Risk Factors for testing positive for SARS-CoV-2 in a national US healthcare system

Vincent S. Fan, MD MPH[1], Jason A. Dominitz MD MHS[2], McKenna C. Eastment MD[3], Emily Locke MPH[4], Pamela Green PhD[4], Kristin Berry PhD[4], Ann M. O'Hare MD[5], Javeed A. Shah MD[3], Kristina Crothers MD[1], George N. Ioannou BMBCh, MS[2]

Divisions of [1]Pulmonary and Critical Care, [2]Gastroenterology, [3]Allergy and Infectious Disease, [4]Research and Development, and [5]Nephrology at the Veterans Affairs Puget Sound Healthcare System and University of Washington, Seattle, WA, USA

Please direct correspondence to:

Vincent S. Fan, MD MPH

Veterans Affairs Puget Sound Healthcare System

1660 S. Columbian Way

Seattle, WA, 98108

Phone: (206) 764-2507

Email: vincent.fan@va.gov

Summary: A positive SARS-CoV-2 PCR test was associated with older age, male sex, geographic burden of disease, non-White race and Hispanic ethnicity, obesity and diabetes. The majority of positive tests were attributed to geographic burden, demographic characteristics and obesity.

ABSTRACT

Background: Identifying risk factors for SARS-CoV-2 infection could help health systems improve testing and screening strategies.

Objectives: Identify demographic factors, comorbid conditions, and symptoms independently associated with testing positive for SARS-CoV-2.

Design: Observational cross-sectional study.

Setting: Veterans Health Administration.

Patients: Persons tested for SARS-CoV-2 nucleic acid by polymerase chain reaction (PCR) between March 1 and May 14, 2020.

Measurements: Associations between demographic characteristics, diagnosed comorbid conditions, and documented symptoms with testing positive for SARS-CoV-2.

Results: Of 88,747 persons tested, 10,131 (11.4%) were SARS-CoV-2 PCR positive. Positivity was associated with older age (≥80 vs. <50 years: aOR 2.16, 95% CI 1.97-2.37), male sex (aOR 1.45, 95% CI 1.34-1.57), regional SARS-CoV-2 burden (≥2,000 vs. <400 cases/million: aOR 5.43, 95% CI 4.97-5.93), urban residence (aOR 1.78, 95% CI 1.70-1.87), Black (aOR 2.15, 95% CI 2.05-2.26) or American Indian/Alaska Native/Pacific Islander (aOR 1.26, 95% CI 1.05-1.52) vs. White race, and Hispanic ethnicity (aOR 1.52, 95% CI 1.40-1.65). Obesity and diabetes were the only two medical conditions associated with testing positive. Documented fevers, chills, cough, and diarrhea were also associated with testing positive. The population attributable fraction of positive tests was highest for regional SARS-CoV-2 burden (35.3%), followed by demographic variables (27.2%), symptoms (12.0%), obesity (10.5%), and diabetes (0.4%).

Limitations: Lack of information on SARS-CoV-2 exposures or the indications for testing which may affect the likelihood of testing positive.

Conclusion: The majority of positive SARS-CoV-2 tests were attributed to regional SARS-CoV-2 burden, demographic characteristics and obesity with a minor contribution of chronic comorbid conditions.

Introduction

Understanding the risk factors for testing positive for SARS-CoV-2 infection could help public health and health system initiatives to target testing, education, and preventive efforts toward those most likely to benefit. Sociodemographic risk factors for a positive SARS-CoV-2 test include advanced age, male sex, Black race, low socioeconomic status, and residence in a high-incidence area.(1-4) Medical conditions such as chronic kidney disease and obesity may be risk factors for infection with SARS-CoV-2, although results have been inconsistent.(2, 3, 5) Most published studies examining the correlates of testing positive for SARS-CoV-2 have been conducted within individual health care facilities or regional health care systems rather than in national health systems.(1, 3, 5, 6)

Symptoms of SARS-CoV-2 including fever, shortness of breath, cough, loss of taste, and loss of smell are frequently included in outpatient SARS-CoV-2 screening questionnaires where laboratory or radiology testing is not routinely available. However, symptoms such as dyspnea or cough are common in the general population, lack specificity for SARS-CoV-2, and overlap with symptoms reported by persons with cardiopulmonary diseases. Whether SARS-CoV-2 symptoms might differ for those with underlying cardiopulmonary comorbidity is not known.

The dual aims of this study were to identify the baseline demographic factors and comorbidities associated with testing positive for SARS-CoV-2 infection in the Veterans Health Administration nationally, and to examine the symptoms associated with a positive SARS-CoV-2 polymerase chain reaction (PCR) test.

Methods

Data source and study population

Data were derived from the Veterans Health Administration (VHA) Corporate Data Warehouse (CDW), a data repository of VHA's electronic medical records, developed by the VA Informatics and Computing Infrastructure (VINCI) to support research. To facilitate research into SARS-CoV-2 infection, VINCI analysts created and are regularly updating the "COVID-19 Shared Data Resource"(7) which includes analytic variables extracted from the CDW for all persons in VHA tested for SARS-CoV-2. We identified all VA patients tested for SARS-CoV-2 nucleic acid by PCR in the inpatient or outpatient setting between 02/28/2020 and 5/14/2020, excluding VA employees. The reasons for SARS-CoV-2 testing were not available in the study data but it is likely that some cohort members were tested as part of routine screening prior to hospital admission (8) or elective procedures.(9)

This study was approved by the Institutional Review Board of the Veterans Affairs Puget Sound Healthcare System.

Outcome definition: positive or negative SARS-CoV-2 status

Patients were considered positive for SARS-CoV-2 if they had at least one positive PCR test during the study period and negative if all of their SARS-CoV-2 PCR tests were negative. Final adjudication of SARS-CoV-2 status was performed by the VA National Surveillance Tool, which is intended to be the single, authoritative data source for determination of positive and negative cases within VHA. The index date was defined as the date of the earliest positive (for those with at least one positive test) or negative (for those with only negative test results) test, unless the patient had been admitted to a VA hospital during the preceding 15 days, in which case the date of admission served as the index date. SARS-CoV-2 testing was considered to have been conducted in the inpatient setting if the test was obtained within a day before hospital admission.

Predictors: Demographic, pre-existing illnesses, and symptoms

Sociodemographic characteristics included age, sex, race, and ethnicity, urban versus rural residence and regional SARS-CoV-2 burden and time period of testing. Urban versus rural residence was based on zip codes using the Rural-Urban Commuting Areas system, with urban areas defined as census tracts with at least 30 percent of the population residing in an urbanized area. Regional SARS-CoV-2 burden was operationalized as the number of cases per million in each participant's state of residence as of 4/10/2020,(10) categorized as <400, 400-999, 1000-1999, ≥2000. The time period of testing was based on quartiles of the cumulative number of tests performed during the study period. (**Table 1**).

Comorbid conditions were defined using ICD-10 codes recorded in VA administrative data during the 2-year period on or before the index date and body mass index (BMI).[25] The Charlson Comorbidity Index (CCI) provides an estimate of overall burden of comorbidity (**Table 2**). Patients were categorized as being underweight (BMI <18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9) or having stage I (BMI 30-34.9) or stages II-III (≥35 BMI) obesity.

Documented symptoms thought to be related to SARS-CoV-2 were identified by VINCI analysts based on a combination of natural language processing of text notes in patients' electronic medical records (i.e., outpatient visit notes, admission notes, progress note, discharge summaries) stored as "text integration utilities" (TIU) notes in CDW, and searching for relevant ICD-10 codes in VA administrative data,(7) occurring on or within 30 days prior to the index date (**Table 3**). We did not include information on the frequency of loss of smell or taste as these were not widely recognized as being symptoms of SARS-CoV-2 during the study period and were rarely reported.

Statistical Analysis

We used multivariable logistic regression models to identify independent risk factors for testing positive for SARS-CoV-2 infection, with a significance threshold set at a $p < 0.05$. Analyses were adjusted for the aforementioned measured sociodemographic characteristics, comorbid conditions, test setting (inpatient or outpatient), and all documented symptoms (Tables 1-3). We also examined the sum of symptoms individually associated with a positive test in unadjusted analyses.

Analyses examining symptoms were stratified by presence or absence of heart failure, chronic obstructive pulmonary disease and asthma, comorbid conditions with prominent respiratory symptoms, with potential interactions examined a likelihood-ratio test. Additional supplementary analyses were conducted after stratifying by test setting (inpatient vs. outpatient).

Multivariate population attributable fractions (PAF) for each major risk factor were estimated by averaging over randomly selected permutations of the PAF when other risk factors were sequentially removed from the model. The number of permutations was sufficient to approximate the true average to 0.1%. Confidence intervals were calculated using Monte Carlo simulation (500 iterations over 5000 samples). The PAF corresponds to the estimated adjusted fraction of the positive SARS-CoV-2 tests that would not have occurred if the risk factor was not present (e.g. BMI ≥35).(11)

RESULTS

Of 88,747 persons tested, 10,131 (11.4%) had at least one positive SARS-CoV-2 PCR test during the study period,**(Figure 1)** among whom 27,062 (30.5%) were tested within a day before hospital admission, and 61,685 (69.5%) were in the outpatient setting. The study cohort included persons tested in all 50 states, with the largest number of tests conducted at VA facilities in California (N= 8,845) and the largest number of positive tests reported in New York (N=1,555) **(Supplemental Figure 1, Supplemental Table 1 and 2)**. Most of those tested were male (88.5%) with a mean age of 61.8±16.0 years, 63.7% were white, 26.6% were Black, 2.8% were Asian, American

Indian, Alaska Native, Native Hawaiian or Pacific Islander, 7.0% were of unknown race, and 9.3% were of Hispanic ethnicity.

Sociodemographic factors

Characteristics independently associated with a positive SARS-CoV-2 test included male sex (adjusted odds ratio (aOR) 1.45, 95% confidence interval (CI) 1.34-1.57), older age (age ≥ 80 vs. 18-49 years: aOR 2.16, 95% CI 1.97-2.37), Black (aOR 2.15, 2.05-2.26) and American Indian/Alaskan Native/Native Hawaiian/Pacific Islander (aOR 1.26, 95% CI 1.05-1.52) vs. White race and Hispanic vs. non-Hispanic ethnicity (aOR 1.52, 95% CI 1.40-1.65) (**Table 1**).

Persons living in geographic regions with a higher burden of SARS-CoV-2 disease at the time of our study had a significantly higher risk of testing positive (living in a state with >2,000 versus <400 cases/million: aOR of 5.34, 95% CI 4.97-5.93). Living in an urban versus rural area was also associated with testing positive for SARS-CoV-2 (aOR 1.78, 1.70-1.87).

Being overweight (aOR 1.16, 95% CI 1.09-1.24) or having class I (aOR 1.32 1.23-1.41) or class II-III obesity (aOR 1.44, 1.34-1.56) were associated with testing positive compared with being of normal weight. Compared to never smokers, former smokers (aOR 0.92, 95% CI 0.88-0.97) and current smokers (aOR 0.52, 95% CI 0.49-0.57) were less likely to test positive.

Comorbid Conditions

Most (68.1%) of those tested had a significant burden of comorbidity with a Charlson comorbidity score ≥ 1. (**Table 2**) Among the individual comorbid conditions examined, only diabetes was associated with a higher odds of testing positive (aOR 1.10, 95% 1.04-1.16). Overall burden of comorbidity measured with the Charlson score, and many individual chronic conditions were associated with a lower risk of testing positive including a cancer, coronary artery disease, congestive heart failure, dialysis, cirrhosis, COPD, obstructive sleep apnea, alcohol dependence, and drug dependence.

Results were similar after adjustment for all documented symptoms **(Tables 1-2)**. In analyses stratified by test setting (inpatient versus outpatient), the association of diabetes with a positive

SARS-CoV-2 test was of greatest magnitude in the outpatient setting, while this association was attenuated and not statistically significant among those tested in the inpatient setting. **(Supplemental Table 3)**. There were some differences in the chronic conditions associated with decreased odds of a positive SARS-CoV-2 test between inpatients and outpatients, although those with cancer, COPD, alcohol dependence and drug dependence had a lower risk of a positive test in both settings.

Symptoms

Among documented symptoms, fever (aOR 1.95, 95% CI 1.85-2.04), chills (aOR 1.42, 95% CI 1.23-1.65), cough (aOR 1.16, 1.09-1.23), and diarrhea (aOR 1.12, 1.01-1.24) were independently associated with a positive SARS-CoV-2 test result whereas there were negative associations between dyspnea, sore throat and abdominal pain (**Table 3**). The total number of symptoms was also independently associated with an increased risk of testing positive.

In analyses stratified by whether patients had a diagnosis of COPD, asthma or heart failure vs. none of these conditions, dyspnea was independently associated with testing positive (aOR 1.09, 95% CI 1.13-1.30) among those without any of these conditions but there was a negative association between dyspnea and testing positive among those with one or more of these conditions (aOR 0.77, 95% CI 0.69-0.84, p-value for interaction <0.001). **(Table 4)** Associations of fever and cough with testing positive were also attenuated in people with COPD, asthma or heart failure (p-value for interaction <0.01).

Population attributable fractions (PAFs) of covariates associated with testing positive for SARS-CoV-2

The largest proportion of positive cases in our study population was attributed to geographic location (burden of SARS-CoV-2 cases and urban residence) with a PAF of 35.3%, followed by symptoms (12.0%), racial-ethnic group (11.4%), being overweight or obese (10.5%), male sex (8.9%), age ≥ 50 (6.9%), and diabetes (0.4%) **(Figure 2, Supplemental Table 4)** . Together, 85.4% of the PAF for testing positive for SARS-CoV-2was attributed to these risk factors.

DISCUSSION

Among persons tested for SARS-CoV-2 in a large national US healthcare system representing all 50 states, the largest number of positive tests were attributed to regional SARS-CoV-2 burden, followed by racial-ethnic group, overweight or obesity, male sex, and age ≥ 50 years, with less than 1% attributable to diabetes. Fever, chills, cough and diarrhea were associated with increased risk of testing positive for SARS-CoV-2 whereas dyspnea, sore throat, and abdominal pain were associated with a lower risk.

The high proportion of positive tests attributed to living in states with a greater SARS-CoV-2 burden after adjusting for individual pre-existing factors underscores the importance of public health measures to mitigate spread of the disease.(12) In our cohort, race and ethnicity were significantly associated with testing positive for SARS-CoV-2. Black cohort members had more than twice the odds of testing positive than white persons and, consistent with prior studies, we also found a higher risk of testing positive for SARS-CoV-2 among Black, American Indian and Hispanic cohort members.(2, 13-15) Hypothesized reasons for the racial and ethnic disparities include differences in underlying chronic medical conditions and socioeconomic factors that increase exposure to the virus due to being less able to social distance at home.(13, 16) Our results likely support the importance of social determinants of health as our analyses adjusted for underlying health conditions and there was likely adequate access to testing since the proportion of Black persons in our cohort (26.5%) is actually higher than Black Veterans getting care in the Veterans Health Administration (15.5%).(17)

Consistent with prior studies, older age, male sex, and obesity were associated with a positive SARS-CoV-2 test,(2, 3, 5) and may be related to differences in the immune response to SARS-CoV-2 (18-20). The relationship between obesity and testing positive persisted even after adjustment for diabetes and hypertension. The finding that current or past smokers were at lower risk for testing positive for SARS-CoV-2 than those who had never smoked was surprising. Our results are consistent with a study by De Lusignan et al. that found a similar 50% reduction in odds of a positive test among outpatients in a large primary care clinic network in the United Kingdom. (2)

De Lusignan suggested several potential reasons for this finding including the fact that smokers may be more likely to be tested due to chronic cough, smoking may reduce the nasopharyngeal viral load decreasing PCR test sensitivity, and that nicotine may downregulate angiotensin-converting enzyme 2 receptors used by SARS-CoV-2 for cell entry. Also, the nicotinic acetylcholine receptor may be involved in SARS-CoV-2 invasion of the central nervous system during infection.(21) Further exploration of the role of smoking and nicotine in the pathogenesis of SARS-CoV-2 infection may offer novel insights into treatment possibilities.

Although pre-existing medical conditions such as cardiac disease, lung disease, liver disease, kidney disease, cancer and obesity have been associated with poor outcomes for those diagnosed with SARS-CoV-2 infection,(22-25) there are relatively few data regarding the relationship between these and other chronic illnesses and risk of testing positive for SARS-CoV-2. While diabetes was associated with a modest increase risk of testing positive for SARS-CoV-2 in our cohort, most other comorbid conditions and overall burden of comorbidity were associated with a lower risk of having a positive test. Prior studies examining the relationship between individual chronic illnesses and risk of testing positive have been mixed, with one study suggesting an increased risk of a positive SARS-CoV-2 test among patients with chronic kidney disease,(2) but others reporting negative associations between asthma,(3, 21), chronic lung disease,(5) alcohol and substance abuse,(5) cancer, coronary artery disease, inflammatory bowel disease, and prior organ transplant with testing positive (3).

The indications for testing for SARS-CoV-2 may influence the positivity rate. As Haimovich et al. suggested, many of the symptoms of SARS-CoV-2 are non-specific and may be common in patients with other medical conditions such as COPD (5). It is also possible that those with more comorbid conditions may have taken more social distancing measures in response to advice from health care providers or public health warnings. The clinical context and indications for testing were not available in this analysis, but likely included testing for infection control purposes such as when patients are admitted to the hospital for reasons other than SARS-CoV2, or those undergoing elective procedures. Changes in regional SARS-CoV-2 burden or the more widespread use of testing

also impact the positivity rate of SARS-CoV2, as supported by a drop in the rate of positive tests over time in our data. To examine this further, we performed several sensitivity analyses to adjust for test setting (inpatient vs. outpatient), COVID-19 symptoms, and the time period, but found similar results.

The Centers for Disease Control lists several symptoms of SARS-CoV-2 infection including fevers, chills, cough, dyspnea, fatigue, muscle aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, or diarrhea. Although commonly used to screen outpatients in health care settings, little is known about whether these symptoms predict a positive SARS-CoV-2 test result. We found that fevers, chills, cough and diarrhea were associated with a positive test, whereas patients with dyspnea, sore throat and abdominal pain were less likely to test positive. Interestingly, our findings suggest that the association between some symptoms and testing positive may vary as a function of patients' underlying comorbid conditions. For example, in our cohort dyspnea was associated with increased risk of a positive test in those without COPD, asthma or heart failure, but negatively associated with testing positive if those conditions were present. Complex interactions between underlying medical conditions and SARS-CoV-2 infection may therefore lead to different manifestations of symptoms, or chronic symptoms may influence the indication for testing.

Strengths of our study include analysis of data from a national integrated healthcare system, the large number of persons tested in both the outpatient and inpatient settings, availability of information on pre-existing chronic medical conditions, the large number of demographic characteristics and comorbidities investigated, and the availability of information on documented symptoms. However, our results in the predominantly male veteran population may not be generalizable to other populations and groups. Other limitations relate to the use of ICD-10 codes to ascertain comorbid conditions. Symptoms were assessed using natural language processing combined with ICD-10 codes, which rely on documentation of symptoms and the performance characteristics of these definitions is not known yet. We focused on predictors that would be

available clinically in the outpatient setting, and therefore did not include laboratory data or imaging results in the models. We also did not have access to detailed information on social determinants of health such as household size or infection prevention behaviors (e.g. social distancing, mask use) which may affect the risk of becoming infected with SARS-CoV-2. In addition, our results likely reflect institutional policies and practices related to testing that might not be generalizable to other health systems.

In summary, the majority of positive SARS-CoV-2 tests within a national US healthcare system were attributed to geographic burden of SARS-CoV-2, male sex, advanced age, belonging to a racial/ethnic minority group and obesity, with only a minor contribution from underlying health conditions. The results of this study have implications for public health practice and for developing rational strategies for SARS-CoV-2 testing and screening.

Notes:

Authors' Contributions and Authorship Statement

Vincent Fan is the guarantor of this paper. All authors approved the final version of the manuscript.

Ioannou: Study concept and design, analysis of data, interpretation of results, drafting of manuscript, critical revision of manuscript

Locke: Study concept, interpretation of results, critical revision of manuscript

Green: Extraction of data, creation of analytic variables, analysis of data, interpretation of results.

Berry: Study concept and design, analysis of data, interpretation of results, drafting of manuscript, critical revision of manuscript

O'Hare: Study concept and design, interpretation of results, critical revision of manuscript

Shah: Study concept and design, interpretation of results, critical revision of manuscript

Crothers: Study concept and design, interpretation of results, critical revision of manuscript

Eastment: Study concept and design, interpretation of results, critical revision of manuscript

Dominitz: Study concept and design, interpretation of results, critical revision of manuscript

Fan: Study concept and design, interpretation of results, drafting of manuscript, critical revision of manuscript

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Table 1. Associations between demographic factors and the likelihood of testing positive for SARS-CoV-2 in the VA healthcare system

Demographic factors	Characteristics of:		Proportion who tested positive (%)	Crude Odds Ratio	Adjusted Odds Ratio*	Adjusted Odds Ratio**
	SARS-CoV-2 Negative N=78,616 (N, %)	**SARS-CoV-2** Positive N=10,131 (N, %)				
Time Period of SARS-CoV-2 test, by quartile of cumulative tests performed						
Feb 20 - Apr 07, 2020	18,172(23.1)	3,675(36.3)	16.8	1	1	1
Apr 08 - Apr 20, 2020	18,354(23.3)	2,185(21.6)	10.6	0.59(0.56-0.62)	0.58(0.54-0.61)	0.63(0.60-0.68)
Apr 21 - Apr 30, 2020	20,956(26.7)	2,411(23.8)	10.3	0.57(0.54-0.60)	0.55(0.52-0.58)	0.64(0.60-0.68)
May 01 - May 14, 2020	21,134(26.9)	1,860(18.4)	8.1	0.44(0.41-0.46)	0.47(0.44-0.50)	0.55(0.51-0.59)
Sex						
Women	9,281(11.8)	910(9.0)	8.9	1	1	1
Men	69,335(88.2)	9,221(91.0)	11.7	1.36(1.26-1.46)	1.47(1.36-1.59)	1.45(1.34-1.57)
Age at test						
18-49	17,653(22.5)	1,973(19.5)	10.1	1	1	1
50-64	23,701(30.1)	2,917(28.8)	11.0	1.10(1.04-1.17)	1.15(1.08-1.24)	1.18(1.10-1.27)
65-79	28,593(36.4)	3,724(36.8)	11.5	1.17(1.10-1.23)	1.41(1.31-1.52)	1.46(1.35-1.57)
>=80	8,669(11.0)	1,517(15.0)	14.9	1.57(1.46-1.68)	2.02(1.85-2.22)	2.16(1.97-2.37)
Race						
White	51,504(65.5)	5,022(49.6)	8.9	1	1	1
Black	19,358(24.6)	4,215(41.6)	17.9	2.23(2.14-2.33)	2.13(2.02-2.23)	2.15(2.05-2.26)
Asian	913(1.2)	80(0.8)	8.1	0.90(0.71-1.13)	1.01(0.80-1.28)	1.01(0.80-1.28)
AI/AN, Native Hawaiian/ Pacific Islander	1,347(1.7)	140(1.4)	9.4	1.07(0.89-1.27)	1.26(1.05-1.51)	1.26(1.05-1.52)
Missing/Unknown	5,494(7.0)	674(6.7)	10.9	1.26(1.16-1.37)	1.17(1.05-1.29)	1.16(1.05-1.29)
Ethnicity						
Non-Hispanic	69,986(89.0)	8,876(87.6)	11.3	1	1	1
Hispanic	5,945(7.6)	944(9.3)	13.7	1.25(1.16-1.35)	1.54(1.42-1.66)	1.52(1.40-1.65)
Missing/Unknown	2,685(3.4)	311(3.1)	10.4	0.91(0.81-1.03)	1.01(0.88-1.17)	1.02(0.89-1.18)
US States by SARS-CoV-2 burden in cases/million**						
<400	10,184(13.0)	671(6.6)	6.2	1	1	1
400-999	42,757(54.4)	2,918(28.8)	6.4	1.04(0.95-1.13)	1.06(0.97-1.15)	1.09(1.00-1.19)
1000-1999	14,839(18.9)	2,453(24.2)	14.2	2.51(2.30-2.74)	2.44(2.22-2.67)	2.47(2.25-2.71)

≥2000	10,836(13.8)	4,089(40.4)	27.4	5.73(5.26-6.24)	5.36(4.91-5.86)	5.43(4.97-5.93)
Urban vs. Rural						
Rural	30,148(38.3)	2,412(23.8)	7.4	1	1	1
Urban	48,406(61.6)	7,714(76.1)	13.7	1.99(1.90-2.09)	1.77(1.69-1.86)	1.78(1.70-1.87)
BMI at index date						
<18.5 (underweight)	2,459(3.1)	281(2.8)	10.3	1.07(0.93-1.22)	1.06(0.92-1.22)	1.06(0.92-1.22)
18.5-24.9 (normal weight)	17,605(22.4)	1,889(18.6)	9.7	1	1	1
25.29.9 (overweight)	24,837(31.6)	3,167(31.3)	11.3	1.19(1.12-1.26)	1.17(1.09-1.24)	1.16(1.09-1.24)
30-34.9 (Obese I)	18,175(23.1)	2,574(25.4)	12.4	1.32(1.24-1.41)	1.32(1.23-1.41)	1.32(1.23-1.41)
≥35 (Obese II and III)	13,480(17.1)	1,968(19.4)	12.7	1.36(1.27-1.45)	1.46(1.35-1.58)	1.44(1.34-1.56)
Missing	2,060(2.6)	252(2.5)	10.9	1.14(0.99-1.31)	1.13(0.97-1.33)	1.19(1.01-1.39)
Smoking						
Never	22,338(28.4)	3,644(36.0)	14.0	1	1	1
Former	29,235(37.2)	4,077(40.2)	12.2	0.85(0.81-0.90)	0.92(0.88-0.97)	0.92(0.88-0.97)
Current	17,149(21.8)	1,135(11.2)	6.2	0.41(0.38-0.43)	0.52(0.48-0.56)	0.52(0.49-0.57)
Unknown	9,894(12.6)	1,275(12.6)	11.4	0.79(0.74-0.85)	0.83(0.77-0.90)	0.84(0.78-0.91)
SARS-CoV-2 test performed in hospitalized persons:						
No	54,385(69.2)	7,300(72.1)	11.8	1	1	1
Yes	24,231(30.8)	2,831(27.9)	10.5	0.87(0.83-0.91)	0.96(0.91-1.01)	0.89(0.84-0.94)

* Adjusted for all the sociodemographic characteristics shown in Table 1 and the comorbid conditions shown in Table 2.

** Adjusted for all the sociodemographic characteristics shown in Table 1, the comorbid conditions shown in Table 2 and the symptoms shown in Table 3.

**Burden of SARS-CoV-2 in a US state in defined by number of case/million in each state as of **Burden of SARS-CoV-2 in a US state in defined by number of case/million in each state as of 4/10/20(10) as <400 (AK, HI, KY, MN, MT, NC, ND, NE, OR, PR, WV), 400-999 (AL, AR, AZ, CA, FL, IA, ID, KS, ME, MO, MS, NH, NM, NV, OH, OK, SC, SD, TN, TX, UT, VA, WI, WY), 1000-1999 (CO, DE, GA, IL, IN, MD, PA, RI, VT, WA), ≥2,000 (CT, DC, LA, MA, MI, NJ, NY).

Table 2. Associations between selected comorbid conditions and the likelihood of testing positive for SARS-CoV-2 in the VA healthcare system

Comorbidities recorded in the preceding 2 years	Characteristics of:		Proportion who tested positive (%)	Crude Odds ratio	Adjusted Odds Ratio*	Adjusted Odds Ratio**
	SARS-CoV-2 NEGATIVE N=78,616 (N, %)	**SARS-CoV-2** POSITIVE N=10,131 (N, %)				
Diabetes						
No	52,324(66.6)	6,270(61.9)	10.7	1	1	1
Yes	26,292(33.4)	3,861(38.1)	12.8	1.23(1.17-1.28)	1.10(1.04-1.16)	1.10(1.04-1.16)
Cancer						
No	58,253(74.1)	7,835(77.3)	11.9	1	1	1
Yes	20,363(25.9)	2,296(22.7)	10.1	0.84(0.80-0.88)	0.78(0.74-0.83)	0.77(0.73-0.82)
Hypertension						
No	31,644(40.3)	3,837(37.9)	10.8	1	1	1
Yes	46,972(59.7)	6,294(62.1)	11.8	1.11(1.06-1.15)	0.96(0.91-1.01)	0.95(0.90-1.01)
Coronary artery disease						
No	60,227(76.6)	7,928(78.3)	11.6	1	1	1
Yes	18,389(23.4)	2,203(21.7)	10.7	0.91(0.87-0.96)	0.93(0.87-0.99)	0.93(0.87-0.99)
Congestive heart failure						
No	68,380(87.0)	9,006(88.9)	11.6	1	1	1
Yes	10,236(13.0)	1,125(11.1)	9.9	0.83(0.78-0.89)	0.83(0.77-0.90)	0.85(0.78-0.92)
Cerebrovascular Disease						
No	75,874(96.5)	9,770(96.4)	11.4	1	1	1
Yes	2,742(3.5)	361(3.6)	11.6	1.02(0.91-1.14)	0.94(0.84-1.06)	0.94(0.83-1.06)
Dialysis						
No	76,034(96.7)	9,786(96.6)	11.4	1	1	1
Yes	2,582(3.3)	345(3.4)	11.8	1.04(0.93-1.16)	0.86(0.76-0.99)	0.83(0.72-0.95)
Chronic kidney disease						
No	64,986(82.7)	8,264(81.6)	11.3	1	1	1
Yes	13,630(17.3)	1,867(18.4)	12.0	1.08(1.02-1.14)	1.02(0.95-1.09)	1.01(0.94-1.08)
Cirrhosis						
No	75,315(95.8)	9,826(97.0)	11.5	1	1	1
Yes	3,301(4.2)	305(3.0)	8.5	0.71(0.63-0.80)	0.86(0.75-0.97)	0.87(0.77-0.99)
Asthma						
No	72,673(92.4)	9,386(92.6)	11.4	1	1	1
Yes	5,943(7.6)	745(7.4)	11.1	0.97(0.90-1.05)	0.97(0.89-1.05)	0.96(0.88-1.05)

COPD						
No	59,135(75.2)	8,228(81.2)	12.2	1	1	1
Yes	19,481(24.8)	1,903(18.8)	8.9	0.70(0.67-0.74)	0.81(0.76-0.86)	0.82(0.77-0.87)
Obstructive Sleep Apnea						
No	55,885(71.1)	7,411(73.2)	11.7	1	1	1
Yes	22,731(28.9)	2,720(26.8)	10.7	0.90(0.86-0.95)	0.86(0.82-0.91)	0.86(0.81-0.90)
Obesity Hypoventilation						
No	77,985(99.2)	10,053(99.2)	11.4	1	1	1
Yes	631(0.8)	78(0.8)	11.0	0.96(0.76-1.21)	1.11(0.86-1.43)	1.16(0.90-1.49)
Alcohol Dependence						
No	65,626(83.5)	9,041(89.2)	12.1	1	1	1
Yes	12,990(16.5)	1,090(10.8)	7.7	0.61(0.57-0.65)	0.80(0.74-0.86)	0.81(0.75-0.88)
Drug Dependence						
No	70,560(89.8)	9,541(94.2)	11.9	1	1	1
Yes	8,056(10.2)	590(5.8)	6.8	0.54(0.50-0.59)	0.68(0.62-0.76)	0.70(0.64-0.78)
Hyperlipidemia						
No	35,742(45.5)	4,501(44.4)	11.2	1	1	1
Yes	42,874(54.5)	5,630(55.6)	11.6	1.04(1.00-1.09)	1.06(1.00-1.11)	1.05(0.99-1.10)
Charlson Comorbidity Index						
0	25,082(31.9)	3,125(30.8)	11.1	1	1	1
1-2	21,466(27.3)	3,037(30.0)	12.4	1.14(1.08-1.20)	1.04(0.98-1.11)	1.04(0.98-1.11)
3-4	13,074(16.6)	1,784(17.6)	12.0	1.10(1.03-1.17)	0.94(0.87-1.01)	0.94(0.87-1.01)
>=5	18,994(24.2)	2,185(21.6)	10.3	0.92(0.87-0.98)	0.72(0.67-0.78)	0.72(0.67-0.78)

* Adjusted for all the sociodemographic characteristics shown in Table 1 and the comorbid conditions shown in Table 2.

** Adjusted for all the sociodemographic characteristics shown in Table 1, the comorbid conditions shown in Table 2 and the symptoms shown in Table 3.

Table 3. Associations between symptoms and the likelihood of testing positive for SARS-CoV-2 in the VA healthcare system

Comorbidities recorded in the preceding 2 years	Characteristics of:		Proportion who tested positive (%)	Crude Odds ratio	Adjusted Odds Ratio*
	SARS-CoV-2 NEGATIVE N=78,616 (N, %)	**SARS-CoV-2** POSITIVE N=10,131 (N, %)			
Fever					
No	58,446(74.3)	5,944(58.7)	9.2	1	1
Yes	20,170(25.7)	4,187(41.3)	17.2	2.04(1.96-2.13)	1.95(1.85-2.04)
Common cold					
No	68,685(87.4)	8,735(86.2)	11.3	1	1
Yes	9,931(12.6)	1,396(13.8)	12.3	1.11(1.04-1.17)	0.96(0.89-1.02)
Chills					
No	77,527(98.6)	9,838(97.1)	11.3	1	1
Yes	1,089(1.4)	293(2.9)	21.2	2.12(1.86-2.42)	1.42(1.23-1.65)
Myalgia					
No	77,621(98.7)	9,934(98.1)	11.3	1	1
Yes	995(1.3)	197(1.9)	16.5	1.55(1.33-1.81)	1.11(0.93-1.32)
Cough					
No	63,719(81.1)	7,511(74.1)	10.5	1	1
Yes	14,897(18.9)	2,620(25.9)	15.0	1.49(1.42-1.57)	1.16(1.09-1.23)
Dyspnea					
No	64,080(81.5)	8,224(81.2)	11.4	1	1
Yes	14,536(18.5)	1,907(18.8)	11.6	1.02(0.97-1.08)	0.86(0.81-0.91)
Sore Throat					
No	77,241(98.3)	10,017(98.9)	11.5	1	1
Yes	1,375(1.7)	114(1.1)	7.7	0.64(0.53-0.77)	0.53(0.43-0.65)
Nausea					
No	75,563(96.1)	9,801(96.7)	11.5	1	1
Yes	3,053(3.9)	330(3.3)	9.8	0.83(0.74-0.94)	0.89(0.79-1.02)
Headache					
No	76,114(96.8)	9,784(96.6)	11.4	1	1
Yes	2,502(3.2)	347(3.4)	12.2	1.08(0.96-1.21)	0.95(0.84-1.08)
Diarrhea					
No	75,066(95.5)	9,585(94.6)	11.3	1	1
Yes	3,550(4.5)	546(5.4)	13.3	1.20(1.10-1.32)	1.12(1.01-1.24)

Abdominal Pain					
No	74,871(95.2)	9,851(97.2)	11.6	1	1
Yes	3,745(4.8)	280(2.8)	7.0	0.57(0.50-0.64)	0.60(0.53-0.68)
Fatigue					
No	72,515(92.2)	9,229(91.1)	11.3	1	1
Yes	6,101(7.8)	902(8.9)	12.9	1.16(1.08-1.25)	1.01(0.93-1.09)
Number of Symptoms**					
0	41,126(52.3)	4,255(42.0)	9.4	1	1
1	22,854(29.1)	2,920(28.8)	11.3	1.23(1.17-1.30)	1.16(1.10-1.22)
2	10,780(13.7)	1,929(19.0)	15.2	1.73(1.63-1.83)	1.55(1.46-1.66)
3+	3,856(4.9)	1,027(10.1)	21.0	2.57(2.39-2.78)	2.16(1.98-2.36)

* Adjusted for all the sociodemographic characteristics shown in Table 1, the comorbid conditions shown in Table 2 and the symptoms shown in Table 3.

** Total number of symptoms associated with an increased risk of a positive SARS-CoV-2 test in unadjusted analyses. Symptoms include: fevers, common cold, chills, cough, myalgia, diarrhea, fatigue.

Table 4. SARS-CoV-2 related symptoms and risk of a positive SARS-CoV-2 test among those with and without conditions with symptoms that overlap with SARS-CoV-2.

Predictor	All persons* N=88,747	Persons without COPD, asthma or heart failure* N=58,488	Persons with COPD, asthma or heart failure* N=30,256	p-value for interaction between diagnosis of COPD/asthma/heart failure and each symptom to predict a positive SARS-CoV-2 test*
Fever				< 0.001
No	1	1	1	
Yes	1.96(1.87-2.06)	2.09(1.98-2.22)	1.70(1.56-1.85)	
Cold				0.75
No	1	1	1	
Yes	1.02(0.96-1.09)	1.02(0.94-1.11)	1.02(0.91-1.16)	
Chills				0.83
No	1	1	1	
Yes	1.72(1.49-1.98)	1.71(1.45-2.03)	1.75(1.33-2.31)	
Myalgia				0.13
No	1	1	1	
Yes	1.31(1.11-1.54)	1.40(1.16-1.68)	1.01(0.69-1.49)	
Cough				0.01
No	1	1	1	
Yes	1.24(1.17-1.31)	1.29(1.21-1.37)	1.13(1.02-1.25)	
Dyspnea				< 0.001
No	1	1	1	
Yes	0.95(0.90-1.01)	1.09(1.01-1.17)	0.77(0.70-0.85)	
Sore throat				0.59
No	1	1	1	
Yes	0.57(0.46-0.69)	0.55(0.43-0.69)	0.63(0.42-0.95)	
Nausea				0.81
No	1	1	1	
Yes	0.91(0.80-1.02)	0.90(0.77-1.05)	0.90(0.72-1.11)	
Headache				0.52
No	1	1	1	

Yes	1.03(0.91-1.17)	1.06(0.92-1.22)	0.97(0.75-1.24)	
Diarrhea				0.74
No	1	1	1	
Yes	1.16(1.05-1.28)	1.16(1.03-1.31)	1.14(0.96-1.37)	
Abdominal pain				0.73
No	1	1	1	
Yes	0.63(0.55-0.72)	0.60(0.52-0.71)	0.66(0.53-0.83)	
Fatigue				0.81
No	1	1	1	
Yes	1.07(0.99-1.16)	1.05(0.95-1.17)	1.10(0.96-1.25)	

* Adjusted for all the sociodemographic characteristics shown in Table 1 and the comorbid conditions shown in Table 2. Not adjusted for other symptoms

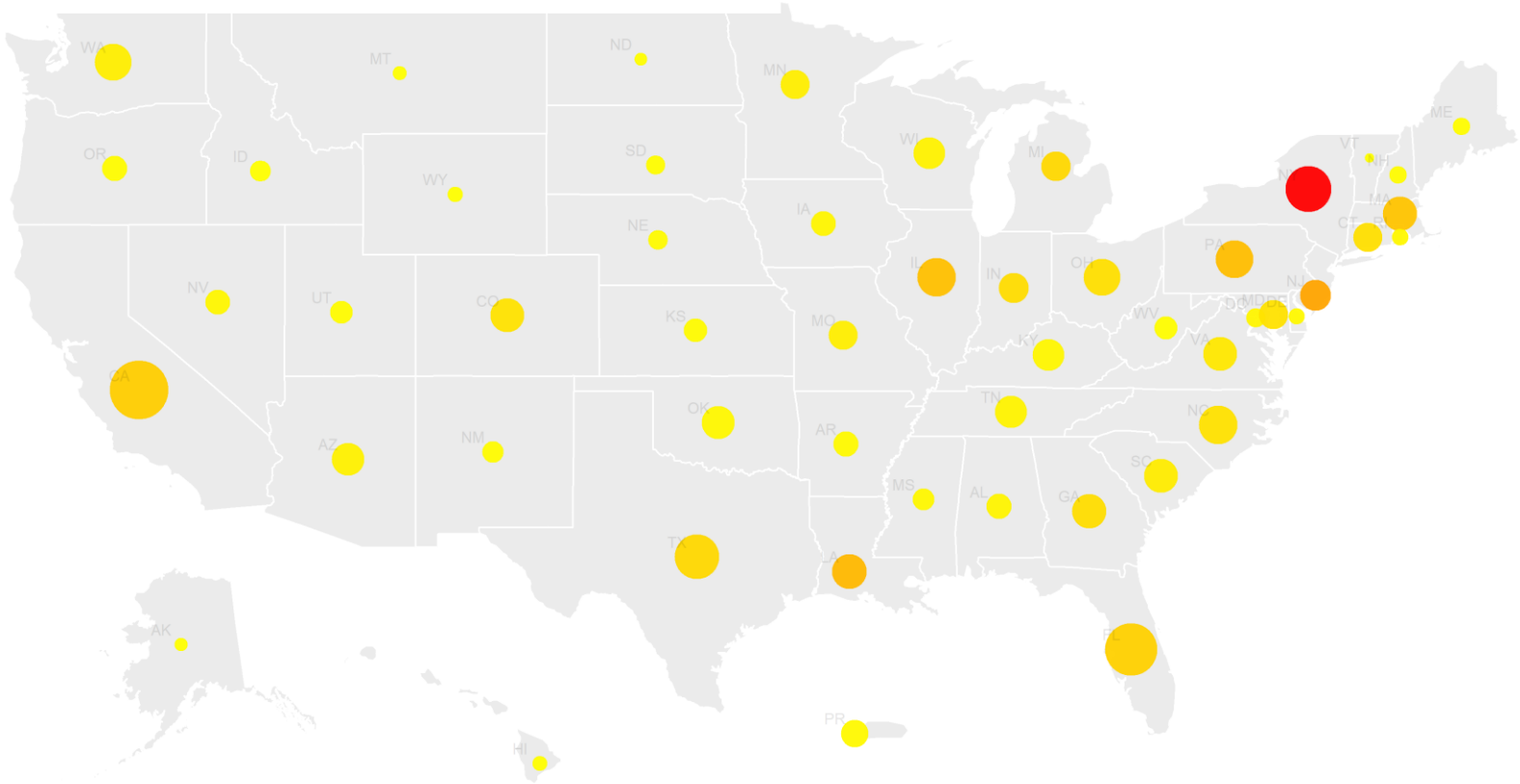
Figure Legends:

Figure 1a: Total number of persons tested for SARS-CoV-2 by state and percent of tests that were positive

Figure 1b. Average number of new SARS-CoV-2 cases per day for each week during the study period.

Figure 2. Population attributable fraction for predicting a positive SARS-CoV-2 test

Figure 1a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PR

Figure 1a legend

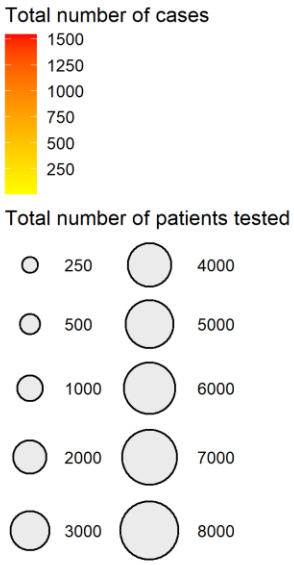


Figure 1b

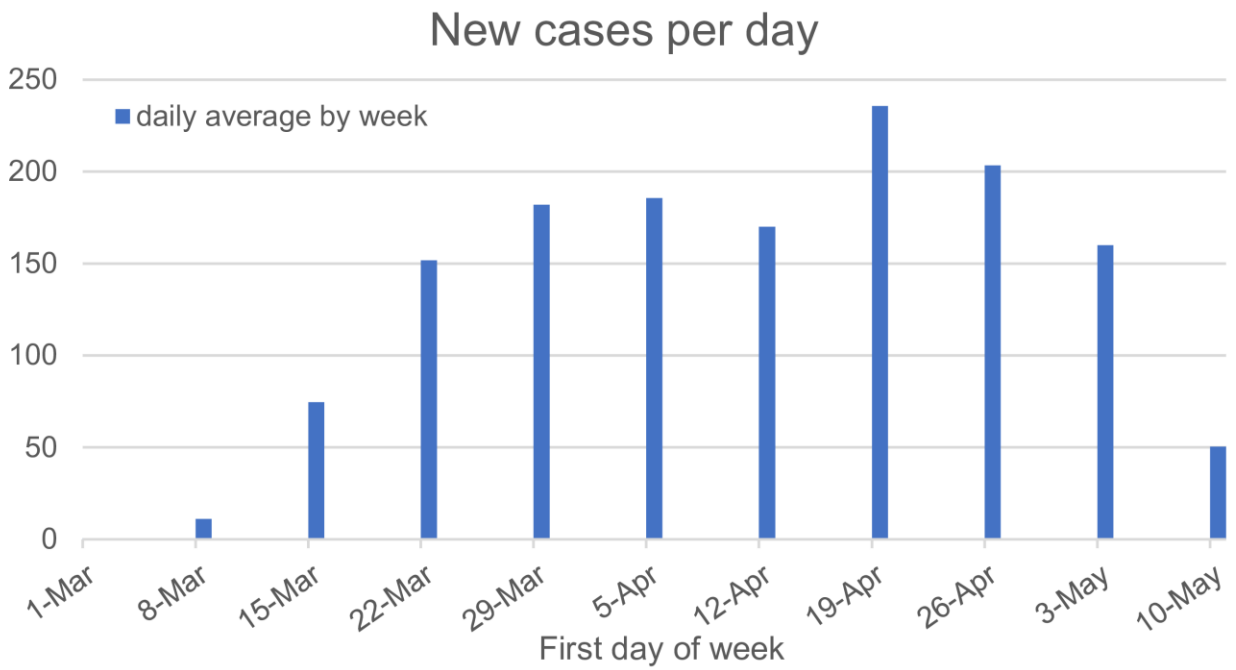
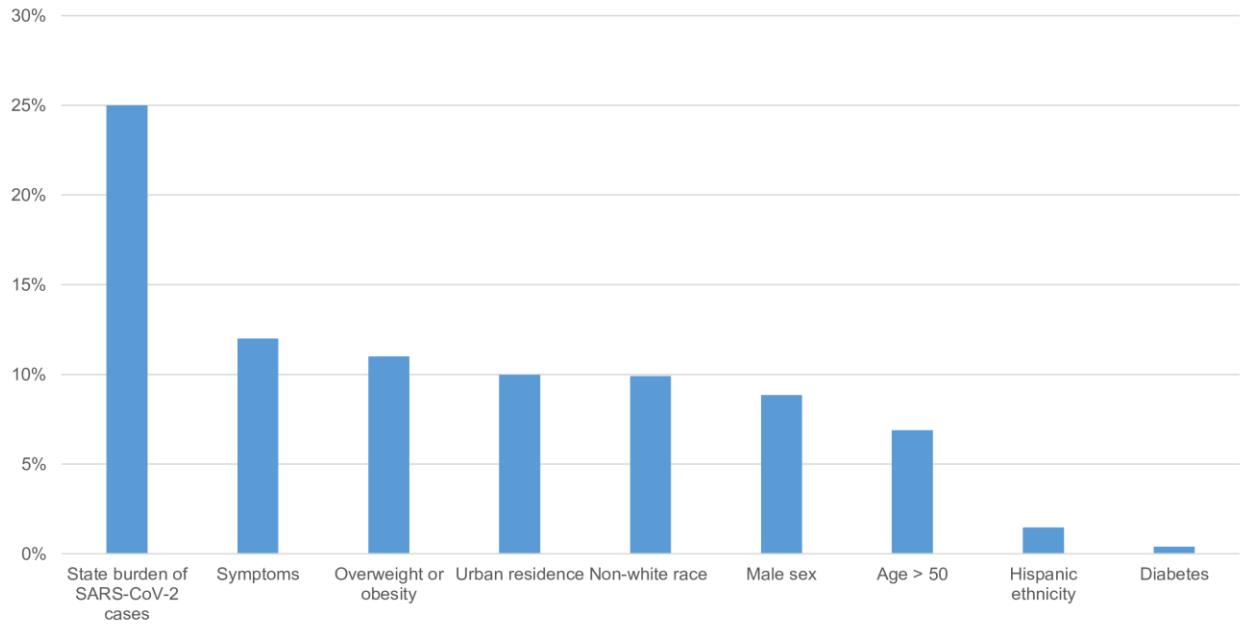

New cases per day
250
200
150
100
50
0
daily average by week
1-Mar
8-Mar
15-Mar
22-Mar
29-Mar
5-Apr
12-Apr
19-Apr
26-Apr
3-May
10-May
First day of week

Figure 2


30%
25%
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0%
State burden of SARS-CoV-2 cases
Symptoms
Overweight or obesity
Urban residence
Non-white race
Male sex
Age > 50
Hispanic ethnicity
Diabetes