Family Medicine and Community Health

Effects of the COVID-19 pandemic on individuals with chemical intolerance

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ABSTRACT

Objective The purpose of this study was to determine if the COVID-19 pandemic had differential effects on individuals with chemical intolerances (CI). CI is characterised by multisystem symptoms initiated by a one-time high dose or persistent low-dose exposure to environmental toxins including chemicals, foods and drugs. With an estimated 20% US prevalence, symptoms include fatigue, headache, weakness, rash, mood changes, musculoskeletal pain, gastrointestinal issues, difficulties with memory, concentration and respiratory problems, which are similar to COVID-19 and its sequelae.

Design A US population-based survey involving 7500 respondents was asked if they ever had COVID-19, what the severity was, and if they had long COVID-19. CI was assessed using the Quick Environmental Exposure and Sensitivity Inventory.

Setting The Center for Disease Control estimates that over 24 million have been infected with COVID-19 in the USA with over 6 700 000 being hospitalised and over 1 174 000 deaths. Other industrialised countries show similar numbers.

Results Those in the High CI class reported a greater COVID-19 prevalence, symptom severity and long COVID-19 than in the medium and low CI groups ($p<0.0001$). These associations were independent of race, ethnicity, income, age and sex. However, there were significantly increased odds of COVID-19 severity among women and those over 45 years old. Asian individuals were least likely to have severe symptoms compared with white individuals (OR=0.53; 95% CI 0.35 to 0.79). Black/African American individuals reported a lower prevalence of COVID-19 than non-Hispanic whites. However, one interaction between CI and race was significant, African Americans with high CI reported greater odds (OR=2.2; 95% CI 1.15 to 3.16) of reporting COVID-19 prevalence. Furthermore, African American individuals had significantly greater odds of increased symptom severity.

Conclusion Prior studies show higher risk for COVID-19 among older age groups, male sex, those with pre-existing comorbidities (eg, challenged immunities) and those from minoritised racial/ethnic groups. The results of this study suggest that those with CI be included in a high-risk group. Various risk subsets may exist and future investigations could identify different risk subsets. Understanding these subgroups would be helpful in mounting targeted prevention efforts.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Prior studies show that individuals at higher risk for COVID-19 include the older age groups, male sex, those with pre-existing comorbidities, and racial/ethnic disparities. The purpose of this study was to determine if the COVID-19 pandemic had differential effects on individuals with chemical intolerances.

WHAT THIS STUDY ADDS

⇒ The results of this study suggest that those with chemical intolerances be included in a high-risk group for COVID-19, particularly if other demographic and comorbid medical conditions exist.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Future investigations could identify those various risk subsets. Understanding the risk subgroups would be helpful in mounting effective targeted prevention efforts that include social media outreach.

INTRODUCTION

COVID-19 first emerged in December 2019. By March 2020, the World Health Organization (WHO) declared the outbreak a global pandemic.[1] The Center for Disease Control (CDC) estimates that 78% of Americans have been infected at least once, and that 97% of adults had antibodies to the virus from either infection, vaccination or a combination of the two.[2] Estimates to date indicate that over 24 million have been infected in the USA with over 6 700 000 being hospitalised, and over 1 174 000 deaths.[2 3] Several other industrialised countries show similar numbers.[3]

Symptoms of COVID-19 range from none or mild, to severe - usually lasting several days after exposure and can include fever, cough, shortness of breath or difficulty breathing, chills, fatigue, muscle pain, body aches, headache, sore throat, loss of taste or smell, congestion, runny nose, nausea, vomiting and/or diarrhoea.[4 5] 'Brain fog' (unusual forgetfulness, word finding deficits and inability to concentrate) has been cited as a 'particularly frustrating persistent symptom'.[5] It is estimated that up to 13% of those infected with COVID-19 will develop long COVID-19 and account for 30% of COVID-19-related hospitalisations.[6]

While there is no universal definition of long COVID-19, most guidelines state that symptoms continue or arise 3 months postinfection with fatigue, shortness of breath and cognitive dysfunction as the most common.[7 8] Several landmark large population studies emphasise four key bodily systems associated with long COVID-19 symptoms. Using national healthcare databases of over 10 million, Xie *et al*[9] report that after 1 year, there is substantial risk of cardiovascular disease in survivors of acute COVID-19 including cerebrovascular disorders, dysrhythmias, ischaemic and non-ischaemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease.

Using a Korean and Japanese nationwide medical claim-based cohort of over 5 million, Choi *et al*[10] found that compared with the general population, the risk of respiratory complications is significantly increased in those with acute and postacute COVID-19.

Bowe *et al*[11] used several key markers of kidney function in a US Veteran sample of over 3 million medical records to investigate long-COVID-19 sequelae of renal function. They report that those who survived COVID-19 were at increased risk of kidney outcomes postacute infection.

In a sample of over 21 million, Kim *et al*[12] report that those persons who were classified as having COVID-19 exhibited a pronounced long-term risk for Guillain-Barré syndrome, cognitive deficit, insomnia, anxiety disorder, encephalitis, ischaemic stroke and mood disorder.

Individuals with the greatest risk of serious illness include older age groups, those with chronic medical conditions such as diabetes, cancer, heart disease and those with weakened immune systems.[8 13] Individuals with chemical intolerance (CI) may also be especially vulnerable to infection and to have more severe symptoms. If so, it is warranted that individuals with CI take extra measures to avoid exposure to COVID-19. Notwithstanding, those with CI have remained vulnerable when workplaces and public spaces were reopened, where disinfectant chemicals were widely used to sanitise the environments.[6]

The purpose of this paper is to investigate if there is a differential effect of COVID-19 among individuals with CI compared with those without CI.

Chemical intolerance

CI develops through exposures to environmental toxins, either through a single large exposure event, or through persistent low-dose exposures over time.[14] Many CI symptoms are similar to those of COVID-19, including respiratory problems, fatigue, mood changes, muscle pain, headache, gastrointestinal problems and difficulties with concentration and/or memory.[15 16]

Prevalence estimates depend on whether CI is clinically diagnosed (0.5%–6.5%) or self-reported (averaging ~20%).[17 18] . Recent estimates from a 2018 nationally representative US population study report prevalence estimates of 25.9% for self-reported CI, and 12.8% for medically diagnosed CI.[19] These temporal estimates indicate an increasing prevalence rate of over 200% for self-reported CI and over 300% for medically diagnosed CI, in just the past several years.[19] In 2018, researchers in Japan corroborated the US findings. Using the Quick Environmental Exposure and Sensitivity Inventory (QEESI), they report that the scores for CIs significantly increased over time. It is believed that the increased prevalence has been attributed to modern lifestyle exposures including industrialised processed foods.[20]

Studies show that those afflicted with CI attribute the initiation to well-defined exposure events, including indoor air contaminants from a multitude of fragranced personal care and/or household cleaning products, pesticide use, new construction and/or mould growth.[15 21]

Study purpose

At the beginning of the COVID-19 pandemic (6/2020), we launched a population survey called the Personal Exposure Inventory (PEI 1).[22] The prevalence of CI in that survey was reported to be 19.3%—commensurate in the range of other population estimates in the literature. Two years later in June 2022, we launched the PEI 2 involving questions concerning the impact of COVID-19 (see online supplemental figure 1, from CDC 2024). In this manuscript, we report the results of the PEI 2. The following research questions and corresponding a-priori hypotheses will be evaluated to determine if the pandemic had differential effects on those individuals with CI.

1. Did the overall prevalence rate of reported CI increase from PEI1 to PEI2?
   Hypothesis 1: the prevalence of CI will be higher in PEI2 compared with PEI1.
2. Did those with CI report higher COVID-19 rates and/or greater symptom severity than those without CI?
   Hypothesis 2: the prevalence of COVID-19 will be higher (*hypothesis a*) with more severe symptoms (*hypothesis* b) among those with CI compared with those without.
3. Are those with CI more likely to experience Long COVID-19?
   Hypothesis 3: the prevalence of long COVID-19 will be higher among those with CI.
4. Are those with CI more likely to experience reactions to the COVID-19 vaccine?
   Hypothesis 4: the prevalence of vaccine reactions will be higher among those with CI.

In addition, we ascertained if the pertinent effects of age, ethnicity, race and sex were associated with the COVID-19 outcomes included in this analysis.

METHODS

Patient and Public Involvement: participant respondents did not contribute to the design, recruitment or dissemination planning. This observational study involved a population-based survey of US adults aged 18 years and older. SurveyMonkey recruitment procedures are available here: www.surveymonkey.com. The survey was deployed on 15 June 2022 and ended 25 June 2022. Respondents answered an 80-item survey called the PEI 2, which included items concerning individuals' demographics, medical diagnoses

and assessment of CI. Age and income were captured as part of SurveyMonkey's panel.

The study's purpose was explained to potential participants who knew the survey would be anonymous. Consent was obtained online before the survey was administered. This research programme was approved by the University of Texas Health Science Center at San Antonio Internal Research Board protocol number 20 220 246EX.

There were 7504 respondents who were randomly selected from nearly 3 million online users of the SurveyMonkey platform. The survey had an abandonment rate of 12.6% and took an average of 12.5 min to complete.

The modelled error estimate for this survey was ±1.19%. Respondents were selected from online panels based on the population sizes of all 50 states plus the District of Columbia as well as by sex, age, race/ethnicity and educational level within each census region to match the US Census Bureau's 2015 American Community Survey targets.

We had previously deployed a similar survey on 1 June 2020. Details of that earlier survey are previously described.[22] In the current study, respondents were classified into high, medium or low CI groups. Self-reported COVID-19, severity and long COVID-19 were assessed. We note that any associations identified in this study cannot be considered causal without a longitudinal design.

Survey

Age was reported as a four-level categorical variable. Income was reported as a 10-level categorical variable, with income increasing by roughly US$25 000 per level. Race and ethnicity were collected following federal guidelines.

Respondents were asked three primary questions to assess COVID-19: 'Have you been diagnosed with, or do you think you have had COVID-19?' Respondents could answer one of five responses: (1) 'Yes, I believe I have had COVID-19 (no test)', (2) 'Yes, I tested positive for COVID-19 with a home test', (3) 'Yes, I tested positive for COVID-19 by a health professional', (4) 'No' and (5) 'I am not sure'. The second question was: 'If yes, please rate the severity of your COVID-19 symptoms on a 0–10 scale'. (0=no symptoms) (5=moderate symptoms) (10=disabling symptom)'. The third question was 'Did your COVID-19 symptoms last for more than 12 weeks (long COVID-19)?' All answers were self-reported, and no clinical confirmation was required. We also ask about vaccination status and if there were reactions to the vaccine (see online supplemental file 1).

CI assessment classification scoring

The QEESI is a widely-used validated tool for assessing intolerances to chemicals, foods and/or drugs with high sensitivity and specificity—differentiating those with CI from the general population.[23 24]

CI was assessed using the QEESI Chemical Exposures and Symptoms scales, which are used to classify participants into three CI severity groups.[23 24] Each scale contains 10 items that are rated from 0 to 10 on a Likert scale: 0='not at all a problem' to 10='severe/disabling symptoms'. Total scores for each scale range from 0 to 100. The published cut-off criteria for 'high CI' are scores greater than or equal to 40 on both the Chemical Exposures and Symptoms Scales. This is regarded as 'very suggestive' or 'high CI. Scores from 20 to 39 on one or both scales are considered 'medium CI'. Scores less than 20 on both scales are classified as 'low CI'.

Data quality control checks

The 7504 survey records were assessed for data quality (DQ) encompassing completeness, validity or accuracy concerns; six measures were required to exclude all surveys indicating one or more DQ concerns. Records with these concerns were excluded from the analytic data set. Online supplemental figure 2 depicts the flow of data exclusions, leading to the final analytic dataset. Some of the DQ measures might technically be accurate (eg, 'male and breast implants'), but with an abundance of caution, they were excluded. The same could be said for the survey time measure: with a survey containing a minimum of 53 questions, it is unlikely that a respondent could read and respond accurately to all questions in under 3 min. By omitting any records that violated one or more DQ measures, 2170 records were excluded (28.9%). We have taken this approach to help ameliorate some well-known DQ concerns associated with web-based surveys, including response probabilities and biases.[25] After applying both the DQ, our final analytic sample was N=5334 (see online supplemental figure 2). This DQ procedure did not differentially affect demographic make-up of the sample, including age and gender distributions.

Statistical modelling

COVID-19 Prevalence: a binary logistic regression was conducted to determine if there was a relationship between CI and COVID-19 prevalence. The binary dependent variable, 'reported COVID-19', was defined as any positive response to the question pertaining to having been diagnosed with COVID-19. We included six independent variables: CI as defined by QEESI (low, medium, high), sex, age, income, race and ethnicity.

Long COVID-19: a similar logistic regression was conducted to determine if there was a relationship between CI and long COVID-19. The binary dependent variable, 'long COVID-19', was created according to the Center for Disease Control definition as a positive response to the question 'Did your COVID-19 symptoms last for more than 12 weeks (long COVID-19)?' We also include the aforementioned CI and covariates.

COVID-19 severity scores: severity scores were normally distributed (determined through QQPlot inspection) and ranged between 0 and 10. This variable was then dichotomised and used as a dependent variable in a logistic regression model. We conducted a sensitivity analysis using 5, 6, 7 or 8 as severity scale cut points.

A p value of 0.05 and 95% CIs were used to determine statistical significance for all models. Correction for multiple comparisons was not necessary given the few models that were run to test the four hypotheses. Analyses were conducted using JMP statistical software.[26]

RESULTS

Table 1 depicts the distribution of the study variables. Non-Hispanic white (NHW) respondents were more prevalent in the sample than other ethnic or racial groups. Nearly one-third (31.3%–1670/5334) of the sample reported having tested positive for COVID-19. The percentage increases to 42.7% (2276/5334) by including those who report they believed they had COVID-19 but were not tested.

Table 2 shows the study variables by CI class. Percentages are row per cents. Compared with the low CI group, those in the high CI group include significantly fewer individuals over 60, more incomes under 25k per year, and more women. Furthermore, 43.5% (241/554) of Hispanic respondents were in the high CI class compared with 29% (1360/4750) of NHW respondents. Black and Asian respondents reported significantly higher rates of CI compared with NHWs.

COVID-19 prevalence, hypothesis 1: this hypothesis tested if the survey estimates of CI administered in 2022 were higher than our baseline survey CI estimates taken in 2020. The prevalence of QEESI criteria for CI significantly increased from 20.6% (1647/7997) to 30.1% (1607/5334) between the 2-year study period (p<0.0001) (see online supplemental figure 1).

COVID-19 *prevalence by CI group, hypothesis 2*a: we found that 53% (791/1487) of those in the highest CI group reported ever having COVID-19, whereas it was 36% (296/820) in the low CI group (p<0.0001). This represents an OR of 1.8 for the high CI group compared with the medium (mid) group (95% CI 1.48 to 2.21); and an OR of 3.3 (95% CI 2.20 to 4.88) comparing the high to low CI group (see figure 1).

51 per cent (51.4%–1895/3685) of those younger than 60 years old reported having COVID-19. In contrast, only 28% (320/1142) who were older than 60 reported COVID-19—corresponding to an OR of 2.5 (95% CI 2.16 to 2.90).

Hispanic/Latino respondents reported 1.6 higher odds (OR=1.6, 95% CI 1.32 to 1.90) of COVID-19 than non-Hispanic or Latino respondents. Younger respondents reported 2.6 higher odds (OR=2.6, 95% CI 2.20 to 2.96) of COVID-19 than older respondents. High CI respondents reported 3.3 higher odds of having COVID-19 than low CI respondents (OR=3.3, 95% CI 2.22 to 2.93). Black or African American respondents reported 0.66 lower odds (33% lower) (OR=0.66, 95% CI 0.50 to 0.86) of COVID-19 than non-Black/African American respondents. However, testing for interactions between CI groups and race, we found a significant interaction among the Black/African American group. Black/African American respondents

Table 1 Sample demographics

N=5334		Sample (%)
Age	18–29	1046/5334 (19.6)
	30–44	1373/5334 (25.7)
	45–60	1500/5334 (28.2)
	61+	1212/5334 (22.7)
	Missing	203/5334 (3.8)
Sex	Male	2320/5334 (43.5)
	Female	2811/5334 (52.7)
	Missing	203/5334 (3.8)
Household income	$0–$24 999	773/5334 (14.5)
	$25 000–$49 999	984/5334 (18.5)
	$50 000–$74 999	847/5334 (17.8)
	$75 000–$99 999	700/5334 (13.1)
	$100 000–$149 999	754/5334 (14.1)
	$150 000+	514/5334 (9.6)
	Missing	662/5334 (12.4)
Ethnicity	Hispanic or Latino	554/5334 (10.4)
	Not Hispanic or Latino	4750/5334 (89.1)
	Missing	30/5334 (0.6)
Race	American Indian or Alaskan Native	101/5334 (1.9)
	Asian	517/5334 (9.7)
	Black/African American	364/5334 (6.8)
	Native Hawaiian or Pacific Islander	42/5334 (0.8)
	White or Caucasian	4280/5334 (80.2)
	Missing	30/5334 (0.6)
COVID-19	I believe I had COVID-19 (no test)	606/5334 (11.4)
	Tested positive with home test	588/5334 (11.0)
	Tested positive by health professional	1082/5334 (20.3)
	No COVID-19	2732/5334 (51.2)
	I am not sure	316/5334 (5.9)
	Missing	10/5334 (0.2)
COVID-19 (simple)	Yes	2276/5334 (42.7)
	No	2732/5334 (51.2)
	Missing	326/5334 (6.1)
COVID-19 cases with long COVID-19	Yes	540/5334 (10.1)
	No	1735/5334 (32.5)
	Missing	3059/5334 (57.4)
COVID-19 vaccination	No COVID-19 vaccination(s)	1051/5334 (19.7)
	Vaccinated with no reaction	1364/5334 (25.6)
	Mild symptoms	1740/5334 (32.6)
	Moderate symptoms	999/5334 (18.7)
	Severe (disabling symptoms)	164/5334 (3.1)
	Missing	16/5334 (0.3)

Table 2 Study variables by chemical intolerance category

Study variables*	Response categories	Low **CI** **864/5334 (16.2%)**	Mid **CI** **2863/5334 (53.7%)**	High **CI** **1607/5334 (30.1%)**
Age	18–29	149/1046 (14.2%)	564/1046 (53.9%)	333/1046 (31.8%)
	30–44	181/1373 (13.2%)	688/1373 (50.1%)	504/1373 (36.7%)
	45–60	183/1500 (12.2%)	808/1500 (53.9%)	509/1500 (33.9%)
	61+	296/1212 (24.4%)	679/1212 (56.0%)	237/1212 (19.6%)
	Missing	55/203 (27.1%)	124/203 (61.1%)	24/203 (11.8%)
Sex	Male	458/2320 (19.7%)	1194/2320 (51.5%)	668/2320 (28.8%)
	Female	351/2811 (12.5%)	1545/2811 (55.0%)	915/2811 (32.6%)
	Missing	55/203 (27.1%)	124/203 (61.1%)	24/203 (11.8%)
Household income	$0–$24 999	71/773 (9.2%)	421/773 (54.5%)	281/773 (36.4%)
	$25 000–$49 999	138/984 (14.0%)	541/984 (55.0%)	305/984 (31.0%)
	$50 000–$74 999	168/947 (17.7%)	486/947 (51.3%)	293/947 (30.9%)
	$75 000–$99 999	113/700 (16.1%)	378/700 (54.0%)	209/700 (29.9%)
	$100 000–$149 999	127/754 (16.8%)	405/754 (53.7%)	222/754 (29.4%)
	$150 000+	99/514 (19.3%)	240/514 (46.7%)	175/514 (34.1%)
	Missing	148/662 (22.4%)	392/662 (59.2%)	122/662 (18.4%)
Ethnicity	Hispanic or Latino	64/554 (11.6%)	249/554 (45.0%)	241/554 (43.5%)
	Not Hispanic or Latino	794/4750 (16.7%)	2596/4750 (54.7%)	1360/4750 (28.6%)
	Missing	6/30 (20.0%)	18/30 (60.0%)	6/30 (20.0%)
Race	American Indian/Alaskan Native	11/101 (10.9%)	47/101 (46.5%)	43/101 (42.6%)
	Asian	65/517 (12.6%)	268/517 (51.8%)	184/517 (35.6%)
	Black/African American	44/364 (12.1%)	151/364 (46.4%)	151/364 (41.5%)
	Native Hawaiian/ Pacific Islander	8/42 (19.1%)	22/42 (52.4%)	12/42 (28.6%)
	White or Caucasian	730/4280 (17.1%)	2339/4280 (54.7%)	1211/4280 (28.3%)
	Missing	6/30 (20.0%)	18/30 (60.0%)	6/30 (20.0%)
COVID-19	I believe I had COVID-19 (no test)	62/606 (10.2%)	325/606 (53.6%)	219/606 (36.1%)
	Tested positive with home test	70/588 (11.9%)	305/588 (51.9%)	213/588 (36.2%)
	Tested positive by health professional	164/1082 (15.2%)	559/1082 (51.7%)	359/1082 (33.2%)
	No COVID-19	524/2732 (19.2%)	1512/2732 (55.3%)	696/2732 (25.5%)
	I am not sure	42/316 (13.3%)	158/316 (50.0%)	116/316 (36.7%)
	Missing	2/10 (20.0%)	4/10 (40.0%)	4/10 (40.0%)
COVID-19 (simple)	Yes	296/2276 (13.0%)	1189/2276 (52.2%)	791/2276 (34.8%)
	No	524/2732 (19.2%)	1512/2732 (55.3%)	696/2732 (25.5%)
	Missing	44/326 (13.5%)	162/326 (49.7%)	120/326 (36.8%)
COVID-19 symptom severity	Rated 0=no symptoms, 10=disabling Mean and (SD)	4.0 (2.4)	5.1 (2.5)	6.3 (2.5)
COVID-19 cases with long COVID-19	Yes	28/540 (5.2%)	196/540 (36.3%)	316/540 (58.5%)
	No	268/1735 (15.5%)	992/1735 (57.2%)	475/1735 (27.4%)
	missing	568/3059 (18.6%)	1675/3059 (54.7%)	816/3059 (26.7%)

Continued

Table 2 Continued

Study variables*	Response categories	Low CI 864/5334 (16.2%)	Mid CI 2863/5334 (53.7%)	High CI 1607/5334 (30.1%)
COVID-19 vaccination symptom severity	No COVID-19 vaccination(s)	145/1051 (13.8%)	582/1051 (55.4%)	324/1051 (30.8%)
	Vaccinated with no reaction	268/1364 (19.7%)	755/1364 (55.4%)	341/1364 (25.0%)
	Mild symptoms	326/1740 (18.7%)	958/1740 (55.1%)	456/1740 (26.2%)
	Moderate symptoms	106/999 (10.6%)	491/999 (49.2%)	402/999 (40.2%)
	Severe (disabling symptoms)	15/164 (9.2%)	70/164 (42.7%)	79/164 (48.2%)
	Missing	4/16 (25.0%)	7/16 (43.8%)	5/16 (31.3%)
Simple vaccination rate*				
	No vaccination	145/860 (16.9%)	582/2856 (20.4%)	324/1607 (20.2%)
	Reporting at least one vaccine with or without symptoms	715/860 (83.1%)	2274/2856 (79.6%)	1278/1607 (79.8%)

*Calculated from the COVID-19 vaccination Symptom Severity data directly above.

with high CI show a 2.2 higher odds (OR=2.2, 95% CI 1.15 to 3.16) of reporting COVID-19 than other races with high CI.

The final logistic model described above demonstrated good fit to the data (lack of fit index x^2 p=0.10).

COVID-19 severity, *hypothesis 2b*: table 3 summarises the results of the logistic model sensitivity analysis described above in the COVID-19 severity scores section. In all four models, compared with those with low CI, those with high CI had an OR of 4.0 or greater. Those with mid CI had at least 2.2 times the likelihood of COVID-19 severity above the 8+ cut point compared with those with low CI (OR=2.2 95% CI 1.87 to 2.67).

Long COVID-19, *hypothesis 3*: QEESI class, ethnicity and race were significant predictors of long COVID-19. Sex, income and age were not significant predictors.

Respondents in the high CI class had 7.6 times the odds of reporting long COVID-19 relative to low classification (95% CI (5.36 to 10.81)). Respondents with mid CI classifications had 2.8 times the odds of reporting long COVID-19 relative to low CI classification (95% CI 2.32 to 3.29) (see figure 2). A significantly higher percentage of long COVID-19 is reported by those with the highest level of CI compared with the mid-level (p<0.012) or low-level CI (p<0.001).

Hispanic or Latino respondents had 1.5 (95% CI 1.12 to 1.94) times the odds of reporting long COVID-19 than NHWs using white/Caucasian as a base, black/African American respondents had 1.7 (95% CI 1.22 to 2.50) times the odds of reporting long COVID-19 than white/Caucasian respondents. The logistic model demonstrated good model fit (lack of fit p x^2=0.07).

Summary of all logistic models: figure 3 is a forest plot summarising the aforementioned logistic models. It depicts that those in the high CI class reported a greater COVID-19 prevalence, severity and long COVID-19 than those in the mid and low CI classes. These associations were independent of race, ethnicity, income, age and

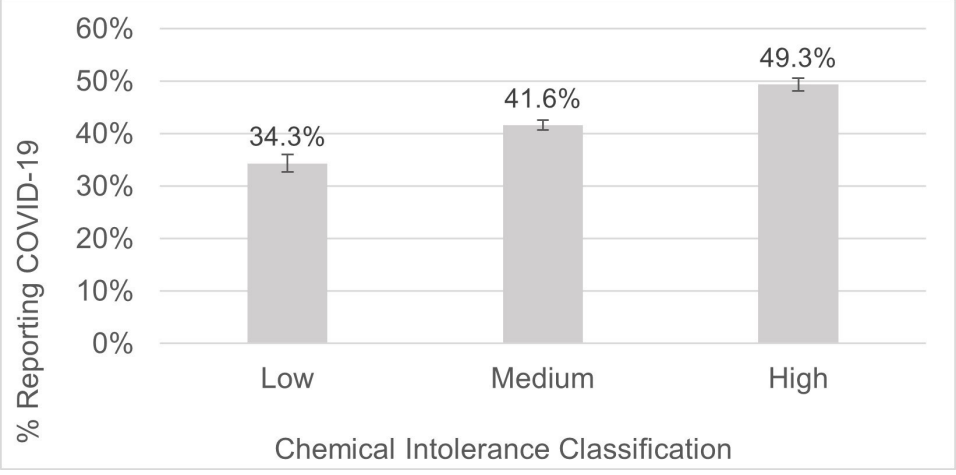

Figure 1 Per cent reporting COVID-19 by chemical intolerance classification.

Table 3 Logistic regression models of different COVID-19 severity cut points

	COVID-19 severity score cut points used in the logistic models			
	5+ OR (95% CI)	**6+ OR (95% CI)**	**7+ OR (95% CI)**	**8+* OR (95% CI)**
High vs low† CI	4.2‡ (3.10 to 5.56)	5.2‡ (3.85 to 5.56)	4.9‡ (3.47 to 6.94)	5.0‡ (3.49 to 7.15)
Medium vs low† CI	1.7‡ (1.31 to 2.23)	1.9‡ (3.10 to 7.10)	2.0‡ (1.44 to 2.85)	2.2‡ (1.87 to 2.67)
Female sex (male referent group)	1.5‡ (1.29 to 1.85)	1.4‡ (1.14 to 1.63)	1.2 p=0.029 (1.02 to 1.47)	1.3 p=0.026 (1.03 to 1.56)
Age 45	ns	ns	ns	1.3 p=0.009 (1.07 to 1.62)
Race	ns	ns	ns	0.6 p=0.012 (0.41 to 0.89)
Model lack of fit (LoF)	0.2378	0.1027	0.0667	0.1528
N	1473/2215 (66.5%)	1083/2215 (48.9%)	780/2215 (35.2%)	516/2215 (23.3%)

*The model with 8+ severity cut-off was selected as the most informative.
†Indicates reference group.
‡P < 0.001.
ns, not significant.

sex. There were significantly increased odds of severity for women and those over 45 years old. The only significant racial coefficient was the comparison between Asian and whites in the 8+ severity cut-off model, where Asian respondents were least likely to have severe symptoms compared with white respondents (OR=0.53, 95% CI 0.35 to 0.79).

Black/African American individuals had an overall lower prevalence of COVID-19 than NHWs; however, an interaction between CI and African American race shows a 2.2 greater odds (OR=2.2, 95% CI 1.15 to 3.16) of reporting COVID-19 prevalence. Furthermore, black, African American respondents had a greater odds of increased symptom severity.

Reactions to the COVID-19 vaccine, hypothesis 4: vaccine rates are presented across CI group at the bottom of table 2. Those in the low CI group were significantly more likely to receive a COVID-19 vaccine than the other two groups (p<0.023). Notwithstanding, table 2 also shows that the mid and high CI groups report a significantly greater percentage of moderate and/or severe symptoms (p<0.001).

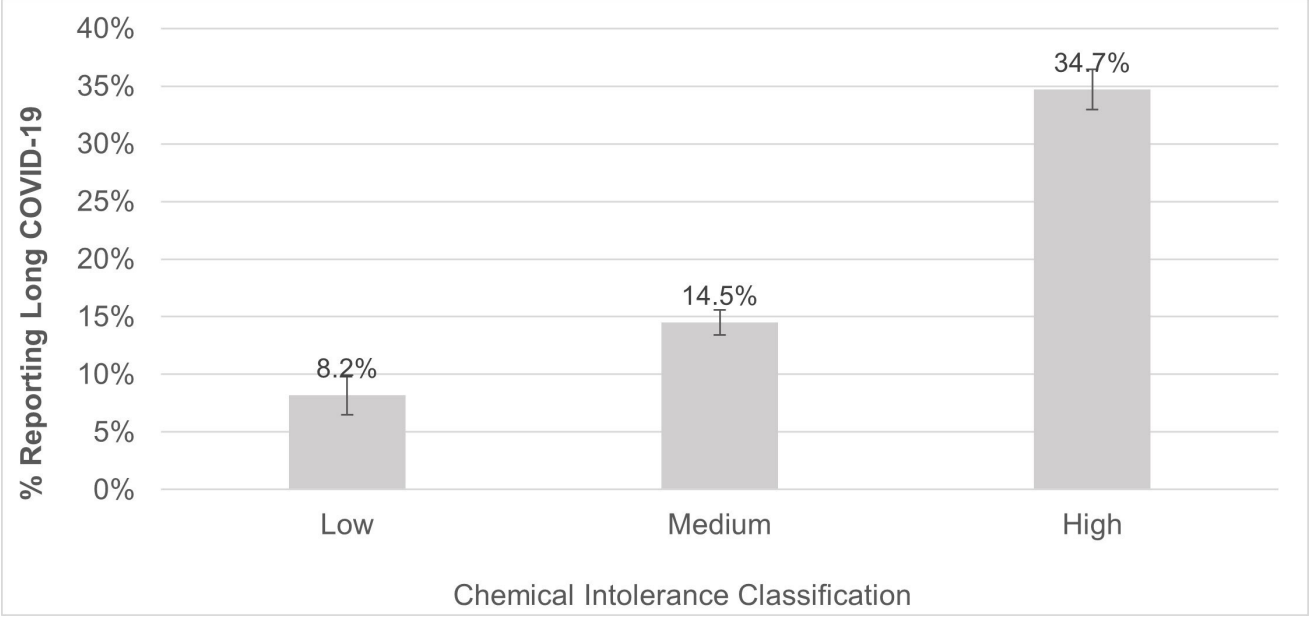

Figure 2 Per cent reporting long-COVID-19 by chemical intolerance classification.

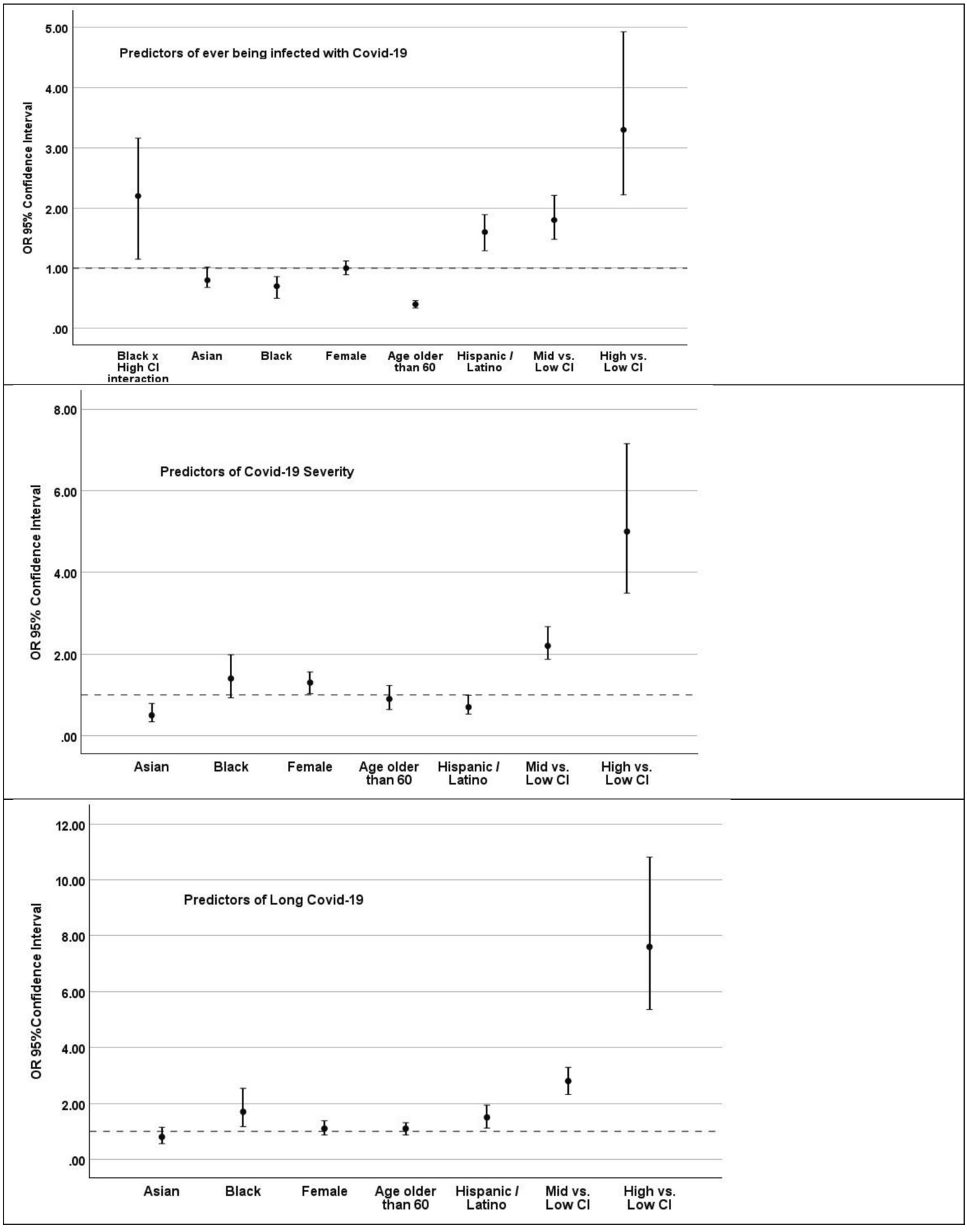

Figure 3 Summary of the ORs for the three logistic regression models.

DISCUSSION

We found that those with CI reported significantly higher rates of COVID-19 compared with those without CI. They also report significantly greater COVID-19 symptom severity scores and higher rates of long COVID-19. One plausible explanation for these findings is that those with CI have a greater number of pre-existing medical conditions than those with low CI.[27] This greater disease burden may further compromise an already taxed immunity response against viruses[28] and/or invoke differential mast cell activation among those with CI.[29 30]

It may also be plausible that being infected with COVID-19 somehow initiated CI. However, the current study has insufficient data to make that determination. Furthermore, to date, there is no evidence in the literature that COVID-19 would initiate CI, this would be a matter for a longitudinal study.

Increased age has been found to be a significant risk factor for COVID-19. In contrast, to the literature, we found that older respondents (>60 years) reported lower COVID-19 prevalence rates. Unim *et al*[31] also reported that the average number of COVID-19 symptoms declined with age, from 2.1 in patients aged <60 years to 1.7 in those aged 90 years or older (p<0.001). They also report that, fever, cough and diarrhoea significantly declined with increasing age.

There may be several reasons for the age discrepancy in our study. Much of the literature centres on cases and death data, whereas these data are self-reported prevalence, where a hospitalisation may well not have occurred. Older adults may be able to better self-isolate (eg, due to the lockdown) than younger age groups, and given the increased risk in the older age groups, may be driven to do so.[32] Canning *et al*[33] report that while the older age groups in their study were just as likely to leave the house as the younger group, those over the age of 50 had less than half the number of close contacts than those less than 30 years old. Notwithstanding, we did find an increased severity to COVID-19 among our older age category.

As discussed in the Study limitations section below, the older age category may be subjected to both an increased health and higher educated bias as well as an increased survivorship bias as cases resulting in death would not be accounted in these data.

We found that women report worse COVID-19 symptom severity than men. But, this is contrary to other reports indicating that men have worse COVID-19 symptomatology than women.[34] However, CI was not assessed in those studies, so it may be plausible to suspect that CI was a confounder of the prior reports of sex differences in COVID-19 symptomatology. This is relevant because women have consistently been reported to have higher CI than men.[35] This suggests a potential subgroup connection between CI and COVID-19 severity in women; however, our analysis did not find any significant sex interactions with the COVID-19 outcome variables.

We found ethnic and racial group differences related to COVID-19 prevalence, COVID-19 reaction severity, and long COVID-19 status. Compared with NHWs, Hispanic individuals reported increased COVID-19 and long COVID-19 prevalence. Hispanic individuals were 1.6 times more likely to report COVID-19 than NHWs. This is highly consistent with prior research using the Household Pulse Survey showing similar results.[36] Kreutzer *et al*[37] reported Hispanic ethnicity was associated with physician-diagnosed multiple chemical sensitivity (OR=1.82, 95% CI 1.21 to 2.73). Concomitantly, we also found that Hispanic individuals reported higher CI rates than NHWs (49% vs 29%, respectively) (p<0.0001)

Given known racial disparities in occupational and other environmental toxic exposures,[38] it is plausible to suspect that exposure to toxins may at least partially explain the disproportionate impact of COVID-19 among racial and ethnic minoritised populations.[39]

Wong *et al*[39] used the US Environmental Protection Agency's Risk-Screening Environmental Indicators (RSEI) Model US EPA (2021)[40] to determine if environmental toxins mediate the association between COVID-19 hospitalisations and race and ethnicity. The RSEI is a measure that considers the amount of toxic chemicals released, the route of exposure, individual chemical toxicity and the number of people potentially exposed. Higher scores indicate higher risk of toxic exposure.[40] They report that higher RSEI scores were associated with increased COVID-19 hospitalisation rates and that all racial and ethnic minority groups had higher odds of hospitalisation compared with the NHW group. They showed that RSEI decile scores mediated the racial and ethnic COVID-19 hospitalisation disparities among Hispanic and non-Hispanic black individuals.[39]

Disparities among Hispanic women might also be accounted for by marked differences in occupational exposures to pesticides and cleaning agents.[34] According to the Economic Policy Institute, women make up the vast majority of domestic house cleaning workers, and 63% of those women are Hispanic.[41 42] Domestic housecleaners are exposed to a myriad of chemical cleaners. Future research could investigate the connection between occupational exposures, CI, COVID-19-risk and ethnicity.

In this study, we found that black/African American respondents reported an increased risk for long COVID-19 despite having a lower COVID-19 prevalence. However, taking into account the significant interaction term, we found that blacks with High CI are at two times the risk of reporting to have had COVID-19. This is consistent with the literature showing that African Americans and Hispanics are about two times as likely to need to stay in the hospital due to COVID-19 than NHWs.[42]

Individuals of Asian race reported a lower COVID-19 severity score than the other ethnic groups. This may be due to an increased willingness among the Asian culture to take greater precaution against infectious disease (eg, mask wearing) than other cultures.[43] The relatively low number of Asian respondents in this study

precluded investigating CI subset interactions between the COVID-19 outcomes.

Another plausible cultural explanation of lower COVID-19 severity scores among Asian individuals may be due to the fact that Asian individuals tend to demonstrate lower extreme response scores than other cultures—believing it is more important to be modest and respond cautiously.[44 45] Studies of cross-cultural differences in response styles show that ordinal response formats (eg, Likert scales) differ across cultures. Asian cultures tend to choose more middle-level items on Likert scales than other cultures.[44 46]

Biological plausibility: in prior work, we have demonstrated a strong association between CI and mast cell proliferation. Approximately 50% of patients with mast cell activation syndrome (MCAS) also have CI, with MCAS patients having similar symptoms as those with CI.[29 30] This suggests that those with CI may more readily respond to environmental insults with greater and a more sustained mast cell immune response. This may include responses to viruses themselves or to vaccinations. Indeed, we demonstrated that those with high CI in this study reported significantly more severe adverse reactions to the COVID-19 vaccine.

Indoor air and COVID-19: several studies indicate that proper indoor air ventilation can mitigate the risk of COVID-19.[45] However, the COVID-19 quarantine may have posed more risk for those who are chemically intolerant. The quarantine may have affected indoor air quality (IAQ) by increasing adverse exposures for longer periods of time—enduring higher levels of indoor air pollutants than before the pandemic. In the face of poorly ventilated spaces, the risk of infectious disease can be compounded through accumulated volatile organic compound (VOC) by everyday product use including scented cleaning or personal care products, pesticide use, combustion through the use of gas stoves or burning candles and plug-in air fresheners.[47]

To sanitise the indoor environment against COVID-19, the use of these toxic cleaning 'air freshener' products may have increased during the lockdown period, therefore potentially triggering CI symptoms. Fragranced cleaning and/or personal care products have been found to be the principal triggers people with CI report.[48] This is consistent with other reports in the literature involving the association between poor IAQ, systemic, health and risk of COVID-19[49]—the new challenge for physicians and healthcare providers.

Interventions: in prior work, we demonstrated that substantial improvements in the symptoms of those with CI were achieved through 'Environmental House Calls' (EHC).[50] In these EHCs, IAQ was assessed in the homes of 37 persons with CI. VOC sources were identified using home air samples analysed by gas chromatography/mass spectrometry. Through a series of home visits, the intervention team taught each person and their families how to reduce their exposures. Pre–post symptom assessments were made. While fragrances were present in every home, the symptoms of those who were able to reduce or eliminate toxic household VOC sources, including fragrances, reported sysmptom improvments at postintervention follow-up. Practical advice for physicians and patients on ways to improve IAQ and how it affects health are shared in online supplements 2 and 3.

Study limitations

This observational study design cannot determine causality without further longitudinal research. The survey was conducted via a paid, computerised survey platform (SurveyMonkey). As such, all respondent answers were self-reported (most with self-diagnosed COVID-19), and therefore prone to several biases, including social acceptability, honesty, differing interpretations of questions and recall bias. Payments to participants were small (less than US$10) and did not constitute 'undue influence'. To address both payment and self-report concerns,[25] extensive DQ procedures were employed to remove surveys completed too quickly or illogically (see the Data quality section).

Although the survey was balanced to reflect state population sizes, a participants' sex, age, race and education, selection bias in computer-based surveys can be marked. Our computerised surveys suggest undersampling of black/African American and Hispanics/Latino respondents, both by nearly 50%. Non-clinical, computerised surveys can lead to a healthy, higher educated bias that may be pronounced in the older population. Indeed, our relatively low COVID-19 prevalence rates among the older group compared with the literature may be due to such a bias. The results of this age group should be taken with caution and further research. Lack of access to the internet, a computer, or a smartphone as well as language limitations, may have also reduced the generalisability of our findings for low-income and minority populations.

Finally, this study design suffers from survivorship bias. All respondents either did not get COVID-19 or survived their encounter with COVID-19. COVID-19 cases that resulted in death are not included in these data.

CONCLUSION

Prior studies show that individuals at higher risk for COVID-19 include older age groups, male sex, those with pre-existing comorbidities (eg, challenged immunities) and racial/ethnic disparities. The results of this study suggest that those with CI be included in a high-risk group, particularly if other demographic and comorbid medical conditions exist. Future investigations could identify those various risk subsets. Understanding the risk subgroups would be helpful in mounting effective targeted prevention efforts that include social media outreach and EHC.

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contributed to the first drafts and approval of the version. The authors agree to be accountable for all aspects of the work in ensuring accuracy and integrity of the paper. RFP is responsible for the overall content as guarantor.

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