COVID-19 related chemosensory changes in individuals with self-reported obesity*

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Abstract

Background/objectives: Self-reported smell loss is a prominent symptom of COVID-19 infection and a potentially useful clinical tool for remote pre-screening of this disease. However, pre-existing chemosensory dysfunction with obesity may diminish the usefulness of self-reported smell loss in this vulnerable group. Here we aim to compare COVID-19 related chemosensory alterations in participants with and without obesity and determine if self-reported smell loss is predictive of lab-based COVID-19 diagnosis in both groups in the context of restrictive clinical data collection.

Subjects/methods: In this secondary analysis of a cross-sectional global dataset, we compared self-reported chemosensory ability in participants with a respiratory illness reporting a positive (C19+; n = 5156) or a negative (C19-; n = 659) COVID-19 laboratory test outcome, who also self-reported to have obesity (C19+; n = 433, C19-; n = 86) or not.

Results: Participants with obesity and without obesity reported a similar decline in smell, taste, and chemesthesis during illness. In C19+ participants with obesity, we observed a greater relative prevalence of non-chemosensory symptoms, including respiratory and GI symptoms. Critically, we found that the model previously proposed also predicts C19+ diagnosis in participants with obesity.

Conclusions: We conclude that COVID-19 respondents with obesity experience a similar self-reported chemosensory loss as those without obesity. In both groups self-reported chemosensory symptoms are similarly predictive of COVID-19 infection, thus highlighting the potential of collecting self-report of symptoms and comorbidities remotely when clinical observations are restrictive.

Key words: COVID-19, smell, taste, chemesthesis, obesity

Introduction

According to the World Health Organization, globally 13% of adults reported to have obesity in 2016[(1)]. Within the context of the COVID-19 pandemic, countries with the highest prevalence of obesity also recorded a high death rate from COVID-19 infection[(2)]. Although an increased susceptibility to viral infection with obesity is unknown, it is a strong determinant of morbidity and mortality in patients infected with SARS-CoV-2, the virus responsible for COVID-19 infection[(3,4)]. A recent analysis also indicated that COVID-19 mortality in patients with obesity is higher than that of other comorbidities[(5)] and they are also at high risk for poor health outcomes. Overall, current evidence suggests that obesity significantly interacts with the pathogenesis of COVID-19.

Obesity has previously been linked to alterations in chemosensory perception. A large body of research suggests that individuals with obesity typically have pre-existing impairment in taste sensitivity and detection threshold and a lower capacity to detect and identify odors than individuals without obesity[(6)]. Though, inconsistencies in the relationship between

excess body weight, olfactory perception[7] and taste sensitivity literature [8] are also reported. These dysfunctions are driven by the production of pro-inflammatory factors from adipose tissue, leading to impairment in olfactory receptors[9] and a decline in taste bud and taste progenitor cells [10,11], respectively. Smell loss was also recently highlighted as an important predictor of COVID-19[12,13] with 67% of COVID-19 patients reporting sudden olfactory and gustatory dysfunctions. Considering that marked inflammation with obesity also seems to favor viral infections[14,15], how existing chemosensory deficiency interacts with obesity and COVID-19 related chemosensory alterations is unknown.

It may be speculated that obesity-driven pre-existing chemosensory deficiency may mask the viral-induced diminished taste and smell self-reported experiences. This may lead to a higher portion of undetected cases in this population[16], thus highlighting the importance of understanding chemosensory alteration in patients with obesity. Furthermore, in light of the potential for using oro-nasal perception as an early marker of SARS-CoV-2 infection[17], it needs to be assessed whether the predictive relation between chemosensory loss and COVID-19 generalizes to participants with obesity. This is particularly relevant given the new waves of infection sweeping through countries worldwide and high death rates in many regions. Here, we systematically describe and compare chemosensory perception (smell, taste, and chemesthesis) and related symptomatology in COVID-19 in non-hospitalized adults with or without obesity. Our measures are self-reported since collecting objective data was impossible on a global scale with strict COVID-19 restrictions. Specifically, our analyses (pre-registered at https://osf.io/xf25v) aimed to describe chemosensory perception and related symptomatology during the COVID-19 illness (Aim 1) and post-vs pre-COVID-19 diagnosis (Aim 2), in participants with self-reported obesity vs without obesity. We predicted lower ratings for smell, taste, and chemesthesis, and more severe COVID-19 symptoms in participants with obesity, compared to those without obesity. We also speculated smaller differences in ratings for smell, taste, and chemesthesis perception post- vs pre- COVID diagnosis in participants with self-reported obesity. Post-COVID-19 chemosensory recovery (Aim 3) was also tested, hypothesizing lower ratings for smell, taste, and chemesthesis in participants with self-reported obesity vs without obesity. Additionally, we assessed COVID-19 severity based on the sum of reported symptoms (Aim 4) and the ability of smell ratings to predict COVID-19 diagnosis (Aim 5) with self-reported obesity vs without obesity.

Materials and methods

Study design

To the best of our knowledge, this study is the first to assess chemosensory alterations in adults with obesity and COVID-19. We conducted a secondary analysis of cross-sectional survey data collected between April 7th and November 4th, 2020 using the Global Consortium for Chemosensory Research (GCCR) core questionnaire. This crowdsourced survey collected data from community-dwelling individuals via social and traditional media, GCCR website, and clinical patients. This survey, currently deployed in 32 languages, used categorical questions, as well as visual analog scales to measure self-reported chemosensory ability and other symptoms in adults with ongoing or recent respiratory illnesses[12]. We also collected self-reported data on the presence of pre-existing diseases, including our condition of interest, obesity, as well as other COVID-19 symptoms. The specific question included in the survey was "Did you have any of the following in the 6 months prior to your recent respiratory illness or diagnosis? (Select all that apply)." Potential responses included: obesity, high blood pressure, heart disease (heart attack or stroke), diabetes (high blood sugar), lung disease (asthma/COPD), head trauma, neurological disease, cancer that required chemotherapy or radiation, cancer that did not require chemotherapy or radiation, chronic sinus problems, sinus allergies/hay fever, none. Whenever in 'prior conditions' question no response was provided or "None" was checked, the response was imputed as indicating no prior conditions. Since we collected this data during the early period of the pandemic when COVID-19 restrictions were stringent and infection rates were high, objective assessments of BMI and chemosensory function were not feasible. Thus, we rely on self-reports. It is also important to note that our data is resistant to collider bias and is supported by independent studies with objective smell tests[18]. All participants included in the study were: 1) ≥18 years old, 2) had a (suspected) respiratory illness within the past two weeks, 3) had onset of respiratory illness after January 1, 2020, 4) reported COVID-19 diagnosis via laboratory test (viral PCR or antigen test). Respondents who did not report having any illness or symptoms within the last two weeks, who had multiple responses, or who responded "Don't know" or "Other" when asked about their diagnosis of COVID-19, were excluded from the analyses. To investigate the recovery of chemosensory functions, only participants who reported the date of onset of respiratory illness symptoms were included. The original study was approved by the Office of Research Protections of The Pennsylvania State University (STUDY00014904). A departure from the pre-registered analyses is the inclusion of age as a factor in all analyses, following differences in age observed between groups. We also report the unregistered analysis of pre-illness ratings, an important addition given the previously reported decreased sensitivity for participants with obesity compared to those without obesity.

Participant description

Figure 1 shows a flow diagram of the inclusion of participants into the various groups. A convenience sample of 52,334 volun-

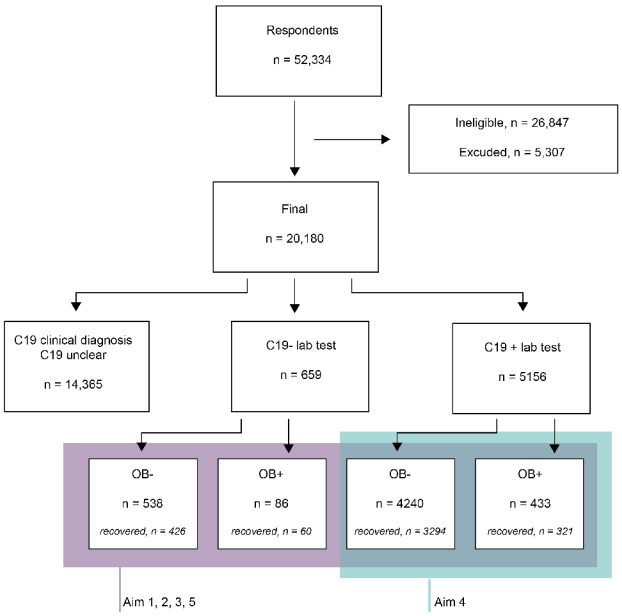

Figure 1. Flow Diagram of Study Participants Based on the STrengthening the Reporting of OBservational Studies in Epidemiology (STROBE) guidelines. Participants included in the prediction of COVID-19 status in participants with obesity vs without obesity are framed in blue. Participants framed in purple are included in all other analyses. n = number of participants; OB+ = self-reported presence of obesity; OB- = self-reported presence of obesity; COVID diagnosis unclear = responses "No - I do not have any symptoms", "Don't know" or "Other" to survey Question 8 ("Have you been diagnosed with COVID-19?").

teers accessed the GCCR questionnaire. Of those, 5815 met the inclusion and exclusion eligibility criteria and were included in the final analysis. A positive COVID-19 diagnosis (C19+) was determined using the self-reported data from COVID-19 lab test or clinical exam outcome. All C19+ patients were further categorized into having obesity if they reported it as one of the pre-existing disease conditions in the questionnaire. C19+ patients who did not report having any medical condition or did not answer this question were categorized as controls without obesity.

Statistical analyses

Statistical analyses were conducted in R via RStudio. The annotated scripts, the information on the computational environment, and dependencies shared for future reproducibility can be found at the OSF project link (https://osf.io/rbcty/). A detailed description of statistical analysis is also included in the Supplementary document. We conducted Bayesian linear regressions using the lmBF function to test whether a difference between groups was present or absent with the lmBF function. Bayes factors for all the analyses are included in the Supplementary document. Please refer to Supplementary Table 1 for the inference rules, which follows the classification scheme proposed by Lee and Wagenmakers[19] and adjusted from[20]. To test for gender differences in the COVID-19 and obesity groups we conducted Pearson's chi-square tests with the R base function "prop.test". For chemosensory perception analysis models, in addition to COVID diagnosis, obesity status, and age, we used "before illness", "during illness", "change due to illness" ("before illness" minus "during illness") and "recovery" ("after illness" minus "during illness") separately as dependent variables. To assess whether participants with obesity experience more and/or different symptoms from those without obesity, we summed all symptoms and used it as a dependent variable in our Bayesian linear regression models. For the subset of C19+ only, we calculated probability tables for the likelihood of experiencing a given symptom for the participants with and without obesity and tested for distribution differences with chi-square tests. We used an alpha of 0.05 to determine significance.

We also tested for model accuracy for predicting COVID-19 illness. We used the ROSE (Random Over-Sampling Examples) package to deal with the binary classification problems in the presence of imbalanced classes. To measure model quality, receiver operating characteristics (ROC) were visualized via the pROC package based on the calculation of hold-out area under the curve (AUC). We focused on "during illness" ratings because those best showed evidence for the effects of illness and were also the most predictive symptom in a previous study with the same questionnaire[18].

Results

Participant characteristics

A total of 5,156 participants reported a positive lab test for COVID-19 (hereafter, C19+), while 659 reported a negative lab test for COVID-19 (hereafter, C19-). Of all participants, 519 (9% of the total group) self-reported to have obesity (C19+ = 433; C19- = 86) (Figure 1). The demographic profile of our participants is summarized in Supplementary Table 2. Age is higher in 'participants who self-reported obesity' (OB+) compared to 'those without obesity' (OB-) (43.1 vs 39.5). After excluding n = 17 participants with gender reporting categories of "prefer not to say" (n = 13) and "other" (n = 4), we observed different proportions of gender ($p = 0.035$), driven primarily by a higher proportion of women in the C19- group with OB+ (87.2%) compared to OB- (77%).

Similar smell, taste, and chemesthesis abilities in participants with and without obesity before COVID-19 illness

Before COVID-19 illness, OB+ did not self-report greater differences in smell, taste, or chemesthesis ability, or greater nasal congestion than OB- (Supplementary Figure 1, Supplementary Table 3). Before COVID-19 illness C19+ participants reported greater ability in smell and taste than C19- participants.

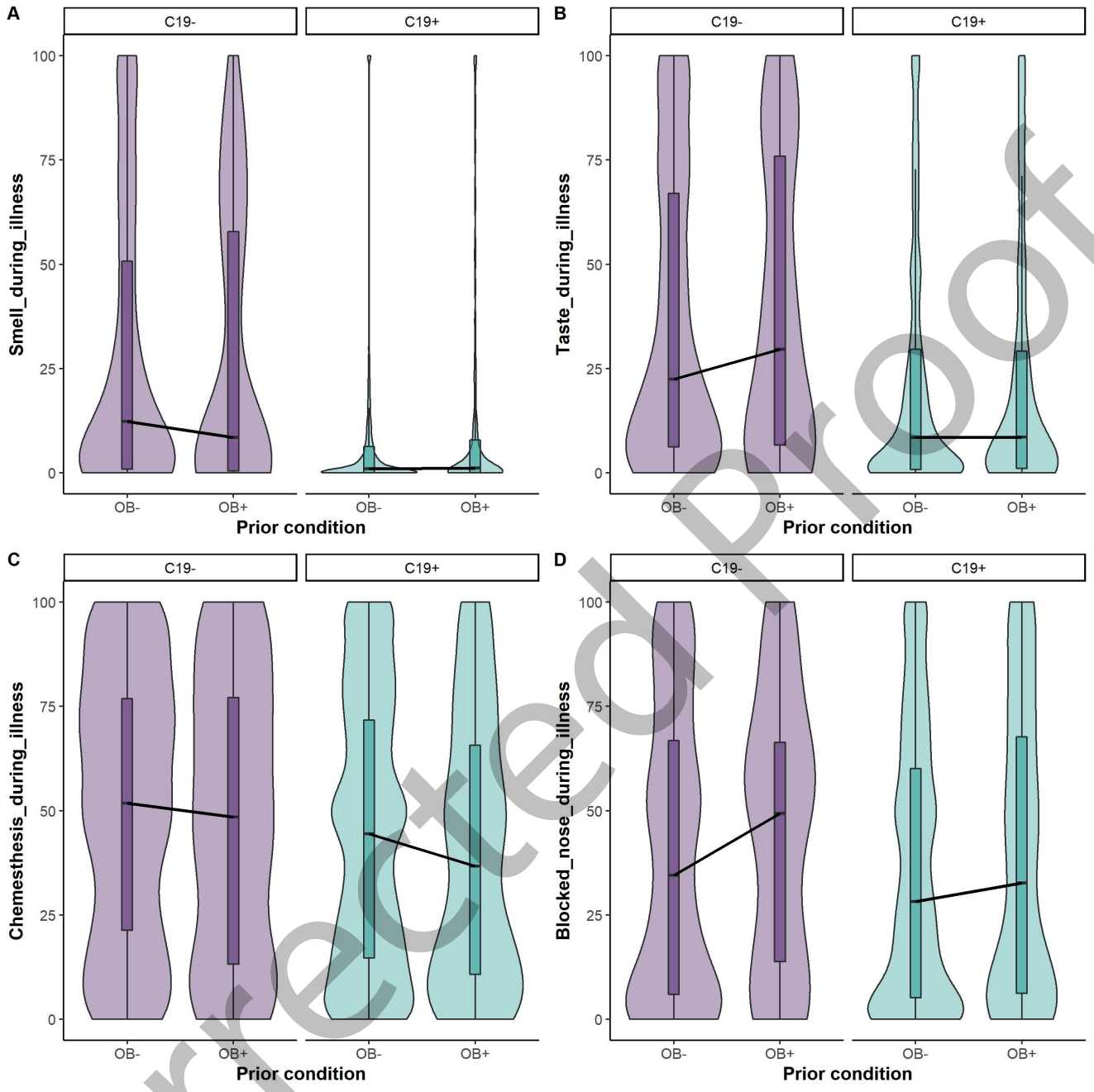

Figure 2. Self-reported smell (A), taste (B), chemesthesis (C), and nasal obstruction (D) ratings during the illness in C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). Ratings were given on 0-100 visual analog scales. Nasal obstruction question was formulated as "How blocked was your nose?") during respiratory illness in C19+ and C19- participants. Each panel presents the mean ratings for chemosensory abilities and nasal blockage. All participants had a diagnosis via a lab test. The thick black horizontal bar indicates the median, the shaded bars within each violin indicates the interquartile range. The shaded violin area in purple and blue represents smoothed histogram of data density along the data points.

Similar smell, taste, and chemesthesis loss in participants with and without obesity during COVID-19 illness

C19+ participants reported greater deficits in smell, taste, and chemesthesis, as compared with C19- participants (Figure 2, Supplementary Table 4). We reported lower deficits in nasal congestion with C19+ participants in our analysis, compared to C19-. Further, these chemosensory variables did not differ between the participants who self-reported OB+ vs OB-, across the COVID groups.

Similar to the above chemosensory findings during the illness, the differences in chemosensory ratings between pre-and during illness varied in C19+ and C19- participants (Figure 3,

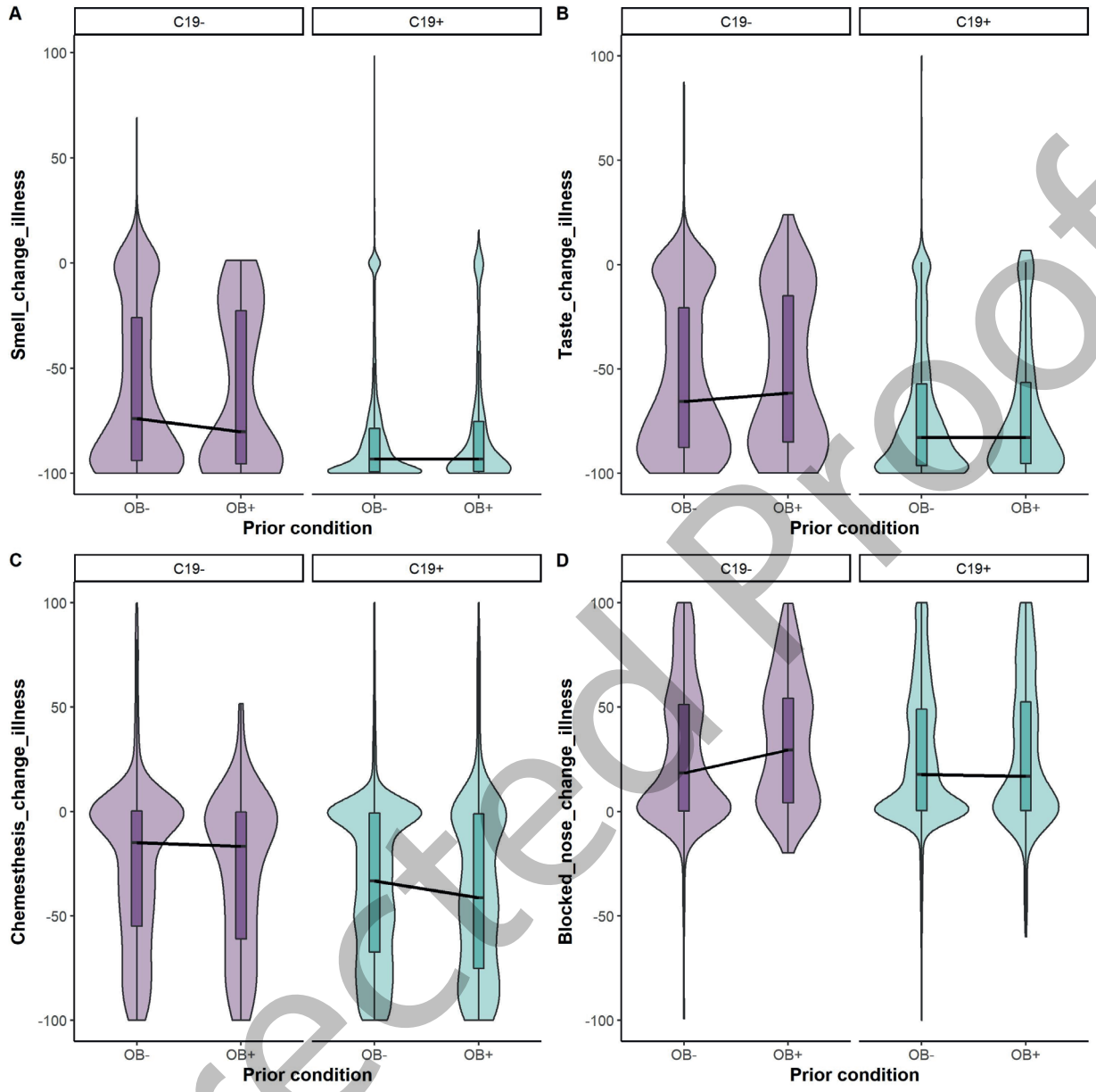

Figure 3. Self-reported change in smell (A), taste (B), chemesthesis (C), and nasal obstruction (D) ratings in C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). Each panel presents the distribution of the change scores, i.e., the rating "before" illness minus the rating "during" illness on the 100-point visual analog scale. All participants had a diagnosis via a lab test. The thick black horizontal bar indicates the median, the shaded bars within each violin indicates the interquartile range. The shaded violin area in purple and blue represents smoothed histogram of data density along the data points.

Supplementary Table 5). In particular, C19+ participants reported greater deficits in smell, taste, and chemesthesis, than the C19- group. However, when estimating the effect of obesity, the three chemosensory variables did not differ between the OB+ and OB- groups across the COVID-19 condition. Interestingly, there was no main effect of COVID-19 condition or obesity status on the nasal obstruction reporting.

Similar smell, taste, and chemesthesis recovery from COVID-19 illness in participants with and without obesity

To further understand changes in chemosensory perception with COVID-19 diagnosis and obesity condition, we looked at the data from participants who reported recovery from the illness (Figure 4, Supplementary Table 6). Recovery was reported by 3970 participants, which is approximately 68% of our sample. Our Bayesian linear models suggest that the ratings for post-recovery chemosensory perception did not differ in C19+ and C19- diagnosis. Of note, some smell/taste/chemosensory symptoms remain post-recovery from the illness in C19+ and C19-. We found no differences in smell, taste, and chemesthetic

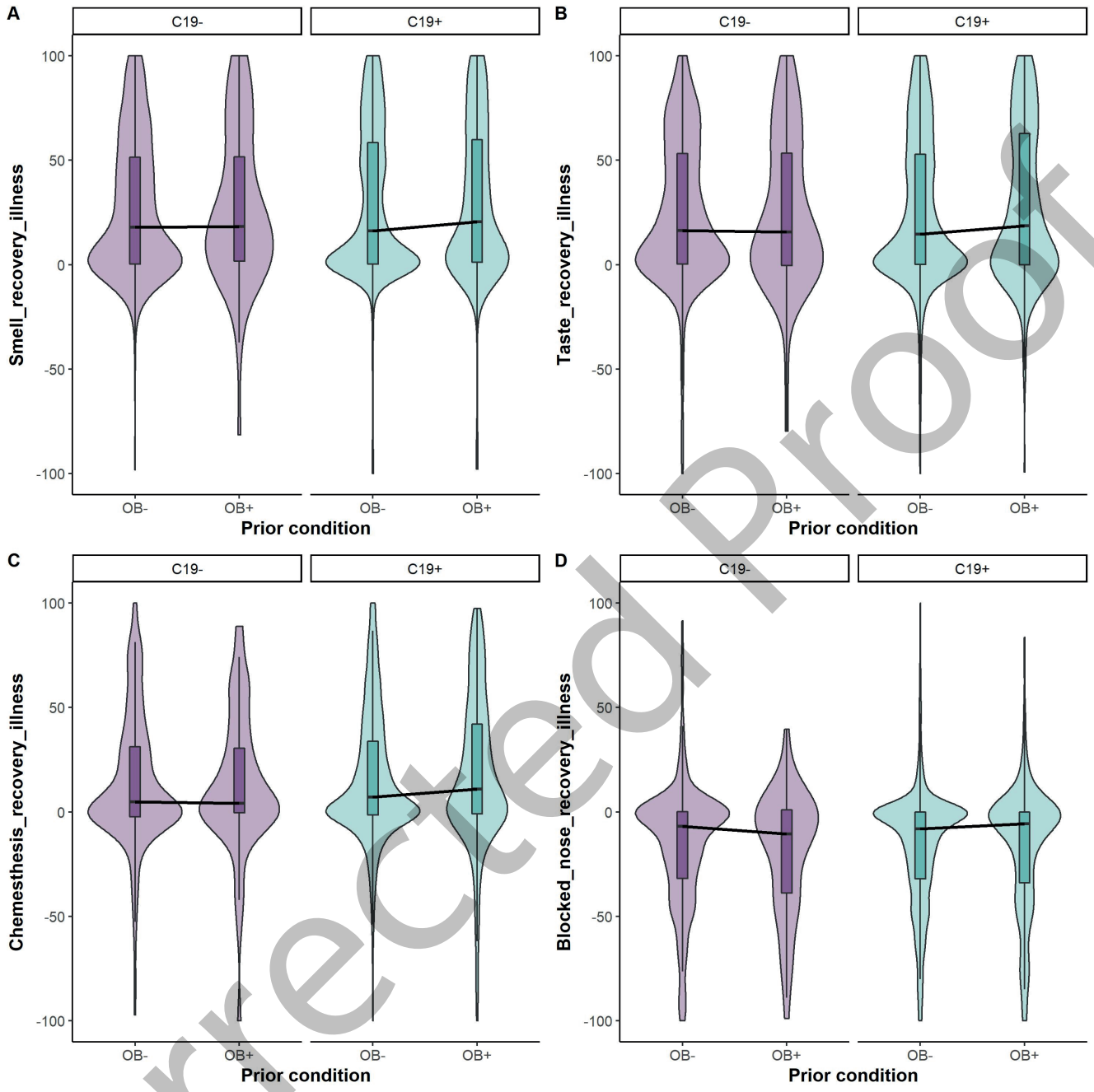

Figure 4. Self-reported change in smell (A), taste (B), chemesthesis (C), and nasal obstruction (D) ratings post-recovery from respiratory illness in C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). Ratings were given on 0-100 visual analog scales. Each panel presents the mean ratings for chemosensory abilities and nasal blockage post-recovery from respiratory illness. All participants had a diagnosis via a lab test. The thick black horizontal bar indicates the median, the shaded bars within each violin indicates the interquartile range. The shaded violin area in purple and blue represents smoothed histogram of data density along the data points.

perception by self-reported obesity. Nasal obstruction did not seem to be affected by either COVID-19 diagnosis or obesity status, post-recovery from the illness.

Participants with obesity report more symptoms overall and more frequently report respiratory and gastrointestinal (GI) symptoms

Based on the evidence from existing clinical and epidemiological studies, one of our goals was to assess whether individuals with OB+ overall have greater symptomatic manifestation with C19+ diagnosis than OB-. To test our hypothesis, we used Bayesian linear regression and compared the sum of the symptoms reported by participants in these samples versus samples without obesity (Figure 5A, Supplementary Table 8). As predic-

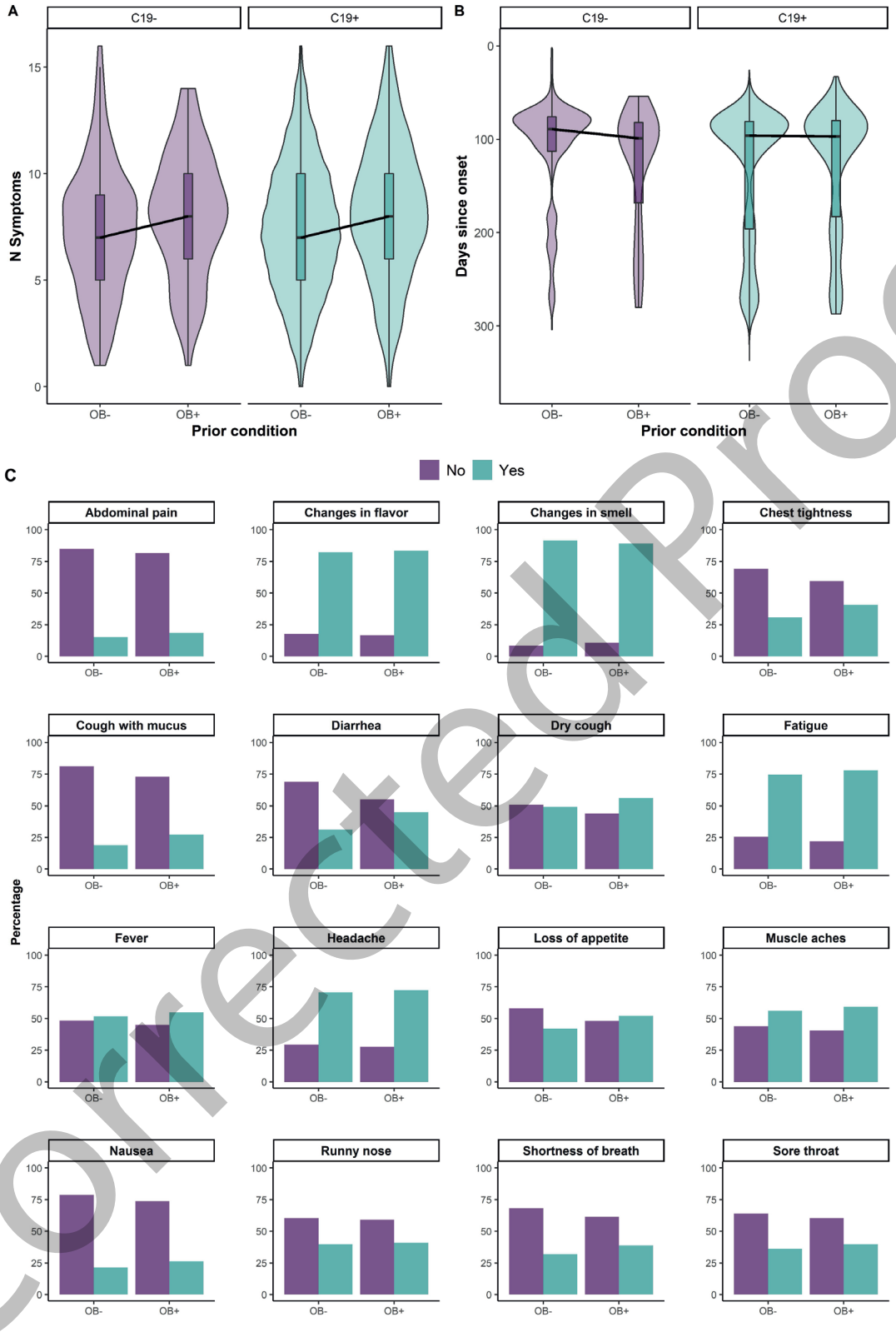

Figure 5. Self-reported symptomatic manifestation reported by C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). (A) Cumulative number of symptoms reported by C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). (B) Self-reported average number of days since onset of respiratory illness symptoms reported by C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). (C) Proportion of participants with C19+ that report specific symptoms by self-reported obesity (OB+) or without obesity (OB-). * $p<0.05$. The thick black horizontal bar indicates the median, the shaded bars within each violin indicates the interquartile range. The shaded violin area in purple and blue represents smoothed histogram of data density along the data points.

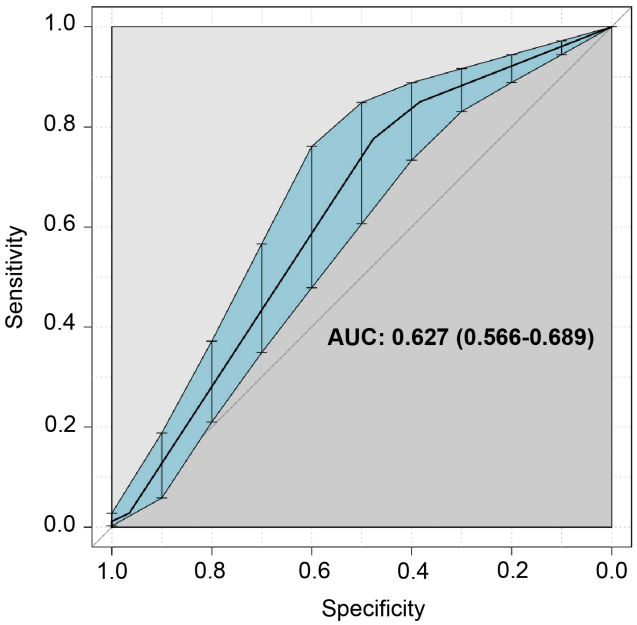

Figure 6. ROC curve in discriminating C19+ vs. C19- in participants with obesity (OB+) after having trained the model with participants without obesity (OB-).

ted, among those with C19+, there is decisive evidence that OB+ report a larger number of symptoms than OB- (average N of symptoms = OB+: 8.22; OB-: 7.42). A similar effect is observed among participants with C19- (average N of symptoms = OB+: 8; OB-: 7.33). Among those with C19+, disease duration is longer in those with obesity, while in C19- such a difference is not observed (Figure 5B, Supplementary Table 7). Looking at the specific symptoms (Figure 5C), smell and taste symptoms are equally reported by OB+ and OB- with a diagnosis of COVID-19. Further, OB+ reported greater frequency in loss of appetite, diarrhea, and nausea, along with shortness of breath, cough (dry or with mucus), and chest tightness.

A classifier trained on participants without obesity accurately predicts C19+ diagnosis in participants with obesity

Based on the self-reports on symptoms, combined with the chemosensory and nasal obstruction ratings, we assessed the accuracy with which we could predict a C19+ diagnosis (Figure 6) in OB-. We then tested the model to predict the accuracy of discrimination of C19+ in OB+. Our results indicate that we can predict the C19+ diagnosis with 63% accuracy. While this number indicates a moderately good estimate, it is important to note that this value is significantly greater than chance (50%) and supports the idea that self-reported chemosensory differences between people with COVID-19 and OB+ or OB- are reasonably irrelevant.

Discussion

Reports of olfactory and gustatory dysfunctions in COVID-19 patients continue to grow. To our knowledge, this study is the first to describe and compare the chemosensory perception and related symptomatology in COVID-19 patients who self-reported to OB+ vs. OB-. Independent of the obesity status, the subjective ratings of smell, taste, and chemesthesis declined with COVID-19 illness. We also found that OB+ showed similar recovery from COVID-19 related loss of smell, taste, and chemesthesis as OB-. Although we do not know the severity of each symptom, OB+ reported a greater frequency of respiratory and GI symptoms and more symptoms overall. Finally, we found that a model of all symptoms combined trained on OB- patients can predict the C19+ diagnosis with 63% of accuracy in OB+. Furthermore, this smell loss was not related to self-reported nasal obstruction, commonly observed in other upper respiratory infections[21,22]. Together, these results confirm and add to previous reports that COVID-19 largely impacts chemosensory function; however, obesity does not mask self-reported chemosensory loss in those with C19+ diagnosis.

Smell and taste disturbances are a typical consequence of nasal inflammation with an upper respiratory tract viral infection[23,24]; however, an acute loss of taste and smell emerged rapidly as a critical neurological manifestation of a C19+ diagnosis[25]. Our current findings are similar to prior reports that showed that approximately 90% of the participants reported a loss of smell. Furthermore, nearly 80% of the participants reported a loss of taste, and 46% had a reduction of chemesthesis, indicating that the chemosensory impairment is not restricted to smell[12,18]. While most cold viruses cause nasal congestion and individuals experience a reduction in the sense of smell, our results showed that nasal congestion was not associated with smell loss. This finding is consistent with other reports[26], suggesting that other mechanisms may play a role in COVID-19 associated smell loss[25].

In addition to being a risk factor for COVID-19 viral infection, excessive body weight is also implicated in chemosensory decline. Adipose tissue in obesity is "pro-inflammatory", causing a surge in levels of IL-6 and C-reactive protein and enhancing the expression of cytokines and adipokines[10]. Interestingly, in diseases where these circulating inflammatory factors are high, smell and taste dysfunction are prevalent[11,14]. Thus, obesity-related inflammation may affect chemosensory function. A major concern with this pre-existing gustatory and olfactory sensory deficiency with obesity is that it may mask the viral-induced diminished taste and smell self-reported experiences. Interestingly, our analysis showed that COVID-19 related chemosensory-related changes were comparable between C19+ participants with OB+ and OB-, suggesting that obesity does not have an effect on the loss of chemosensory perception with COVID diagnosis. These findings need to be taken with caution, especially when

considering severe cases. For example, if a patient is in critical condition, they cannot pay attention to their chemosensory alterations, and chemosensory perception will likely not be tested or self-reported. This does not mean that the chemosensory perception is not affected.

In terms of chemosensory recovery, we found no differences between OB+ and OB-. While none of the studies to date has compared the recovery rates between C19+ participants with OB+ vs OB-, our overall recovery rate of 65% is comparable to our previous analysis[18] but slightly lower than other studies[15,27]. There are residual smell/taste/chemosensory symptoms reported post-recovery from the illness in C19+ and C19- groups. In particular, quantitative studies using psychophysical methods have shown that nearly 25% of people continue to report chemosensory problems when evaluated 30 - 60 days after the onset of COVID-19[15]. This insufficient recovery rate may significantly increase the number of patients with chemosensory disturbances, ultimately influencing eating behaviors[28], quality of life[29], and psychological health[30] in the general population. But most importantly, it may significantly impact OB+ who have an added burden of lower chemosensory acuity[6,31]. Thus, it is imperative to prepare healthcare workers to detect and treat chemosensory disorders in this high-risk population.

As we hypothesized, non-chemosensory symptoms were more severe in C19+ participants with OB+ than OB-. Specifically, OB+ reported a greater frequency of respiratory and GI symptoms. In general, it is known that obesity is associated with GI symptoms disturbances, such as upper abdominal pain, nausea, vomiting, retching, and gastritis accompanied by inflammation or alterations of intestinal permeability[32]. C19+ patients also experienced several GI symptoms such as diarrhea (24.2%), anorexia (17.9%), and nausea (17.9%)[33], though they vary widely and are less understood. This may not be surprising since some viral infections are known to cause alterations in intestinal permeability as well[34]. The mediation of ACE2 cell receptors could elucidate the mechanism related to GI tract involvement in SARS-CoV-2 infection. While ACE2 is expressed in abundance in the lungs' alveolar cells, the receptor is also highly expressed in the GI tract, especially in the small and large intestines[35].

Nine percent of our participant population reported to have obesity, compared to the global obesity rate of 13% and higher obesity rates in some countries, which suggests our sample is a biased sample. Self-reports of body weight or obesity are generally accurate[36,37]. However, there is also evidence that self-reported body mass index data may lead to underestimation of overweight and obesity. This bias is specifically present in adults with overweight and obesity, compared to normal weight individuals[38]. Slight underreporting of obesity in our dataset may reflect that those at the lower end of obesity may categorize themselves as not having obesity. Consequently, one may say that the OB- groups include a small subset of people with obesity and may contribute to a lack of difference in the chemosensory ratings between groups. The proportion of participants obesity may also be smaller than expected because C19+ patients with obesity are reported to have high hospitalization rates and greater severity of respiratory symptoms requiring intubation. If both these two biases exist in our sample, this means that our sample is biased towards the middle of the distribution of degree of obesity, and we may not be over-or underestimating the differences between groups. Three observations in our data validate the accuracy of self-reported obesity: First, there is a higher likelihood of respiratory symptoms for participants with all obesity participants across the C19+ and C19-. Second, epidemiological data indicates that prevalence of obesity increases with age, which is also observed in our dataset with OB+ (43.1 yr) reporting higher age vs OB- (39.5 yr). Third, given the rates of diabetes are high in adults with obesity, of the total sample with obesity, 9% of individuals were diabetic (46/519).

Our study has some limitations. Our online survey and sampling methodology likely selected participants with a heightened interest in smell and taste and/or their disturbances. We also acknowledge that due to the nature of our data being collected in several countries, the definition of obesity may vary and there may be regional and cultural factors that may influence stigma and biases towards self-report of obesity. Ideally, future studies using quantitative taste and smell measures will be conducted in this population.

Despite the limitations, our study shows differences in participants with obesity compared to participants without obesity with other symptoms. However, those differences potentially do not affect the chemosensory symptoms.

Conclusion

It is evident from our analysis that chemosensory loss as a symptom of COVID-19 in combination with other non-chemosensory symptoms is a robust surveillance tool for COVID-19 infection regardless of body weight. Though, more evidence is needed to understand biological mechanisms related to alterations in taste and smell loss in individuals with COVID-19. Understanding how the alteration initiates and progresses will provide molecular and cellular bases for diagnosis and treatment of chemosensory disorders for those with COVID-19 and others who lose their sense of taste and smell due to other conditions with underlying inflammation. It is therefore imperative to include chemosensory assessments for screening and treatment purposes in COVID-19, as well as other health conditions relevant for people with obesity.

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Authorship contribution

All authors conceived the project idea. MGV and VP analyzed the data. SB, GC, PJ drafted the manuscript. All authors were involved in editing the paper and had final approval of the submitted and published versions.

Conflict of interest

The authors declare no competing financial interests in relation to the work described.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Methods

Statistical analysis

Demographics

Cognizant of possible null effects in all our analyses, we opted to implement a Bayesian approach, which allows us to estimate the strength of the evidence supporting the null hypothesis. To test via a between-participant sequential Bayes factor design whether a difference between groups was present (H1) or absent (H0), we conducted Bayesian linear regressions with the lmBF function from the BayesFactor package 32. We used the default Cauchy prior on the effect sizes under the H1 as the scale parameter spread, which was set at its default value of r = sqrt(2)/2. To test for a difference in age between groups, we used the following full model: Age ~ COVID diagnosis + Obesity Age + COVID diagnosis x Obesity. Additive models (no interaction) and main effect models were also computed and compared to determine the model that best explained the data pattern, aka the model comparison with the most extreme Bayes Factor. Please refer to Supplementary Table 1 for the inference rules, which follows the classification scheme proposed by Lee and Wagenmakers and adjusted from. To interpret the strength and the direction of the effects identified, we have additionally sampled from the models' posterior distributions (iterations = 1e4). To test for gender differences between groups, we calculated probability tables of women and men in each of the COVID-19 and obesity groups and tested for distribution differences with Pearson's chi-square tests with the R base function "prop.test". We used an alpha of 0.05 to determine significance.

Self-reported Chemosensory perception analyses

For chemosensory perception analyses, we also conducted Bayesian linear regressions with the lmBF function. The full model included the following terms: Dependent variable ~ COVID diagnosis + Obesity Age + COVID diagnosis x Obesity. Additive models (no interaction) and main effect models were also computed and compared to determine the model that best explained the data pattern. Age was included in all models to factor in significant associations between age and obesity. We used "before illness", "during illness", "change due to illness" ("before illness" minus "during illness") and "recovery" ("after illness" minus "during illness") separately as dependent variables.

Other illness symptomatology analyses

To assess whether participants with obesity experience more and/or different symptoms from those without obesity, we summed all symptoms that participants reported (each symptom that was reported was assigned a value of 1). We then conducted Bayesian linear regressions with the lmBF function as above with summed symptoms as the dependent variable (as above in the chemosensory analyses). We operationalized disease duration as the number of days since onset of the illness and used "days since onset" as the dependent variable in Bayesian linear regression (models as above). For the subset of C19+ only, we calculated probability tables for the likelihood of experiencing a given symptom for the participants with and without obesity and tested for distribution differences with chi-square tests (details as above under demographics). We used an alpha of 0.05 to determine significance.

Model accuracy for predicting COVID-19 illness

To deal with binary classification problems in the presence of imbalanced classes, we used the ROSE (Random Over-Sampling Examples) package, which generates synthetic balanced samples and thus allows to strengthen the subsequent estimation of any binary classifier. To measure model quality, receiver operating characteristic (ROC) were visualized via the pROC package based on the calculation of hold-out area under the curve (AUC), which summarizes the tradeoff between sensitivity (fraction of correctly identified C19+ cases in the sample with obesity and without obesity) and specificity (fraction of correctly identified C19- cases in the sample with obesity and without obesity) as the threshold value for the predictor is varied. We used symptoms (binary), number of symptoms, chemosensory ratings during illness, COVID diagnosis, and days since onset of the respiratory illness. We focused on "during illness" ratings because those best showed evidence for the effects of illness and were also the most predictive symptom in a previous study with the same questionnaire 9. Moreover, this question (rather than pre-illness ratings or change in ratings) is best suited for being asked when making an inventory of symptoms in a clinical setting.

Supplementary Table 1. Interpretation of Bayes factors BF10 following the classification proposed by Lee and Wagenmakers (2013) and adjusted from Jeffreys (1961).

Bayes factor	Evidence category
>100	Extreme evidence for H1
30–100	Very strong evidence for H1
10–30	Strong evidence for H1
3–10	Moderate evidence for H1
1–3	Anecdotal evidence for H1
1	No evidence
1/3–1	Anecdotal evidence for H0
1/10–1/3	Moderate evidence for H0
1/30–1/10	Strong evidence for H0
1/100–1/30	Very strong evidence for H0
<1/100	Extreme evidence for H0

Supplementary Table 2a. Participant gender between C19+ and C19- participants who self-reported to have obesity (OB+) or no obesity (OB-).

	All		C19+		C19-	
	OB+	OB-	OB+	OB-	OB+	OB-
Women, n	412	3571	337	3165	75	406
Women proportion	0.793834	0.750999	0.778291	0.748581	0.872093	0.770398
Men, n	107	1184	96	1063	11	121
Men proportion	0.206166	0.249001	0.221709	0.251419	0.127907	0.229602
Chi Sq statistic (p-value)	4.4155 (0.03561)		1.7001 (0.1923)		3.9434 (0.04705)	

C19+ = positive COVID-19 diagnosis; C19- = negative COVID-19 diagnosis; OB+ = with obesity; OB+ = without obesity.

Supplementary Table 2b. Participant age between C19+ and C19- participants who self-reported to have obesity (OB+) or no obesity (OB-).

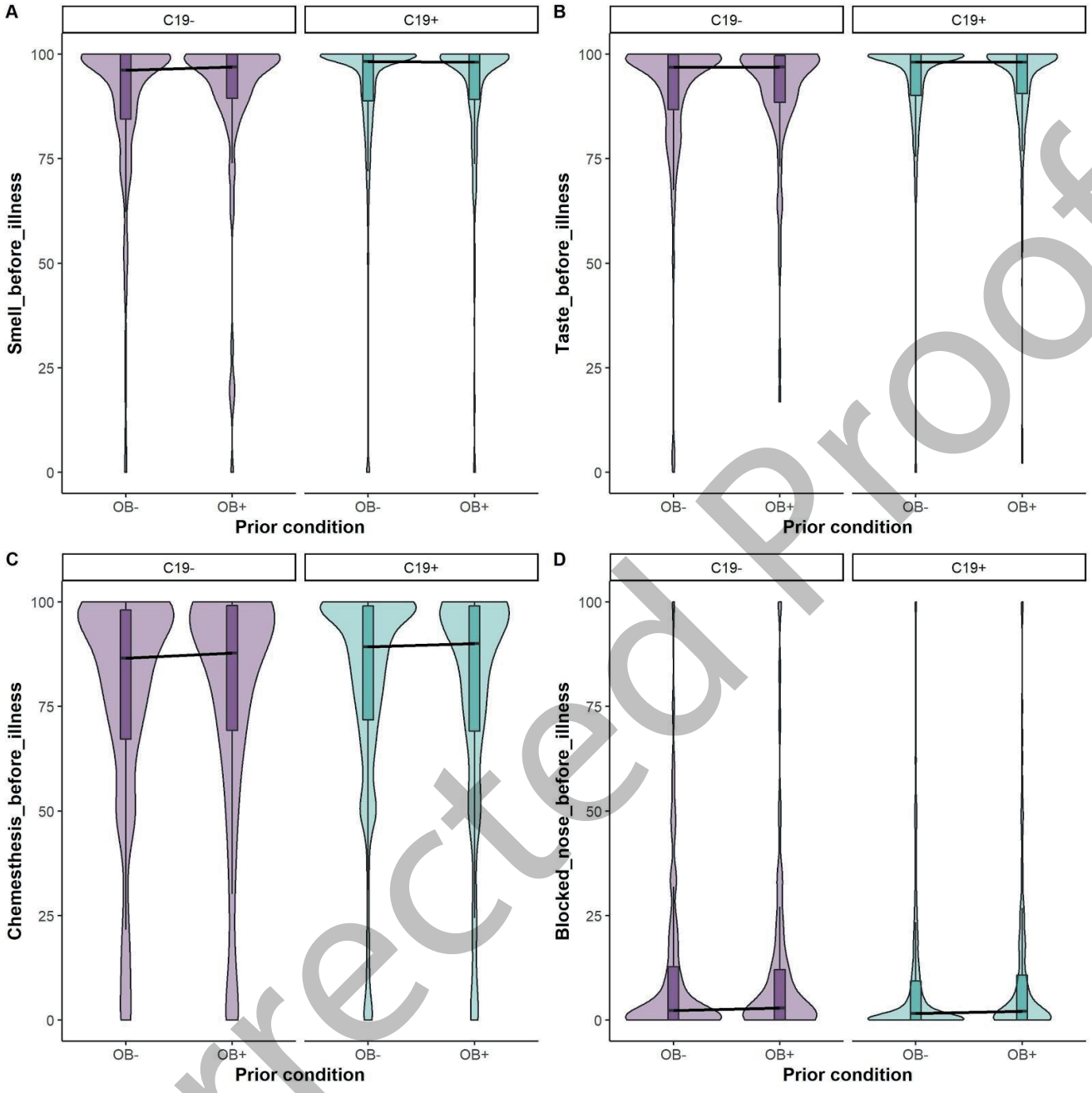
Model (lmBF, on data and with random effect of ID)	Bayes Factor (JZS)	± error%
Age ~ Group+Obesity+Group:Obesity	2.60E+10	1.46E-02
Age ~ Group+Obesity	5.63E+10	1.02E-02
Age ~ Group	7.52E+03	1.62E-12
Age ~ Obesity	3.07E+07	1.48E-16
Effect of Obesity:(X ~ Group+Obesity)/ (X ~ Group)	7.48E+06	1.02E-02
Effect of Group:(X ~ Group+Obesity)/(X ~ Obesity)	1.83E+03	1.02E-02

C19+ = positive COVID-19 diagnosis; C19- = negative COVID-19 diagnosis; OB+ = with obesity; OB+ = without obesity. lmBF = Function to compute Bayes Factors for specific linear models. JZS = JeffreysZellner-Siow priors.

Supplementary Table 3. Chemosensory and nasal obstruction ratings before the respiratory illness in C19+ and C19- participants who self-reported to have obesity (OB+) or no obesity (OB-).

	Model (lmBF, on data and with random effect of ID)	Bayes Factor (JZS)	± error%
Smell	Smell_before_illness ~ Group+Obesity+Age+Group:Obesity	1.46E+00	2.84E-01
	Smell_before_illness ~ Group+Obesity+Age	8.94E+00	1.59E-02
	Smell_before_illness ~ Group+Age	**1.38E+02**	3.37E-02
	Smell_before_illness ~ Obesity+Age	4.14E-01	2.17E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	6.48E-02	3.72E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**2.16E+01**	2.69E-02
Taste	Taste_before_illness ~ Group+Obesity+Age+Group:Obesity	9.37E+00	2.09E-02
	Taste_before_illness ~ Group+Obesity+Age	**8.88E+01**	2.42E-02
	Taste_before_illness ~ Group+Age	**1.23E+03**	2.29E-02
	Taste_before_illness ~ Obesity+Age	2.57E-01	1.18E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	7.24E-02	3.33E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**3.45E+02**	2.69E-02
Chemesthesis	Chemesthesis_before_illness ~ Group+Obesity+Age+Group:Obesity	7.86E-04	2.49E-02
	Chemesthesis_before_illness ~ Group+Obesity+Age	6.99E-03	2.07E-02
	Chemesthesis_before_illness ~ Group+Age	8.86E-02	1.18E-02
	Chemesthesis_before_illness ~ Obesity+Age	4.89E-03	1.45E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	7.89E-02	2.38E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	1.43E+00	2.52E-02
Blocked nose	Blocked_nose_before_illness ~ Group+Obesity+Age+Group:Obesity	6.31E-04	2.20E-02
	Blocked_nose_before_illness ~ Group+Obesity+Age	6.45E-03	3.29E-02
	Blocked_nose_before_illness ~ Group+Age	9.48E-02	1.17E-02
	Blocked_nose_before_illness ~ Obesity+Age	7.64E-03	1.87E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	6.80E-02	3.49E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	8.44E-01	3.79E-02

Ratings were given on 0-100 visual analog scales. In the second column "model", the effect of Obesity is made bold, because that is our most important model. In column "BF" any value for strong evidence (BF>10) for H1 is bold, any value indicative of strong evidence for H0 (no difference) is underlined. lmBF = Function to compute Bayes Factors for specific linear models. JZS = JeffreysZellner-Siow priors.



Supplementary Figure 1. Self-reported smell (A), taste (B), chemesthesis (C), and nasal obstruction (D) ratings before the respiratory illness in C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-). Ratings were given on 0-100 visual analog scales. Nasal obstruction question was formulated as "How blocked was your nose?") before the respiratory illness in C19+ and C19- participants. Each panel presents the mean ratings for chemosensory abilities and nasal blockage. All participants had a diagnosis via a lab test. The thick black horizontal bar connects medians, the shaded bars within each violin indicates the interquartile range. The shaded violin area in purple and blue represents smoothed histogram of data density along the data points.

Supplementary Table 4. Chemosensory and nasal obstruction ratings during the respiratory illness in C19+ and C19- participants who self-reported to have obesity (OB+) or no obesity (OB-).

	Model (lmBF, on data and with random effect of ID)	Bayes Factor (JZS)	± error%
Smell	Smell_during_illness ~ Group+Obesity+Age+Group:Obesity	**1.76E+84**	3.54E-02
	Smell_during_illness ~ Group+Obesity+Age	**1.33E+85**	1.36E-02
	Smell_during_illness ~ Group+Age	**9.23E+85**	1.71E-02
	Smell_during_illness ~ Obesity+Age	**1.11E+10**	1.53E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	1.44E-01	2.19E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**1.20E+75**	2.05E-02
Taste	Taste_during_illness ~ Group+Obesity+Age+Group:Obesity	**5.20E+25**	5.23E-02
	Taste_during_illness ~ Group+Obesity+Age	**4.31E+26**	2.39E-02
	Taste_during_illness ~ Group+Age	**7.57E+27**	9.70E-03
	Taste_during_illness ~ Obesity+Age	2.85E-03	1.58E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	5.70E-02	2.58E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**1.51E+29**	2.87E-02
Chemesthesis	Chemesthesis_during_illness ~ Group+Obesity+Age+Group:Obesity	**1.83E+09**	3.83E-02
	Chemesthesis_during_illness ~ Group+Obesity+Age	**1.85E+10**	1.52E-02
	Chemesthesis_during_illness ~ Group+Age	**2.25E+10**	1.27E-02
	Chemesthesis_during_illness ~ Obesity+Age	**1.09E+05**	4.24E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	8.22E-01	1.98E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**1.69E+05**	4.50E-02
Blocked nose	Blocked_nose_during_illness ~ Group+Obesity+Age+Group:Obesity	**2.31E+07**	5.67E-02
	Blocked_nose_during_illness ~ Group+Obesity+Age	**2.03E+08**	1.52E-02
	Blocked_nose_during_illness ~ Group+Age	**5.97E+07**	3.48E-02
	Blocked_nose_during_illness ~ Obesity+Age	**1.30E+07**	1.11E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	3.40E+00	3.80E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**1.56E+01**	1.88E-02

Ratings were given on 0-100 visual analog scales. In the second column "model", the effect of Obesity is made bold, because that is our most important model. In column "BF" any value for strong evidence (BF>10) for H1 is bold, any value indicative of strong evidence for H0 (no difference) is underlined. lmBF = Function to compute Bayes Factors for specific linear models. JZS = JeffreysZellner-Siow priors.

Supplementary Table 5. Change in chemosensory and nasal obstruction ratings in C19+ (in purple) and C19- (in blue) participants who self-reported to have obesity (OB+) or no obesity (OB-).

	Model (lmBF, on data and with random effect of ID)	Bayes Factor (JZS)	± error%
Smell	Smell_change_illness ~ Group+Obesity+Age+Group:Obesity	**3.75E+69**	3.61E-02
	Smell_change_illness ~ Group+Obesity+Age	**2.51E+70**	1.33E-02
	Smell_change_illness ~ Group+Age	**3.74E+71**	1.86E-02
	Smell_change_illness ~ Obesity+Age	**4.85E+10**	1.44E-01
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	6.71E-02	2.29E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**5.18E+59**	1.45E-01
Taste	Taste_change_illness ~ Group+Obesity+Age+Group:Obesity	**1.39E+29**	3.20E-01
	Taste_change_illness ~ Group+Obesity+Age	**9.56E+29**	1.46E-02
	Taste_change_illness ~ Group+Age	**1.81E+31**	9.62E-03
	Taste_change_illness ~ Obesity+Age	6.55E-03	3.47E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	5.28E-02	1.75E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**1.46E+32**	3.77E-02
Chemesthesis	Chemesthesis_change_illness ~ Group+Obesity+Age+Group:Obesity	**8.90E+07**	2.96E-02
	Chemesthesis_change_illness ~ Group+Obesity+Age	**9.45E+08**	1.51E-02
	Chemesthesis_change_illness ~ Group+Age	**7.48E+09**	2.93E-02
	Chemesthesis_change_illness ~ Obesity+Age	**1.39E+01**	1.68E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	1.26E-01	3.29E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	**6.82E+07**	2.26E-02
Blocked nose	Blocked_nose_change_illness ~ Group+Obesity+Age+Group:Obesity	**1.97E+07**	2.58E-02
	Blocked_nose_change_illness ~ Group+Obesity+Age	**1.76E+08**	3.70E-02
	Blocked_nose_change_illness ~ Group+Age	**1.88E+08**	2.89E-02
	Blocked_nose_change_illness ~ Obesity+Age	**4.64E+08**	1.13E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	9.34E-01	4.70E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	3.79E-01	3.87E-02

Ratings were given on 0-100 visual analog scales. In the second column "model", the effect of Obesity is made bold, because that is our most important model. In column "BF" any value for strong evidence (BF>10) for H1 is bold, any value indicative of strong evidence for H0 (no difference) is underlined. lmBF = Function to compute Bayes Factors for specific linear models. JZS = JeffreysZellner-Siow priors.

Supplementary Table 6. Chemosensory and nasal obstruction ratings post-recovery from respiratory illness in C19+ and C19- participants who self-reported to have obesity (OB+) or no obesity (OB-).

	Model (lmBF, on data and with random effect of ID)	Bayes Factor (JZS)	± error%
Smell	Smell_recovery_illness ~ Group+Obesity+Age+Group:Obesity	1.76E+84	4.32E-02
	Smell_recovery_illness ~ Group+Obesity+Age	1.33E+85	1.71E-02
	Smell_recovery_illness ~ Group+Age	9.23E+85	1.49E-02
	Smell_recovery_illness ~ Obesity+Age	1.11E+10	1.22E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	1.44E-01	2.27E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	1.20E+75	2.10E-02
Taste	Taste_recovery_illness ~ Group+Obesity+Age+Group:Obesity	5.84E-05	1.13E-01
	Taste_recovery_illness ~ Group+Obesity+Age	3.72E-04	2.43E-02
	Taste_recovery_illness ~ Group+Age	3.47E-03	1.55E-02
	Taste_recovery_illness ~ Obesity+Age	5.77E-03	4.08E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	1.07E-01	2.88E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	6.44E-02	4.75E-02
Chemesthesis	Chemesthesis_recovery_illness ~ Group+Obesity+Age+Group:Obesity	2.70E-04	3.63E-02
	Chemesthesis_recovery_illness ~ Group+Obesity+Age	1.81E-03	8.19E-02
	Chemesthesis_recovery_illness ~ Group+Age	1.82E-02	1.17E-02
	Chemesthesis_recovery_illness ~ Obesity+Age	8.32E-03	1.18E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	9.96E-02	8.27E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	2.18E-01	8.27E-02
Blocked nose	Blocked_nose_recovery_illness ~ Group+Obesity+Age+Group:Obesity	6.00E-01	2.19E-02
	Blocked_nose_recovery_illness ~ Group+Obesity+Age	4.57E+00	2.14E-02
	Blocked_nose_recovery_illness ~ Group+Age	**5.59E+01**	1.16E-02
	Blocked_nose_recovery_illness ~ Obesity+Age	**8.56E+01**	2.17E-02
	Effect of Obesity:(X ~ Group+Obesity+Age)/ (X ~ Group+Age)	8.16E-02	2.44E-02
	Effect of Group:(X ~ Group+Obesity+Age)/(X ~ Obesity+Age)	5.33E-02	3.05E-02

Ratings were given on 0-100 visual analog scales. In the second column "model", the effect of Obesity is made bold, because that is our most important model. In column "BF" any value for strong evidence (BF>10) for H1 is bold, any value indicative of strong evidence for H0 (no difference) is underlined. lmBF = Function to compute Bayes Factors for specific linear models. JZS = JeffreysZellner-Siow priors.

Supplementary Table 7. Severity of symptoms and days since onset in C19+ (in purple) and C19- (in blue) participants with obesity (OB+) or without obesity (OB-).

Model (lmBF, on data and with random effect of ID)	Bayes Factor (JZS)	± error%
N symptoms ~ Obesity+Age	**3.01E+03**	1.11E-02
N symptom ~ Obesity	2.95E-01	1.84E-05
Effect of Obesity:(X ~ Obesity+Age)/ (X ~ Age)	**1.02E+04**	1.11E-02
N symptoms ~ Obesity+Age	**2.92E+03**	1.11E-02
N symptom ~ Obesity	2.95E-01	1.84E-05
Effect of Obesity:(X ~ Obesity+Age)/ (X ~ Age)	**9.91E+03**	1.11E-02
Days since onset ~ Obesity+Age	**2.90E+03**	2.49E-02
Days since onset ~ Obesity	2.95E-01	1.84E-05
Effect of Obesity:(X ~ Obesity+Age)/ (X ~ Age)	**1.02E+04**	1.10E-02
Days since onset ~ Obesity+Age	3.23E-01	1.04E-02
Days since onset ~ Obesity	2.65E-01	2.76E-05
Effect of Obesity:(X ~ Obesity+Age)/ (X ~ Age)	1.21E+00	2.86E-02

In the second column "model", the effect of Obesity is made bold, because that is our most important model. In column "BF" any value for strong evidence (BF>10) for H1 is bold, any value indicative of strong evidence for H0 (no difference) is underlined. lmBF = Function to compute Bayes Factors for specific linear models. JZS = JeffreysZellner-Siow priors.

Supplementary Table 8. Symptoms reported by C19+ participants with obesity (OB+) or without obesity (OB-).

Symptom	"Yes"				"No"					
	OB+		OB-		OB+		OB-			
	n	prop	n	prop	n	prop	n	prop	Chi-square	P-value
fever	238	0.55	2190	0.52	195	0.45	2050	0.48	1.60	0.206
dry cough	243	0.56	2089	0.49	190	0.44	2151	0.51	7.11	0.008
cough with mucus	117	0.27	798	0.19	316	0.73	3442	0.81	16.26	0.000
difficulty breathing/ shortness of breath	168	0.39	1352	0.32	265	0.61	2888	0.68	8.24	0.004
chest tightness	176	0.41	1308	0.31	257	0.59	2932	0.69	16.95	0.000
runny nose	177	0.41	1683	0.40	256	0.59	2557	0.60	0.18	0.669
sore throat	172	0.40	1535	0.36	261	0.60	2705	0.64	1.95	0.163
changes in food flavor	361	0.83	3488	0.82	72	0.17	752	0.18	0.26	0.610
changes in smell	386	0.89	3876	0.91	47	0.11	364	0.09	2.25	0.134
loss of appetite	225	0.52	1781	0.42	208	0.48	2459	0.58	15.50	0.000
headache	313	0.72	2994	0.71	120	0.28	1246	0.29	0.45	0.501
muscle aches	257	0.59	2376	0.56	176	0.41	1864	0.44	1.62	0.203
fatigue	338	0.78	3161	0.75	95	0.22	1079	0.25	2.39	0.122
diarrhea	195	0.45	1320	0.31	238	0.55	2920	0.69	34.03	0.000
abdominal pain	80	0.18	641	0.15	353	0.82	3599	0.85	3.14	0.076
nausea	114	0.26	907	0.21	319	0.74	3333	0.79	5.32	0.021

C19+ = positive COVID-19 diagnosis; OB+ = with obesity; OB+ = without obesity.