Recent smell loss is the best predictor of COVID-19: a preregistered, cross-sectional study

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Abstract (247)

Background: COVID-19 has heterogeneous manifestations, though one of the most common symptoms is a sudden loss of smell (anosmia or hyposmia). We investigated whether olfactory loss is a reliable predictor of COVID-19.

Methods: This preregistered, cross-sectional study used a crowdsourced questionnaire in 23 languages to assess symptoms in individuals self-reporting recent respiratory illness. We quantified changes in chemosensory abilities during the course of the respiratory illness using 0-100 visual analog scales (VAS) for participants reporting a positive (C19+; n=4148) or negative (C19-; n=546) COVID-19 laboratory test outcome. Logistic regression models identified singular and cumulative predictors of COVID-19 status and post-COVID-19 olfactory recovery.

Results: Both C19+ and C19- groups exhibited smell loss, but it was significantly larger in C19+ participants (mean±SD, C19+: -82.5±27.2 points; C19-: -59.8±37.7). Smell loss during illness was the best predictor of COVID-19 in both single and cumulative feature models (ROC AUC=0.72), with additional features providing no significant model improvement. VAS ratings of smell loss were more predictive than binary chemosensory yes/no-questions or other cardinal symptoms, such as fever or cough. Olfactory recovery within 40 days was reported for ~50% of participants and was best predicted by time since illness onset.

Conclusions: As smell loss is the best predictor of COVID-19, we developed the ODoR-19 tool, a 0-10 scale to screen for recent olfactory loss. Numeric ratings ≤2 indicate high odds of symptomatic COVID-19 ($10<OR<4$), especially when viral lab tests are impractical or unavailable.

Introduction (334)

The novel coronavirus SARS-CoV-2 is responsible for the worldwide global COVID-19 pandemic that has left a staggering level of morbidity, mortality, and societal and economic disruption in its wake.[1] Several early publications,[2–7] including our own work,[8] indicate that sudden loss of smell and taste are cardinal, early and potentially specific symptoms of COVID-19,[9] including individuals who are otherwise asymptomatic.[10–13] While fever and cough are common symptoms of diverse viral infections, the potential specificity of early smell and taste loss to COVID-19 could make it valuable in screening and diagnosis.

Anosmia and other chemosensory disorders have serious health and quality of life consequences for affected patients. However, there is a general lack of awareness of chemosensory disorders by clinicians and the public, including the association of disorders such as anosmia with upper respiratory infections.[14] In the case of COVID-19 this lack of awareness led to an underappreciation of the role of chemosensory symptoms in the diagnosis of COVID-19. In addition, the impact of smell loss as a clinical consequence of COVID-19 has not been adequately addressed. Thus, there is an urgent need to better define the chemosensory dysfunctions associated with COVID-19 and to determine their relevance as predictors of this disease. It is critical to develop rapid clinical tools to efficiently and effectively integrate chemosensory assessments into COVID-19 screening and treatment protocols. Information on the duration and reversibility of post-COVID-19 chemosensory impairment is also lacking.

We used a combination of quantitative, binary, and categorical self-report measures to determine the chemosensory phenotype, along with other symptoms and characteristics, of COVID-19-positive (C19+) and COVID-19-negative (C19-) individuals who had reported recent symptoms of respiratory illness. We used those results in logistic regression models to identify predictors of COVID-19 and recovery from smell loss. Finally, we propose the **O**lfactory **D**eterminati**o**n **R**ating scale for COVID-19 (ODoR-19), a quick, simple to use, telemedicine-friendly tool to improve the utility of current COVID-19 screening protocols, particularly when access to rapid testing for SARS-CoV-2 is limited.

Methods

Study design (175)

This preregistered,[15] cross-sectional online study was approved by the Office of Research Protections of The Pennsylvania State University (STUDY00014904); it is in accordance with the revised Declaration of Helsinki, and compliant with privacy laws in the U.S.A. and the European Union. The data reported here were collected between April 7 and July 2, 2020 from the Global Consortium for Chemosensory Research (GCCR) core questionnaire,[16] an online crowdsourced survey deployed in 32 languages to measure self-reported smell, taste, and chemesthesis ability and nasal blockage – as well as dozens of other symptoms – in adults with current or recent respiratory illness (**Appendix 1** and https://gcchemosensr.org). The GCCR questionnaire contains questions about symptoms using both binary responses (e.g. **Appendix 1**, Question 9) and visual analog scales (e.g., **Appendix 1**, Question 13). The data reported here include responses in Arabic, Bengali,

Chinese (Simplified and Traditional), Danish, Dutch, English, Farsi, Finnish, French, German, Greek, Hebrew, Hindi, Italian, Japanese, Korean, Norwegian, Portuguese, Russian, Spanish, Swedish, Turkish, and Urdu.

Participants (247)

A convenience sample of 52,334 volunteers accessed the GCCR questionnaire and 25,620 met eligibility criteria (≥19 years old, respiratory illness or suspicion thereof within the past two weeks). After applying preregistered exclusion criteria, 15,747 participants were included in reported analyses (**Figure 1**).

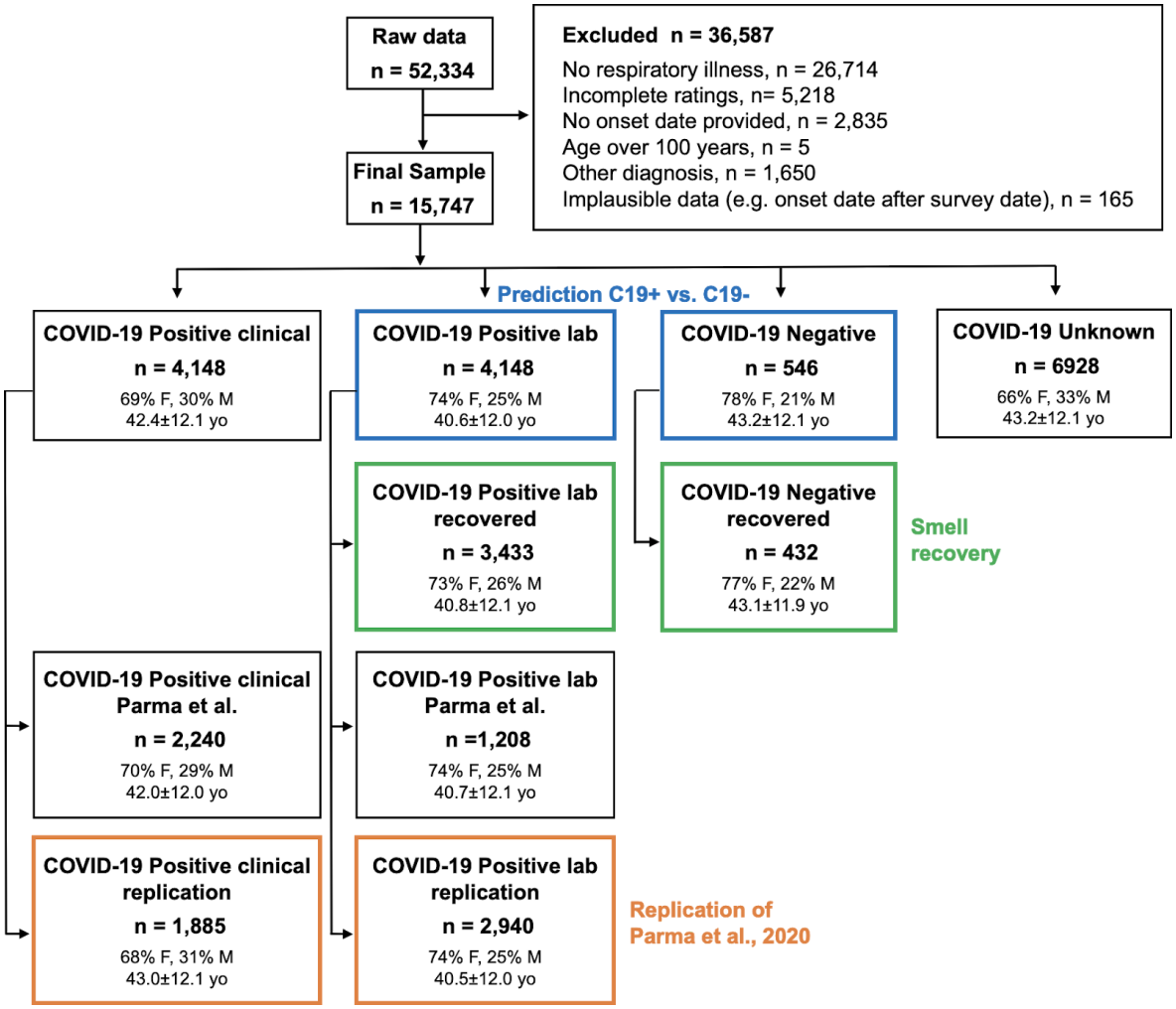


Figure 1. Flow diagram showing the demographics of participants included and excluded in the present analyses. Participants included inr the prediction of COVID-19 status are highlighted in blue. Participants included in the smell recovery models are highlighted in green. Participants included in the replication of our prior work are highlighted in orange. . N = number of participants; yo = age in years; F = female; M = male. Gender percentages do not include <1% of participants who answered “other” or “preferred not to say”.

Based on the reported outcome of a COVID-19 lab test, participants were labeled as either C19+ (positive result) or C19- (negative result). The specific collider bias characterizing this sample (greater fraction of C19+ than C19- participants and greater prevalence of chemosensory disorders across both groups) underestimates the positive correlation between smell loss and COVID-19 (**Figure S1**). Thus, it represents a conservative scenario to test the hypothesis that smell loss reliably predicts COVID-19 status. We also

benchmarked the GCCR dataset to the representative samples collected with the Imperial College London YouGov Covid 19 Behavior Tracker by the international online survey research firm YouGov (henceforth, YouGov; countries shared across datasets: Brazil, Canada, Denmark, Finland, France, Germany, Italy, Mexico, Netherlands, Norway, Spain, Sweden, UK, USA; YouGov: N=8,674, GCCR: N=3,962; data publicly available at https://github.com/YouGov-Data/covid-19-tracker). Benchmarking shows the GCCR sample underestimates the positive correlation between smell loss and COVID-19-positive status (**Figure S1E, Table S1**). The country-wise fraction of C19+ participants is correlated (r~0.5) when responses from the same calendar week are aligned (**Figure S2)**. These findings are in line with other comparisons between crowdsourced versus representative health data,[17] confirming that trends identified in crowdsourced data reasonably approximate population data. Nonetheless, because our cohort is not demographically balanced, it should not be used to estimate prevalence.

Statistical analyses (190)

Statistical analyses were performed in Python 3.7.6 using the pandas,[18] scikit-learn,[19] and statsmodels[20] packages. The data and annotated code will be available on GitHub (http://github.com/GCCR/GCCR002) upon publication. Missing values in prediction models of COVID-19 status and smell recovery were imputed as follows: binary features = 0.5, numeric features = median, categorical variables = "Missing". Responses incompatible with model generalization (e.g., open ended questions) were excluded. A one-hot encoding was applied to all categorical variables to produce binary indicators of category membership. L1-regularized logistic regression (penalty α=1) consistently produced sparse models with comparable cross-validation accuracy and were therefore the prediction test of choice. Model quality was measured using receiver operating characteristic (ROC) area under the curve (AUC). Cross-validation was performed in 100 random splits of 80% training set and 20% test set, and ROC curves are averages over each test set. Note that for single feature models, AUC is independent of most modeling details, including all rank-invariant decisions. To correctly compute p-values for model coefficients, the normalized data were standardized (mean 0, variance 1) and then coefficients back-transformed to normalized form after fitting.

Results

Chemosensory loss associates with COVID-19 (190)

A preregistered replication of our prior study[16] confirmed that reported smell, taste, and chemesthesis abilities drop significantly in both lab tested C19+ participants and those diagnosed by clinical assessment (**Figure S3, Table S2**).

Next, we compared lab tested C19+ and C19- participants. C19+ participants reported a greater loss of smell (C19+: -82.5±27.2 points; C19-: -59.8±37.7 points, p=2.2e-46, extreme evidence of difference: BF_{10}=8.97e+61, **Figure 2A,B, Table S3**), taste (C19+: -71.6±31.8 points; C19-: -55.2±37.5 points, p=6.7e-26, extreme evidence of difference: BF_{10}=6.67e+24, **Figure 2C,D, Table S3**) and chemesthesis ability (C19+: -36.8±37.1 points; C19-: -28.7±37.1 points, p=1.6e-07, extreme evidence of difference: BF_{10}=3182, **Figure 2E,F, Table S3**). However, both groups reported a similar degree of nasal obstruction (**Figure 2G,H, Table S3**). Self-reported changes in smell, taste, and chemesthesis were highly correlated in both groups (C19+: 0.71<r<0.83; C19-: 0.76<r<0.87) and orthogonal to nasal obstruction changes (C19+: r=-0.20; C19-: r=-0.13).

Prediction of COVID-19 status from survey responses (436)

Examining binary (yes/no) reported symptoms, we found COVID-19 has a stronger association with chemosensory symptoms than with non-chemosensory symptoms, including fever, cough, and shortness of breath, which are the cardinal symptoms currently highlighted by the US Centers for Disease Control and Prevention (CDC; **Figure 3A**). Using AUC to assess prediction quality (**Figure 3B**), we found the single survey question most predictive of COVID-19 status was self-reported smell ability during illness, reported on a continuous scale (AUC=0.71). Changes in smell as a result of illness, calculated from the difference between smell ability during and before illness, was similarly predictive (AUC=0.69). Changes in taste ability (assessed via rating) were the next most predictive features (AUC=0.64-0.65) (**Figure 3B**). Models fit to the same data but with shuffled COVID-19 status consistently produced AUC ~0.5 for all features. The most predictive non-chemosensory symptom sore throat, which was negatively associated with COVID-19, was substantially less predictive (AUC=0.58) than the top chemosensory symptoms. Nasal obstruction was not predictive (AUC=0.52). Notably, responses given on a continuous scale were more predictive (AUC=0.71) than binary yes/no responses to parallel questions (e.g., **Appendix 1**, Question 13 versus 14) (AUC=0.60-0.62), likely because a continuous scale contains a greater amount of diagnostic information (**Figure S4**).

Next, we examined which simple multi-feature model would best predict COVID-19 status. As some questions have highly correlated responses, the question most complementary to “Smell during illness” is unlikely to be one that carries redundant information. Adding “Days since onset of respiratory symptoms” (DOS) to “Smell during illness” (Smell Only) produced the largest incremental gain in predictive performance (AUC=0.72, +0.01 versus the Smell Only model) (**Figure 3C**).

We then directly compared the Smell Only+DOS model to other candidate models. The Smell Only+DOS model (AUC=0.72, **Figure 3D**) yielded an equal or higher AUC than the model including the three cardinal CDC symptoms (AUC=0.55) or the full model using 70 features (AUC=0.72). The Smell Only+DOS model exhibits the same AUC as the Smell Only model and strikes a good balance between model parsimony and predictive accuracy for C19+. However, the Smell Only model also offers reasonable sensitivity of 0.85 (at specificity=0.51, cutoff=13 on the 100-point VAS) and/or specificity of 0.75 (at sensitivity=0.51, cutoff=1) as desired. By sharp contrast, fever has a sensitivity of only 0.54 with specificity of 0.49 and dry cough has sensitivity of 0.52 and specificity of 0.46.

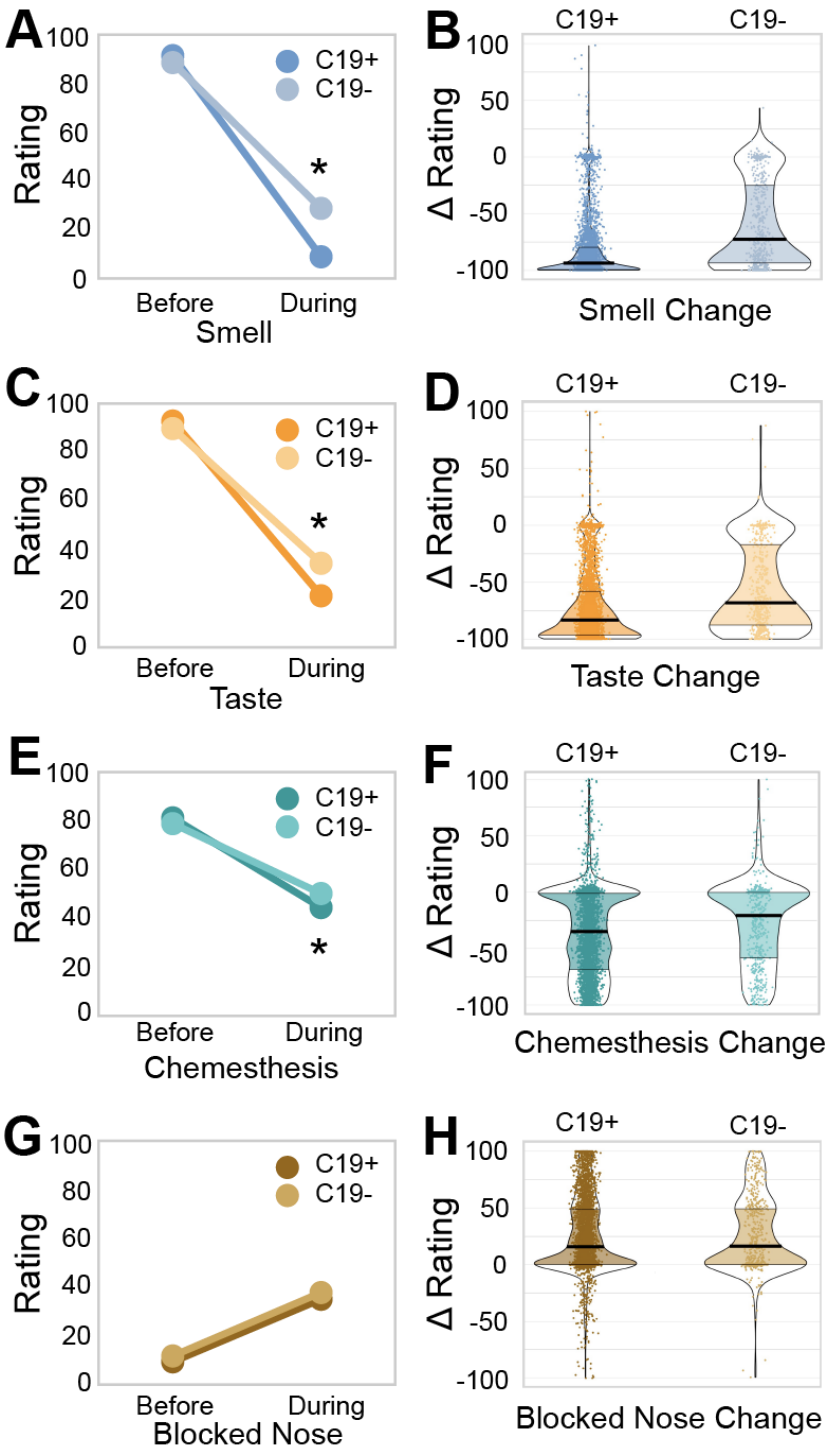


Figure 2. Chemosensory ability and nasal obstruction in C19+ and C19- participants. Self-reported smell (**A,B**), taste (**C,D**), chemesthesis (**E,F**), and nasal obstruction (**G,H;** formulated as "How blocked was your nose?") before and during respiratory illness in C19+ (darker shades) and C19- (lighter shades) participants. Ratings were given on 0-100 visual analog scales. Left panels (A,C,E,G) show mean values. Right panels (B,D,F,H) show distributions of the change scores (during minus before). Thicker sections indicate relatively more subjects (higher density of responses). The thick black horizontal bar indicates the median, the shaded area within each violin indicates the interquartile range. Each dot represents the rating of a single participant.

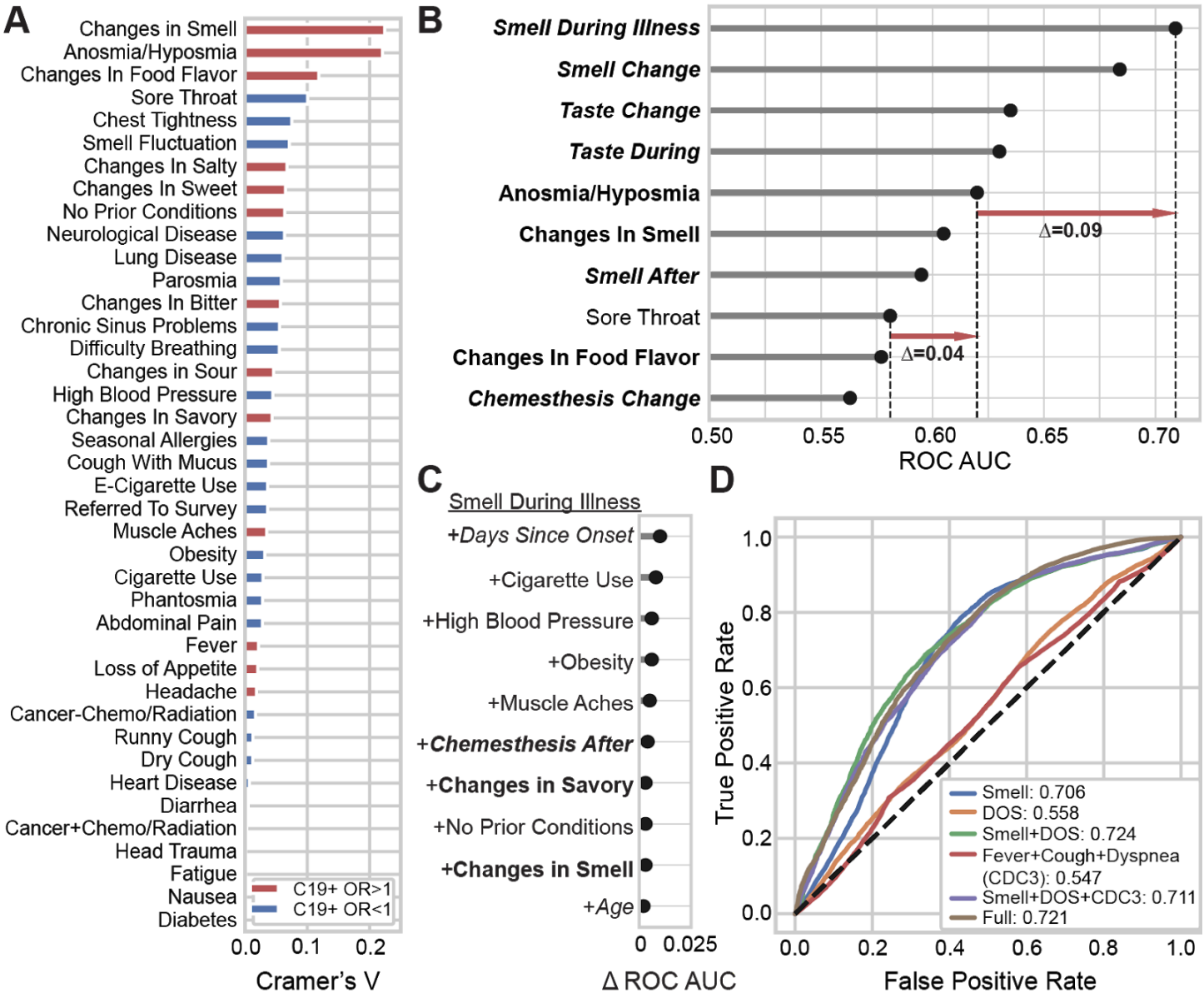


Figure 3. Smell loss is the strongest predictor of COVID-19 status. (**A**) A normalized measure of association (Cramer's V) between binary or categorical responses on COVID-19 status. V=0 reflects no association between the response and COVID-19 status; V=1 reflects a perfect association; V>0.1 is considered a meaningful association. Features in red are positively associated with C19+ (odds ratio > 1); features in blue are negatively associated with C19+ (odds ratio < 1). (**B**) Logistic regression is used to predict COVID-19 status from individual features. Top-10 single features are ranked by performance (cross-validated area under the ROC curve, AUC). Chemosensory-related features (bold) show greater predictive accuracy than non-chemosensory features (non-bold). Responses provided on the numeric scale (italic) were more informative than binary responses (non-italic). Red arrows indicate differences in prediction quality (in AUC) between features. (**C**) Adding features to "Smell During Illness" results in little improvement to the model; only **D**ays Since **O**nset of Respiratory **S**ymptoms (DOS) yields meaningful improvement. (**D**) ROC curves for several models. A model using "Smell during illness" (Smell Only, abbreviated "Smell" in figure) is compared against models containing this feature along with DOS, as well as models including the three cardinal CDC features (fever, dry cough, difficulty breathing). "Full" indicates a regularized model fit using 70 dozen survey features, which achieves prediction accuracy similar to the parsimonious model "Smell Only+DOS".

Recovery from smell loss (312)

In the subset of C19+ participants with full or partial resolution of respiratory symptoms, recovery from smell loss was modest (approximately half the initial average loss). Overall, self-reported post-illness olfactory ability was still lower for C19+ (39.9±34.7) than C19- (52.2±35.2, p=2.8e-11, **Figure S5A**). However, the mean recovery of smell (after illness relative to during illness) was greater for C19+ (30.5±35.7) than C19- (24.6±31.9, p=0.0002, **Figure S5B**). A similar (but smaller) effect of COVID-19 status on recovery was observed for taste (**Figure S5C**, **D**), while little to no association with COVID-19 was observed for recovery of chemesthesis (**Figure S5E, F**) or nasal obstruction (**Figure S5G, H**). When illness-induced change in olfactory function (during versus before illness) and recovery of olfactory function (after versus during illness) were evaluated, we identified three respondent clusters: those who self-reported no loss of smell (Intact Smell), those who reported a loss of smell with recovery (Recovered Smell), and those who reported smell loss without recovery by up to 40 days (Persistent Smell Loss, **Figure 4, Table S4).** Intact smell was reported by only 8.5% of the participants in the C19+ group but by 27.5% in the C19- group. A greater proportion of C19+ participants were included in both the Recovered Smell group (C19+: 40.9%, C19-: 33.3%) and the Persistent Smell Loss group (C19+: 50.7%, C19-: 39.2%; **Figure 4A, B**). C19+ participants in both the Recovered Smell and Persistent Smell Loss clusters reported similar extent of olfactory loss, irrespective of the number of days since respiratory symptom onset. By contrast, the rate of self-reported smell recovery increased over time, with a plateau at 30 days (**Figure 4C**). Finally, DOS was the best predictor (AUC=0.62) between the Persistent Smell Loss and the Recovered Smell groups (**Figure S6A, Table S4**).

Simple screening for COVID-19: the **O**lfactory **D**etermination **R**ating scale in COVID-**19** (ODoR-19) (103)

Our results indicate that a continuous rating of current olfactory function is the single best predictor of COVID-19 and improves the discrimination between C19+ and C19- over a binary (y/n) question on smell loss. We propose here a simple numeric variation of the rating scale (0-10), the ODoR-19, that can be administered in person or via telemedicine to improve early COVID-19 screening for individuals without preexisting smell and/or taste disorders. Responses to the ODoR-19 scale ≤2 indicate high odds of COVID-19 positivity (4<OR<10, **Figure 5D**). An ODoR-19 response of 3 indicates a borderline risk (OR=1.2) of COVID-19.

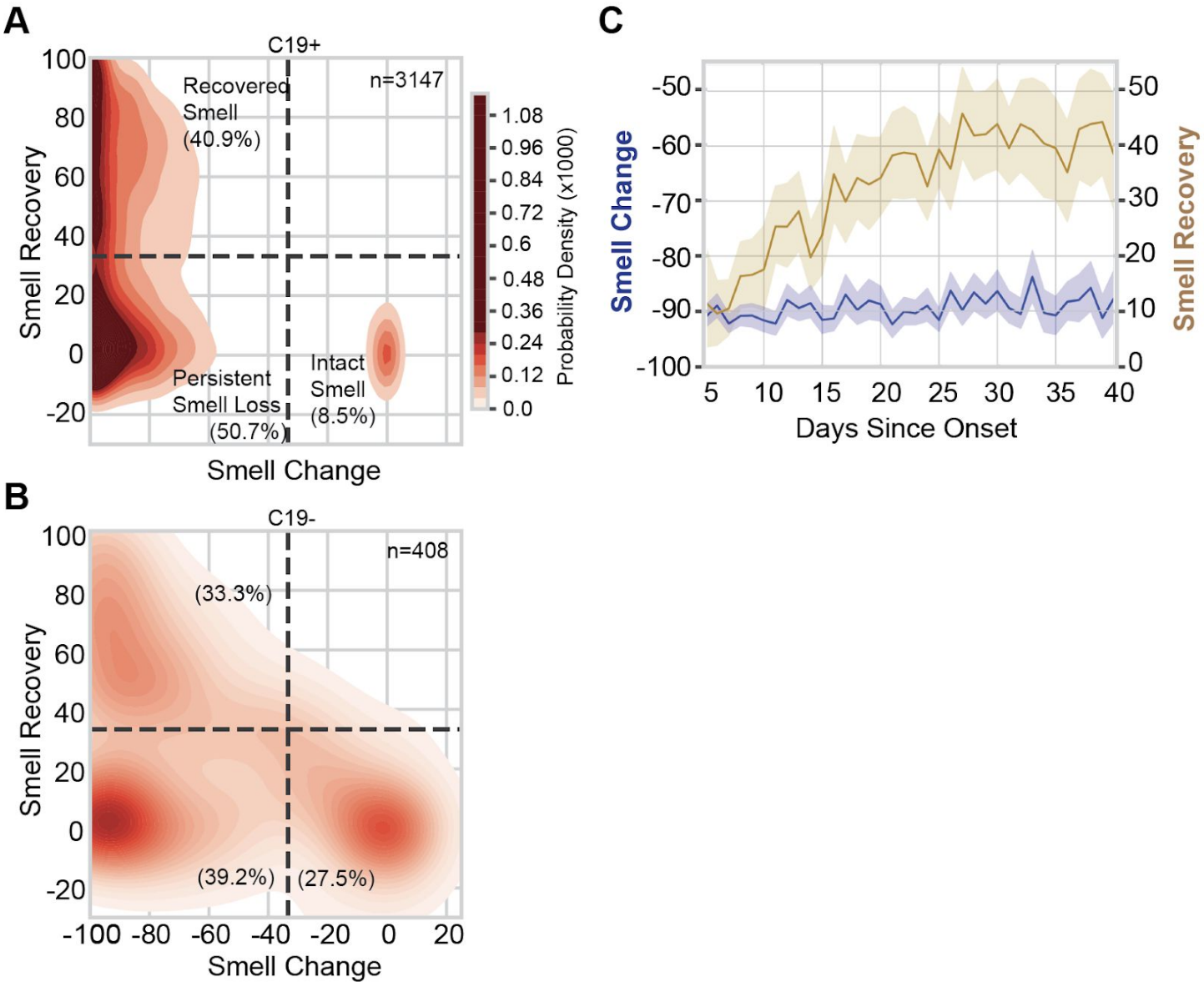


Figure 4: Smell loss, recovery, and time course. (**A, B)** Joint distribution of smell loss (during minus before illness ratings) and smell recovery (after minus during illness ratings) for C19+ (A) and C19- (B) participants. Darker color indicates a higher probability density; the color map is shared between (A) and (B); dashed lines are placed at a third of the way across the rating scale to aid visualization of the clusters. Severe smell loss that is either persistent (lower left) or recovered (upper left) was more common in C19+ than C19-. *n* indicates the number of participants in each panel. % indicates the percentage of participants in each quadrant. (**C**) In C19+ participants who lost their sense of smell (Recovered Smell + Persistent Smell Loss), the degree of smell recovery (right y axis) increased over ~30 days since onset of respiratory symptoms before plateauing; the degree of smell change (left y axis) did not change in that window of observation. Solid lines indicate the mean of the measure, the shaded region indicates the 95% confidence interval.

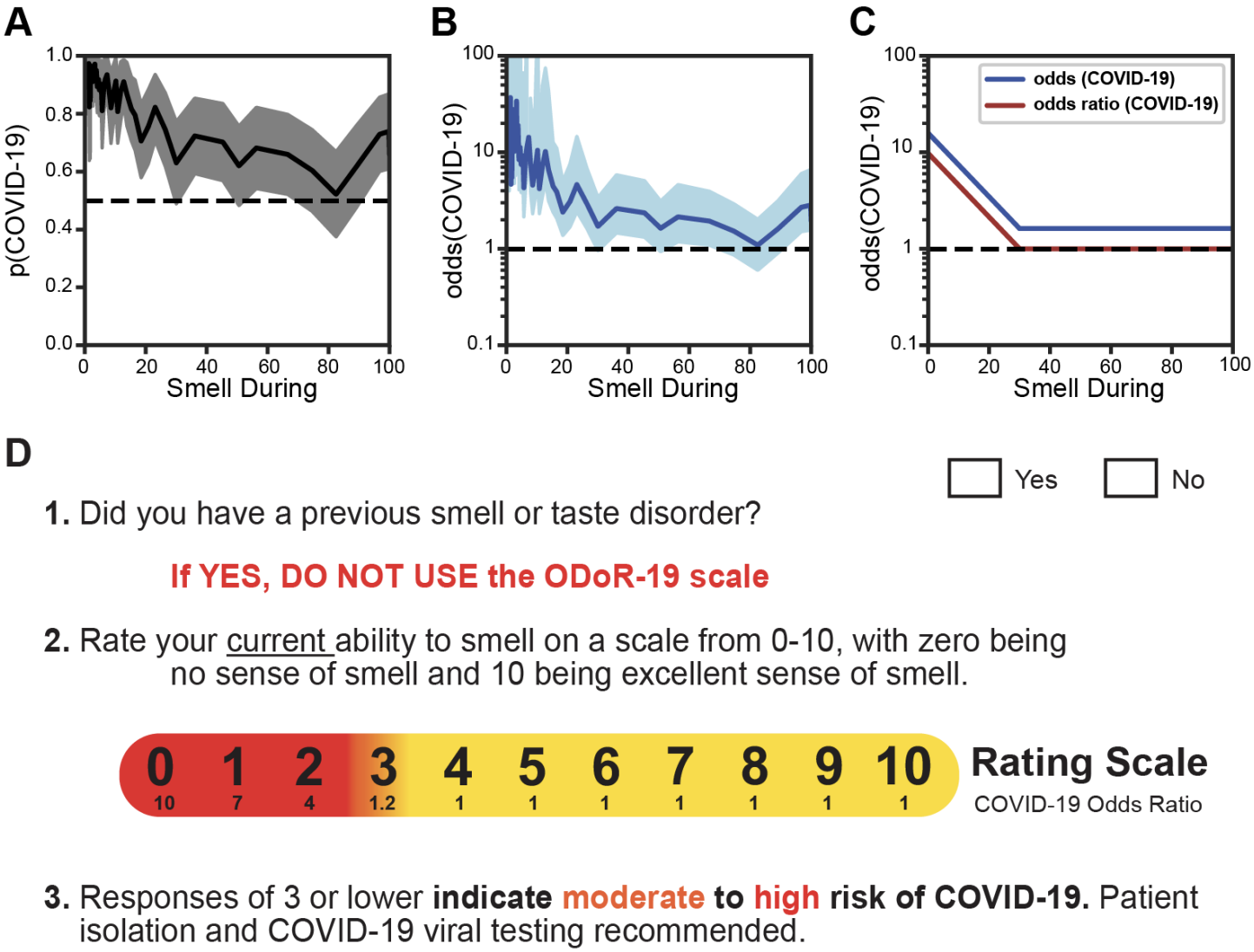


Figure 5. The odds of a COVID-19 diagnosis as a function of olfactory loss. (**A**) The solid line indicates the probability of a COVID-19 diagnosis as a function of "Smell during illness" ratings. The shaded region indicates the 95% confidence interval. (**B**) The solid line expresses the probability of a COVID-19+ diagnosis as a function of "Smell during illness" in odds (p/(1-p)); it is shown on a logarithmic scale. The shaded region indicates the 95% confidence interval. (**C**) Stylized depiction of change in the odds of a COVID-19 diagnosis and of the odds ratio. (**D**) The ODoR-19 screening tool. After healthcare providers or contact tracers have excluded previous smell and/or taste disorders such as those resulting from head trauma, chronic rhinosinusitis, or previous viral illness, the patient can be asked to rate their current ability to smell on a scale from 0-10, with 0 being no sense of smell and 10 being excellent sense of smell. If the patient reports a value below or equal to 3, there is a high (red) or moderate (orange) probability that the patient has COVID-19. Values in yellow (ratings above 3) cannot rule out COVID-19.

Discussion (706)

Self-reported smell loss was present in both C19+ and C19- participants, but more common in the C19+ group. The use of a VAS to assess olfactory loss better predicted COVID-19 status than using a binary (yes/no) question. We found that the best predictor of COVID-19-associated smell recovery, within the time frame captured by the survey (~40 days), was days since onset of COVID-19.

The SARS-CoV-2 pandemic requires healthcare providers and contact tracers to quickly and reliably assess an individual's COVID-19 risk and is often performed remotely. Thus, reliable screening tools are critical to assess a person's likelihood of having COVID-19 and to justify self-quarantine and/or testing recommendations. Indeed, some reports suggest that COVID-19-associated smell loss might be an indicator of disease severity.[2,21] Current screening measures and symptom criteria (e.g., travel history, fever, dry cough) are less specific than severe olfactory loss. Indeed, the value of our ODoR-19 tool lies in the high specificity of values ≤2 for indicating COVID-19 positivity, therefore representing a valuable addition to the current repertoire of COVID-19 screening tools.

Our online survey and sampling methodology likely selected participants with a heightened interest in smell and taste and/or their disturbances. This could be viewed as a limitation since the C19- group also showed chemosensory loss. However, the finding of a difference between groups in a sample with a higher barrier for discriminating between C19+ and C19- supports the robustness of this tool when used in a typical clinical population.

Our results suggest that chemosensory impairment has strong COVID-19 predictive value when access to viral testing is limited or absent. While it is important to recognize that the self-selection bias of our sample could limit the generalizability of these results, our collider bias (**Figure S3**) suggests that our findings are likely conservative estimates. As with any self-report measure, veracity of self-reports cannot be guaranteed, however the ability to screen individuals in real-time should outweigh this potential confound[22]. Finally, while objective smell tests are the gold standard for assessing olfactory function,[23,24] they are costly, time consuming to administer, and can require in-person interactions with a potentially infectious patient.[24,25] By contrast, the ODoR-19 is free, quick, and can be administered in person or remotely. We cannot exclude that our C19- sample contains COVID-19 false negatives.[26] However, self-reported smell during illness distinguishes between C19+ and C19-, but not between randomly shuffled C19+ cases, suggesting that the difference between C19+ and C19-, even in a sample with over-represented chemosensory dysfunction, is substantial and can be captured via self-report. Those who receive a negative outcome from a COVID-19 viral test, yet report significant idiopathic smell loss, should be considered as high-priority candidates for COVID-19 re-testing.

Approximately half of the participants in the C19+ group recovered their sense of smell within 40 days from the onset of respiratory symptoms. This finding suggests the presence of at least two subgroups of patients: one that recovers quickly (<40 days, 40.9%) and another that may present a more variable time course of recovery (50.7%). Since these data are collected before the full recovery of all symptoms, we cannot offer a complete picture of recovery from olfactory loss in COVID-19-positive individuals, but they align with other early reports.[27]The COVID-19 pandemic will greatly increase the number of patients suffering from anosmia and other chemosensory disorders,[28] conditions that significantly affect quality of life,[29,30] dietary behavior,[31] cardiovascular health[32], and mental health.[33,34] Thus, it is necessary to prepare healthcare providers to address the long-term needs of these patients.

Based on our results, we propose the use of the ODoR-19 tool, a quick, free, and effective smell-based screening method for COVID-19. This 0-10 rating scale accurately predicts COVID-19 in individuals without pre-existing smell and taste disorders (e.g., from head trauma, chronic rhinosinusitis[35]). ODoR-19 combines the utility of a continuous scale with the ease and speed needed for a screening tool. ODoR-19 is safe for remote administration during an illness with high viral spread and can precede and complement viral testing, especially when lab tests are unavailable, impractical or cost prohibitive. This tool will improve screening for patients with limited or no access to medical care around the globe.

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Conflict of interest

Richard C. Gerkin is an advisor for Climax Foods, Equity Compensation (RCG); John E. Hayes has received speaker honoraria, consulting fees, and/or travel expenses from numerous organizations, including federal agencies, universities, nonprofit organizations, trade groups, and for-profit corporations, to present data on taste biology, perception and consumer behavior. Additionally, the Sensory Evaluation Center at Penn State routinely conducts product tests for industrial clients to facilitate experiential learning for students. Since 2018 Thomas Hummel did research together with and received funding from Sony, Stuttgart, Germany; Smell and Taste Lab, Geneva, Switzerland; Takasago, Paris, France: aspuraclip, Berlin, Germany. Christine E Kelly is the founder of AbScent, a charity registered in England and Wales, No. 1183468. Christophe Laudamiel has received fundings from scent related institutions and corporations, however for work totally unrelated to the field of the present study.

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Supplementary Material

Collider bias results in underestimation of an association between smell loss and COVID-19

As others have noted,[36] collider bias, resulting from selection or conditioning on variables involved in the analysis, may result in the distorted association between COVID-19 and candidate symptoms or patient attributes. In the present sample, it is likely that we have selected for both a higher probability of COVID-19 and a higher probability of smell and taste disorders than the population at large. However, rather than leading to an overestimation of the positive correlation between smell loss and COVID-19, collider bias is expected to lead to an underestimation of this correlation (**Figure S1)**. If we consider the hypothetical scenario in which there is no association between smell loss and COVID-19 status in the general population, we would expect a distribution similar to that depicted in **Figure S1A**, where the correlation between the likelihood of smell change and likelihood of COVID-19 is r = 0. Based on our recruitment method, we expect that the participants who elected to complete the GCCR core questionnaire were likely to have COVID-19, smell loss, or both. We can simulate participant selection to reflect this hypothesis by censoring subjects which do not meet a fixed sum of smell loss and COVID-19 probabilities (i.e., the red dots are excluded from the calculation of the correlation; **Figure S1B**). As a result, the estimated correlation between smell loss and COVID-19 status originating from a population with r = 0 would be negative (**Figure S1B)**. A similar scenario would manifest if the association between smell loss and COVID-19 status in the general population is positive (**Figure S1C**)**.** Again, simulating the removal of participants with low likelihood of having COVID-19 and/or reporting smell loss would result in a bias of the estimated correlation towards more negative values (**Figure S1D**). This collider bias indicates that the positive correlation between smell loss and C19+ is underestimated in the present sample. Therefore, our analyses represent a conservative scenario for the prediction of C19+ and C19- based on chemosensory alterations.

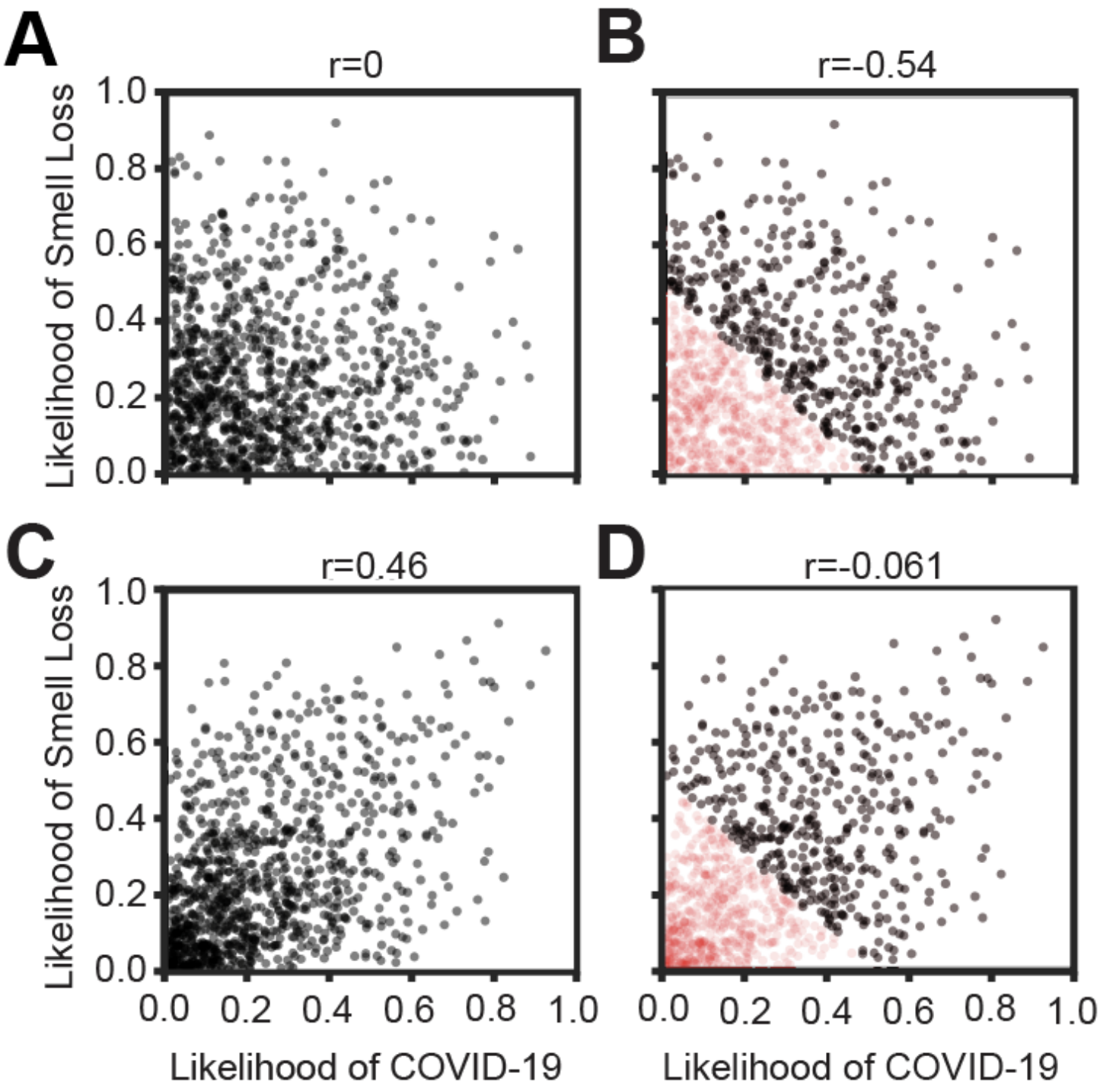


Figure S1. Collider bias leads to underestimation of the positive correlation between smell loss and COVID-19-positive status. **(A)** Hypothetical scenario depicting no relationship between smell change and likelihood of COVID-19 positive status. Black dots indicate individual potential subjects, each of whom has a latent likelihood of COVID-19 and of smell loss. **(B)** Hypothetical scenario depicting the emergence of a negative correlation between smell change and likelihood of COVID-19 positive status following a baseline lack of correlation, if participants with greater smell loss and/or COVID-19 positive are preferentially included in the sample. Red dots indicate subjects not observed due to this selection bias; subjects observed remain in black. **(C)** Hypothetical scenario depicting a positive relationship between smell change and likelihood of COVID-19 positive status. **(D)** Hypothetical scenario depicting the emergence of a negative correlation between smell change and likelihood of COVID-19 positive status following a positive baseline correlation, if participants with greater smell loss and/or COVID-19 positive are preferentially included in the sample.

Table S1. Comparison with the representative YouGov database shows that the GCCR sample underestimates the positive correlation between smell loss and COVID-19 positive status.

	N	p(C19+)	OR (C19+ vs C19-)	OR (C19+ vs Not Tested)	OR (C19- vs Not Tested)	p(Smell Loss | C19+)
Global	109395	0.01	5.96	49.66	8.33	0.33
Brazil	4167	0.01	8.39	33.87	4.04	0.47
Canada	5524	0	7.76	71.55	9.22	0.35
Denmark	5839	0	9.35	77.83	8.32	0.33
Finland	5927	0	1.85	27.84	15.07	0.21
France	9820	0	7	57.87	8.27	0.29
Germany	9468	0	4.56	94.24	20.66	0.37
Italy	9790	0	9.17	50.81	5.54	0.22
Mexico	5840	0	8.91	27.61	3.1	0.21
Netherlands	3822	0.01	2.73	16.14	5.92	0.3
Norway	5794	0.01	5.82	51.2	8.8	0.32
Spain	9789	0	5.81	43.48	7.48	0.33
Sweden	9741	0	3.69	38.02	10.32	0.35
United Kingdom	13565	0	23.14	107.75	4.66	0.5
United States	10309	0.01	4.61	54.65	11.86	0.34

Column 1 includes the list of countries available in the YouGov database. Column 2 indicates the number of participants over the history of their survey up to July 3, 2020. Minimum N=1000 per time point. Column 3 reports the fraction of the participants who reported C19+. Columns 4-6 report the odds ratios using Smell Loss for either C19+ vs. C19- (Column 4, and as reported in Figure 5 based on the data of the GCCR survey), for C19+ vs. untested individuals (Column 5) and C19- vs. untested individuals (Column 6). Untested individuals in YouGov's survey are those who did not report to be sick, but were contacted as representative participants of a country. The first row indicates the Global average (across countries) weighted by sample size. The global odds ratio for Smell loss calculated from a binary question for the group C19+ vs. C19- is 6.72, which is greater than what we identify in the GCCR survey (OR for changes in smell (binary question) = 4.89). The OR for C19+ vs. untested individuals is 58, and lowers to 11 for C19-. This confirms that smell loss is also associated with other etiologies, but is not nearly as prevalent as in participants with C19+. The last column indicates the probability of having smell loss due to COVID-19 in a representative sample.

How representative is the GCCR sample?

As with most COVID-19 studies,[19] the sample studied here is not representative of the general population. To better understand the extent to which this is the case, we computed a cross-correlation between GCCR and YouGov data.[37] These data were aligned by weighting YouGov samples to achieve an identical survey date

distribution to the GCCR samples. Specifically, GCCR survey dates were converted to a YouGov "week number" because YouGov surveys only weekly. The distribution of week numbers was computed for each country in the GCCR data. The YouGov data for the same country was then weighted by week number to match the corresponding GCCR distribution for that country. So, for example, if a country had 10 GCCR survey responses in week 1 of the YouGov survey period, and 30 in week 2 of that period, then the YouGov data in week 1 would be weighted at 25% and in the YouGov data in week 2 at 75%. This procedure was applied independently for each country, and the weights were used to compute a weighted mean COVID-19-positive rate for each country from the YouGov data. This was then directly compared against the raw COVID-19-positive rate for each country in the GCCR data. A lag (x-axis value in **Figure S2**) of 0 exactly reflects the above description. Other values of the lag indicate that the alignment was shifted: for example, a lag of one week means that the YouGov data would be weighted 25/75 towards weeks 2 and 3, instead of weeks 1 and 2. Under the hypothesis that the COVID-19-positive rates in the two surveys are related, but may have different temporal dynamics, changing the lag allows these dynamics to be estimated. **Figure S2** depicts the country-wise correlation in participants with a positive COVID-19 test results (C19+) fraction between the two datasets, as a function of the lag between GCCR survey date and YouGov survey date. The country-wise C19+ fraction is correlated (r ~ 0.5) when responses from the same calendar week are aligned, but GCCR COVID-19 status also anticipates YouGov status by up to 4 weeks (r~0.4).

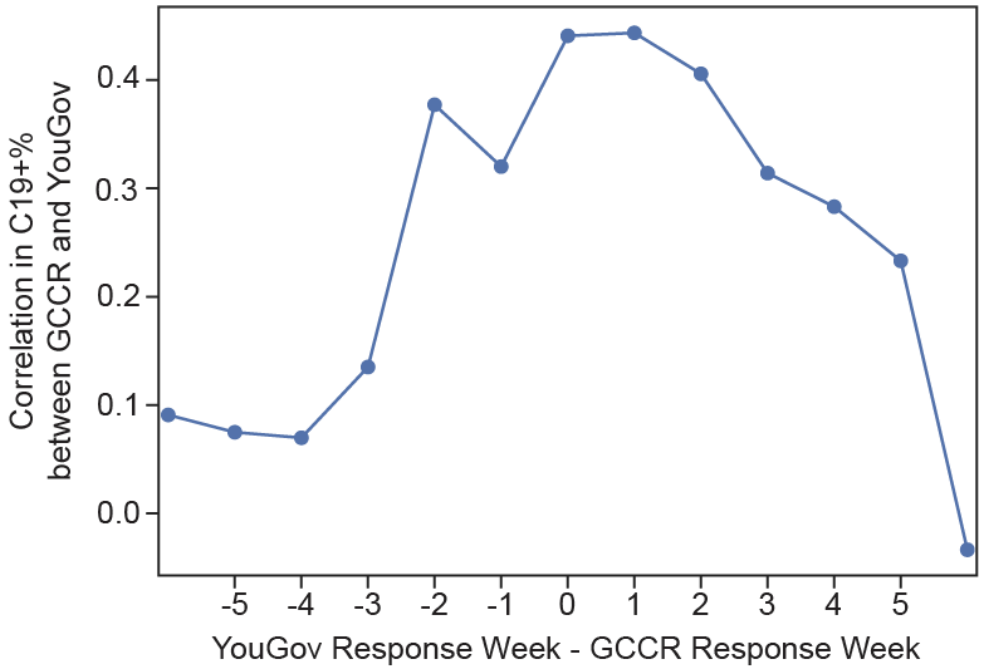


Figure S2. COVID-19 status in the GCCR cohort is correlated with – and in advance of – a representative YouGov sample.

Sample description

Based on responses to question 7 of the GCCR survey ("Have you been diagnosed with COVID-19?", **Appendix 1**), participants can be split into six groups (see **Figure 1**). Participants who responded with Option 2 ("Yes – diagnosed with viral swab") or 3 ("Yes – diagnosed with another lab test") were classified as C19+; participants who responded with option 5 ("No – I had a negative test, but I have symptoms") were classified as symptomatic C19-; participants who responded with option 4 ("No – I was not diagnosed, but I have symptoms") were classified as C19 Unknown; participants who responded with option 6 ("No – I do not have any symptoms"), with option 7 ("Don't know"), or with option 8 ("Other") were classified as undefinable and excluded from the final analyses. To replicate our previous findings,[8] we first compared individuals newly included in the GCCR dataset (responses from 14 May to 2 July, 2020, replication sample in **Figure 1**) with COVID-19 who were lab tested and those who were diagnosed by a clinician based on the self-reported quantitative changes in smell, taste, chemesthesis, and nasal obstruction (**Figure S3)**. Participants with lab-test confirmed C19+ did show slightly greater chemosensory deficits than did those diagnosed with C19+ clinically, but the difference was not clinically meaningful (smell: 4.4±28.6, p=2.7e-13) (**Figure S3, Table S2**). We then focused our descriptive and predictive analyses of participants who received a positive (C19+) or a negative (C19-) lab test for COVID-19. We also computed descriptive and predictive analysis for the C19+ subsample who reported partial or full signs of recovery from their recent respiratory illness. Lastly, the unknown group was originally hypothesized as similar to the C19- group. Yet, the ratings of smell ability during illness suggest that the majority of these participants has a smell profile closer to C19+ than C19- (**Figure S4**). To maximize the validity of the COVID-19 diagnosis in our sample, we therefore excluded the C19 Unknown group from further analyses.

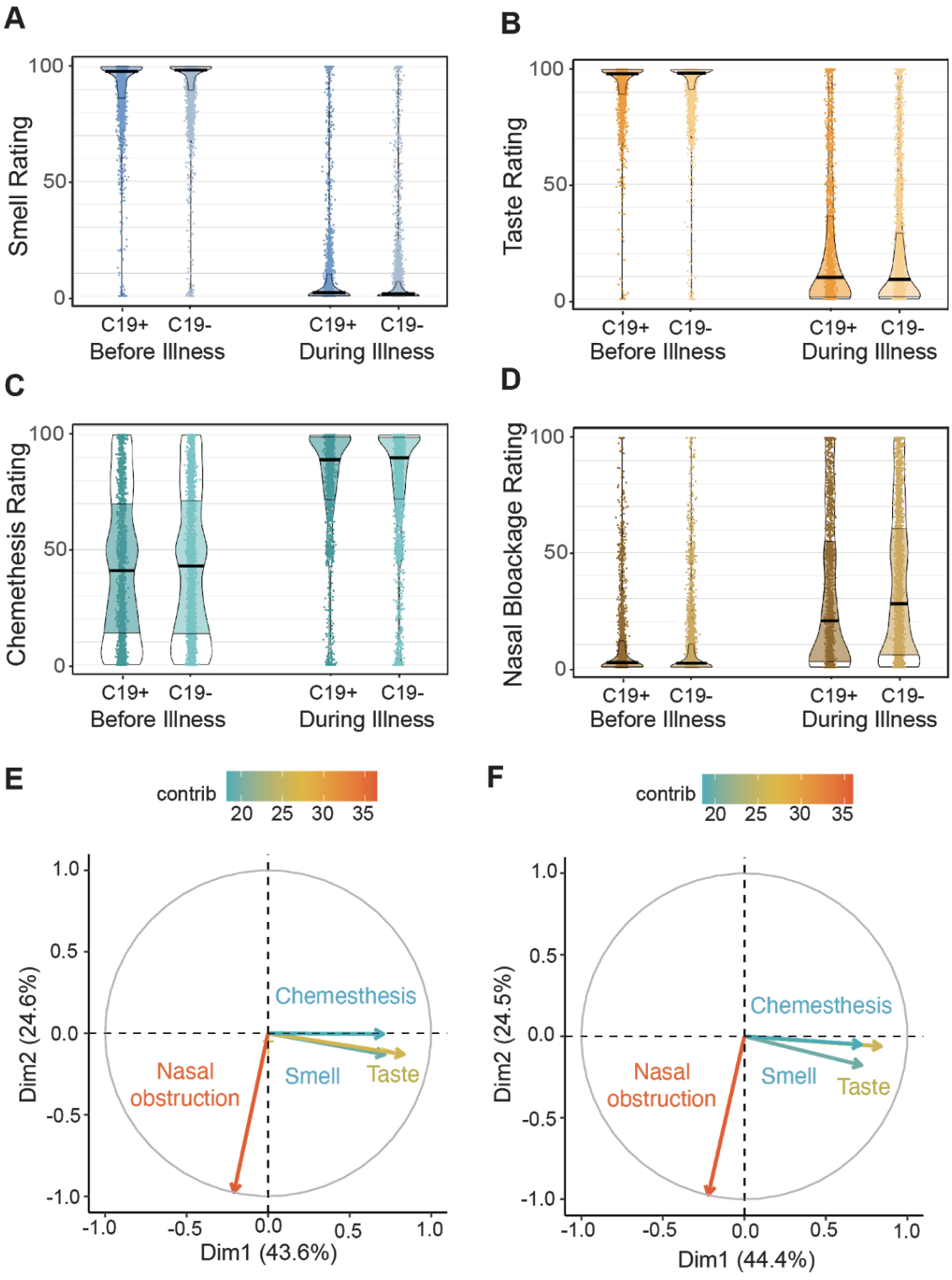


Figure S3. This figure describes a pre-registered replication of Parma et al, 2020 and includes only new data collected between May 14th and July 2nd 2020 via the GCCR survey. *(***A-D**) Changes in smell (A), taste (B), chemesthesis (C) and nasal blockage (D) during versus before in COVID-19-positive individuals (Groups 1, 2 and 3, see Figure 1). All subjects had a COVID-19-postive status either via lab test (darker shades) or via clinical assessment (lighter shades). (**E-F**) Principal component analysis shows that smell, taste, and chemesthesis changes in both the lab test (E) and clinical assessment (F) groups) were orthogonal to blocked nose changes, i.e., the three chemosensory changes were highly correlated across subjects whereas blocked nose changes were mostly uncorrelated.

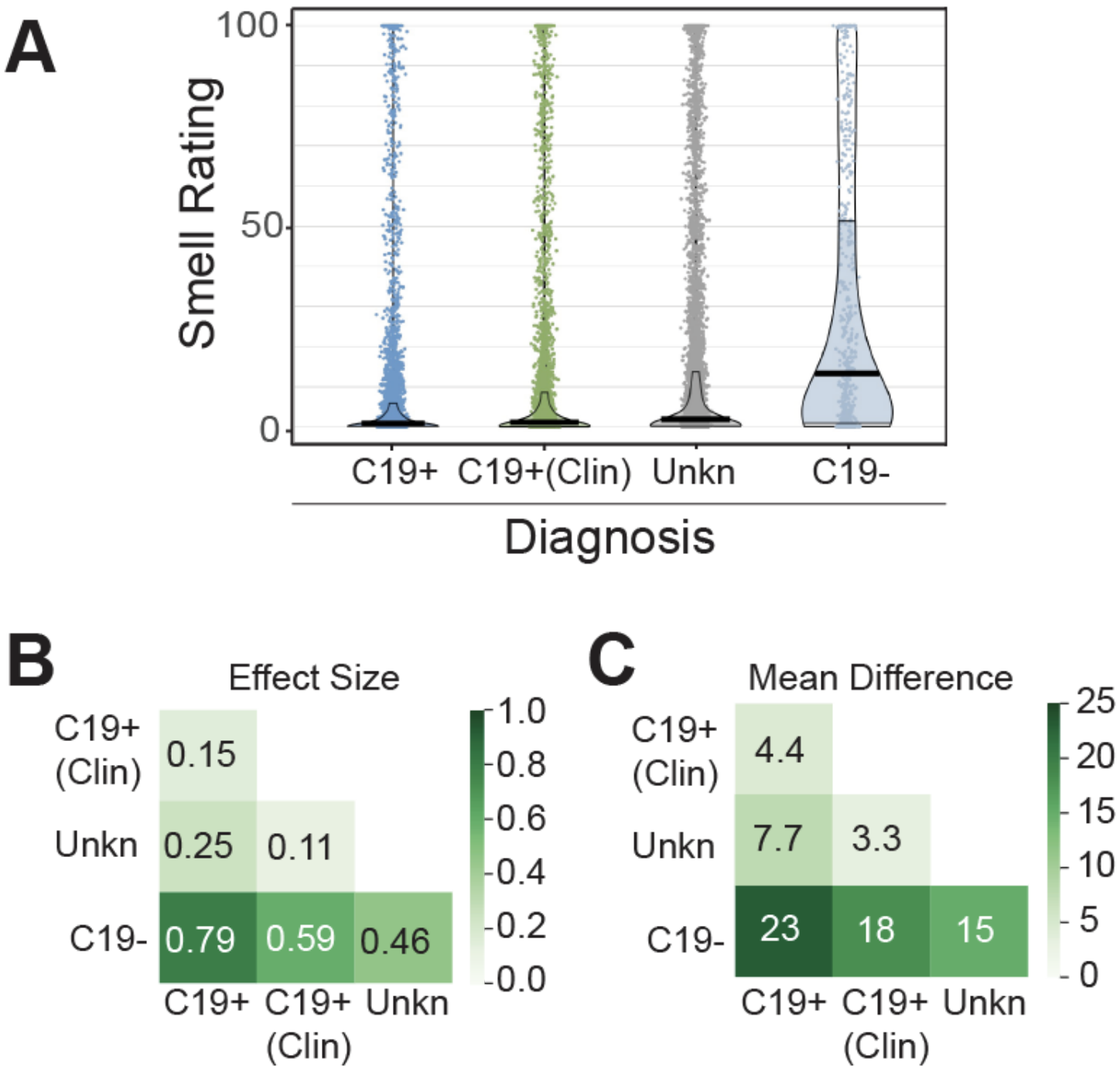


Figure S4. (**A**) Self-reported smell change and comparison of smell change between four diagnosis groups: Positive COVID-19 lab-test (C19+), positive COVID-19 clinical assessment (C19+ (Clin)), COVID-19 Unknown (Unkn; lack of clinical and lab test diagnosis, but report symptomats), and negative COVID-19 lab test (C19-). Solid horizontal lines reflect the median; dashed lines reflect the quartiles. (**B, C**) Differences between groups, in terms of (B) effect size (Cohen's D) and (C) means (on a 0-100 scale).

Replication of previous analyses

The replication of Parma et al.[8] used the same Bayesian linear regression approach with Cauchy prior [r = sqrt(2)/2]. This approach is appropriate for estimating the strength of the evidence in support of the null hypothesis: the clinical assessment and the lab test C19+ groups show similar smell, taste, chemesthesis and nasal obstruction changes before vs. during the illness. The interpretation of the Bayes factors BF follows the classification scheme proposed by Lee and Wagenmakers[38] and adjusted from Jeffreys[39], which considers BF > 3 as moderate evidence, BF > 10 as strong evidence, BF > 30 as very strong evidence and BF > 100 as extreme evidence for H_0 or H_1.

Table S2. Differences between lab-tested and clinically-diagnosed COVID-19-positive participants on changes in smell, taste, chemesthesis and nasal blockage.

	Smell Change	Taste Change	Chemesthesis Change	Change in Nasal Blockage
Δ	-4.4	-3.4	0.37	3.9
σ	0	0	37	33
seΔ	-0.048	-0.037	0.0041	0.043
D	-0.15	-0.1	0.01	0.12
p	2.70E-13	2.00E-06	0.38	4.00E-09

Change means the rating "before" illness minus the rating "during" illness on the 101-point visual-analog scale. Δ indicates the mean difference in change between lab-test and clinically-diagnosed COVID-19-positive subjects. *D* indicates effect size (Cohen's D). *p* indicates p-value from a Mann-Whitney U-test. In contrast to the prediction of the pre-registration, we found statistically significant differences between groups. However, the effect sizes are small and thus unlikely to be of practical importance.

Chemosensory characterization of C19+ and C19-

We asked how accurately COVID-19 status could be predicted from the survey responses. The data matrix had strictly non-negative values and was normalized (column-wise min=0, max=1) to apply regularization in an equitable fashion across features and give regression coefficients the same interpretation for each feature. Compared with the main text, similar results (but with non-zero coefficients for additional, likely spurious features) were obtained for smaller values of α, and inferior results for larger ones (which contained fewer or no non-zero coefficients). Quantitatively similar AUC values were obtained for other models predicting COVID-19 status using multiple features including ridge regression and random forest, but L1-regularized logistic regression consistently produced sparser models with comparable cross-validation accuracy. Each logistic regression model included an intercept term and one or more normalized features. Each model attempted to predict, using the value of the response to a single question (and an additive constant), whether a subject reported a C19+ or C19- status. Each ROC curve -- constructed using predictions on holdout test sets and averaged over these test sets -- summarizes the tradeoff between sensitivity (fraction of C19+ cases

correctly identified) and specificity (fraction of predicted C19+ cases who were actually C19+) as the threshold value for the predictor is varied.

Value of using a scale rather than a binary response to detect C19+

We quantified the information entropy for each survey question used the following standard equation: I=sum_i(-p_i*log2(p_i)). Re-binning to mimic new scales was achieved by dividing response values by a constant and rounding to the nearest integer. Relative mutual information was calculated by computing the mutual information based on the following standard equation: MI=sum_i_j(p_i_j*log2(p_ij/(p_i*p_j)) between each feature and the C19+/C19- status, and then dividing by the entropy available from that same status distribution. Results indicate that soliciting responses on either a continuous 100-point scale or a downsampled 10-point numeric version of the scale is more informative about symptoms themselves and about COVID-19 status (given the symptoms) than soliciting binary responses (**Figure S5**).

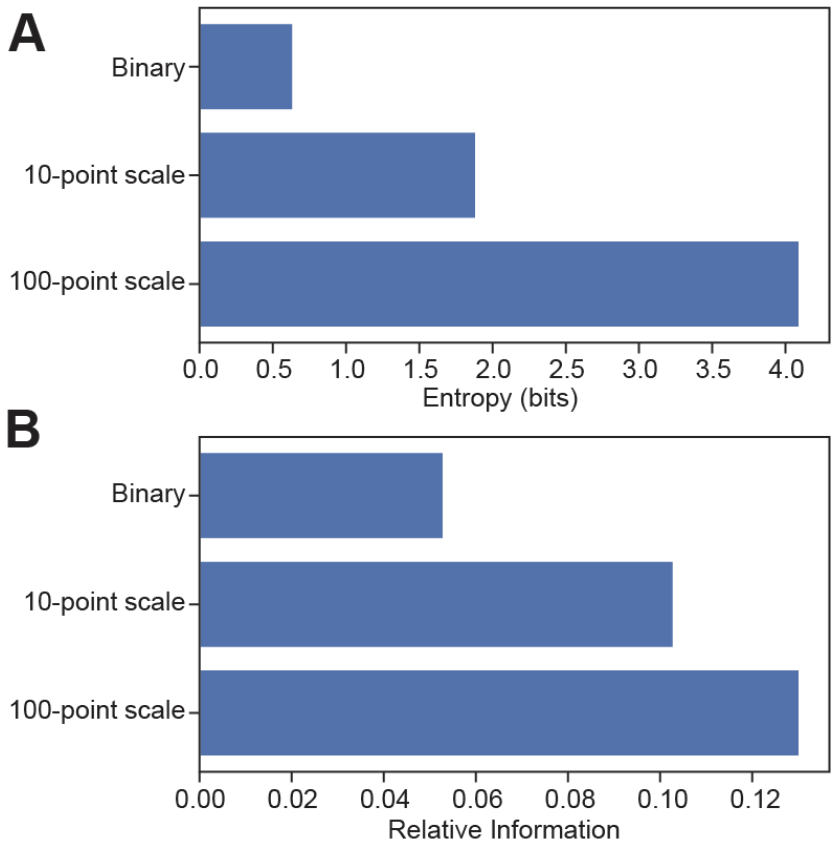


Figure S5. (A) Relative information available from the distribution of responses to the two primary "Smell" survey questions. *Binary* refers to the yes/no question about symptomatic smell loss. A relative information of 1 would correspond to a question whose response is perfectly informative about COVID-19 status. By contrast, a similar question asked on a numeric scale (0-100, the original scale; or a hypothetical 10-point scale obtained by rounding responses) contains substantially more information due to the resolution of the scale. A 10-point scale may be familiar from clinical self-reports of pain. (**B)** ROC Area-under-the-curve (AUC) is also higher for the full numeric scale or the hypothetical 10-point scale than for the binary question.

Prediction of recovery from COVID-19-associated smell loss

We applied the same predictive modeling framework used in **Figure 4** to try to predict smell recovery in C19+ participants. In other words, we asked which survey responses predicted that a subject would fall into the Recovered Smell rather than the Persistent Smell Loss cluster, given both smell loss during the disease and C19+ status. The only predictive feature of any practical significance was “Days Since Onset” of respiratory symptoms (AUC=0.62), indicating that those who experienced their first respiratory symptoms less recently are more likely to have Recovered Smell (**Figure S6A**). Adding additional features to the model provided modest improvement (AUC=0.65 for the optimal model), but overall it was difficult to predict whether a C19+ participant would exhibit Recovered Smell or Persistent Smell Loss based on the data available (**Figure S6B**). **Table S3** includes the means and SD by recovery group for C19+ and C19-participants.

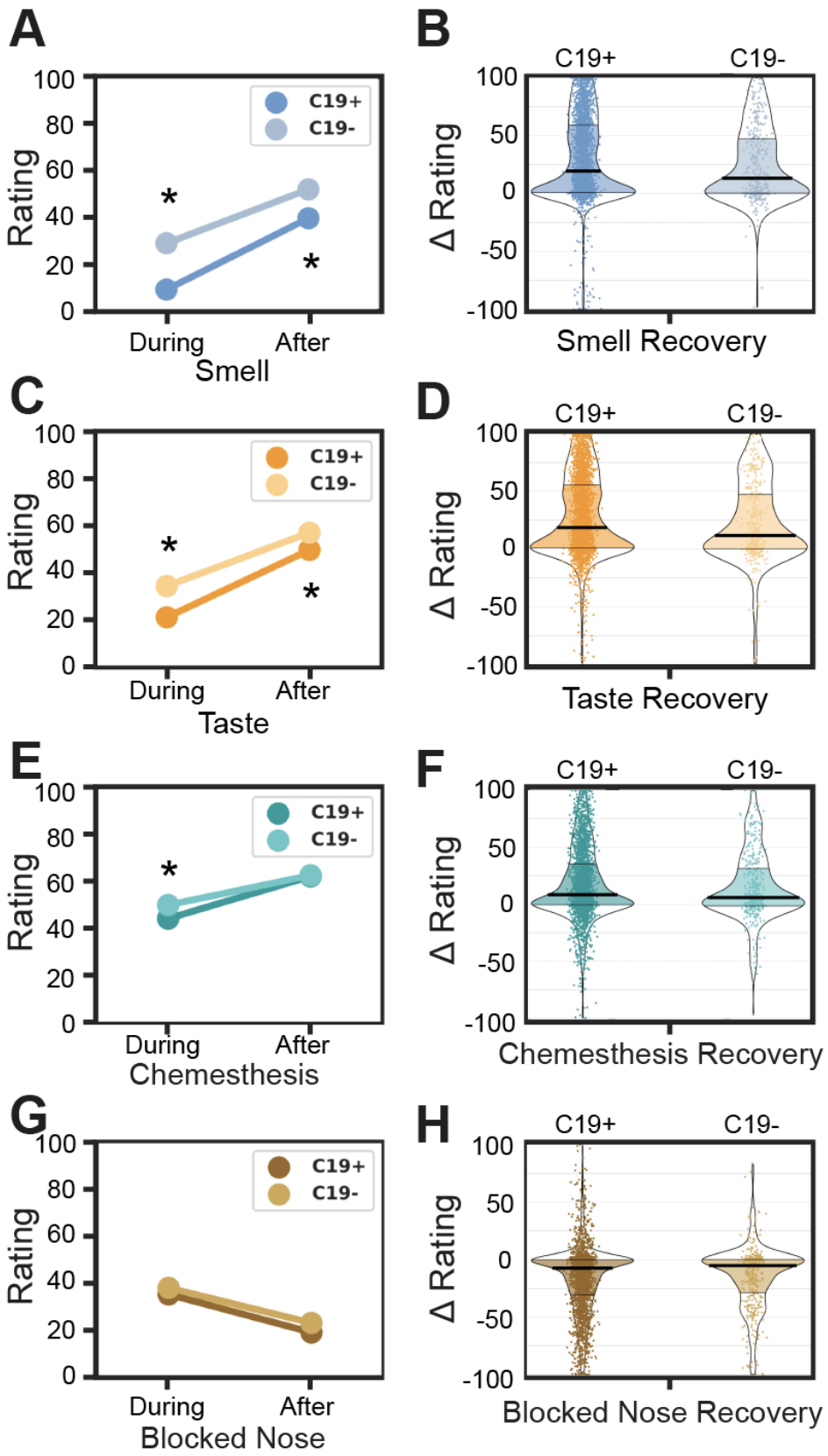


Figure S6. COVID-19 recovery. Similar to Figure 1, but self-reported smell (**A,B**), taste (**C,D**), chemesthesis (**E,F**), and nasal blockage(**G,H**) during and after respiratory illness in C19+ (darker) versus C19- (lighter). (A,C,E,G) mean values during and after respiratory illness, respectively. (B,D,F,H) Change (after minus during) as a distribution over subjects.

Table S3. Main chemosensory and relevant demographic features in the three clusters of recovering C19+ and C19- participants.

	Intact Smell			Persistent Smell Loss			Recovered Smell		
	C19+	**C19-**	**p**	**C19+**	**C19-**	**p**	**C19+**	**C19-**	**p**
Taste Change	-34 ± 39	-21 ± 30	0.011	-75 ± 28	-68 ± 32	0.0018	-75 ± 29	-69 ± 31	0.0043
Chemesthesis Change	-17 ± 32	-5.9 ± 25	0.016	-40 ± 37	-42 ± 38	0.2	-36 ± 37	-37 ± 39	0.41
Changes In Sweet	0.31 ± 0.46	0.19 ± 0.39	0.0067	0.46 ± 0.5	0.4 ± 0.49	0.067	0.47 ± 0.5	0.45 ± 0.5	0.36
Changes In Sour	0.27 ± 0.45	0.14 ± 0.35	0.0037	0.43 ± 0.5	0.42 ± 0.5	0.42	0.4 ± 0.49	0.42 ± 0.5	0.29
Smell Change	-3.6 ± 14	-8.1 ± 12	0.022	-89 ± 13	-82 ± 19	1.50E-07	-89 ± 13	-83 ± 17	4.20E-05
Phantosmia	0.09 ± 0.29	0.11 ± 0.31	0.35	0.09 ± 0.28	0.11 ± 0.31	0.21	0.08 ± 0.28	0.10 ± 0.3	0.32
Days Since Onset	28 ± 18	27 ± 17	0.35	27 ± 20	33 ± 26	0.0039	32 ± 17	33 ± 20	0.32
Parosmia	0.15 ± 0.36	0.15 ± 0.36	0.48	0.09 ± 0.28	0.12 ± 0.33	0.063	0.12 ± 0.33	0.15 ± 0.36	0.19
Changes In Savory	0.18 ± 0.39	0.16 ± 0.37	0.32	0.4 ± 0.49	0.36 ± 0.48	0.17	0.32 ± 0.47	0.35 ± 0.48	0.26
Onset Day	95 ± 24	91 ± 23	0.078	1e+02 ± 29	95 ± 30	0.00036	90 ± 21	91 ± 27	0.47
Taste Recovery	15 ± 33	13 ± 28	0.43	9.2 ± 23	6 ± 29	0.07	55 ± 30	50 ± 31	0.043
Changes In Bitter	0.27 ± 0.45	0.17 ± 0.38	0.018	0.43 ± 0.5	0.4 ± 0.49	0.2	0.41 ± 0.49	0.4 ± 0.49	0.41
Changes In Salty	0.36 ± 0.48	0.21 ± 0.41	0.0026	0.47 ± 0.5	0.42 ± 0.49	0.12	0.47 ± 0.5	0.44 ± 0.5	0.23
Fraction Women	0.63 ± 0.48	0.79 ± 0.41	0.0017	0.76 ± 0.43	0.77 ± 0.42	0.38	0.73 ± 0.44	0.75 ± 0.43	0.32
Anosmia/ Hyposmia	0.43 ± 0.5	0.14 ± 0.35	3.50E-08	0.94 ± 0.23	0.86 ± 0.35	1.40E-05	0.88 ± 0.32	0.86 ± 0.35	0.23
Chemesthesis Recovery	8.3 ± 27	8.3 ± 24	0.24	9.5 ± 26	10 ± 27	0.41	29 ± 33	25 ± 38	0.25
Smell Recovery	-3.8 ± 39	4.4 ± 22	0.14	6.3 ± 10	6.3 ± 11	0.22	67 ± 19	62 ± 18	0.007
Age	44 ± 13	44 ± 13	0.33	41 ± 12	42 ± 12	0.092	40 ± 12	43 ± 12	0.0015

APPENDIX 1

GCCR core questionnaire

The core questionnaire of the Global Consortium for Chemosensory Research (GCCR) has been deployed in Compusense Cloud in 32 languages. The questionnaire was published previously[16] and also appears in the NIH Office of Behavioral and Social Sciences Research (OBSSR) research tools for COVID-19.[40] Responses to the GCCR core questionnaire in 23 languages were collected between April 7 and July 2, 2020 and included in the final dataset, on which we conducted the analyses reported in this paper.

Global Consortium for Chemosensory Research (GCCR) Questionnaire

GCCR
Global Consortium for Chemosensory Research

Welcome and Consent

1. I consent to participate.
   - ◯ [1] Yes
   - ◯ [0] No

Question Type: Choose only 1
Branching logic: if [0]=checked, then go to Section 4) End of test

About your illness

---

2. In which year (YYYY) were you born?

Question Type: Numeric
Branching logic: if year of birth greater than 2001 then go to Section 4) End of test

---

3. What is your current country of residence?

Question Type: Comment _____

---

4. Optional: What city, town, or region do you currently live in?

Question Type: Comment _____

---

5. Which gender do you most identify with?
   - ◯ [1] Female
   - ◯ [2] Male
   - ◯ [3] Another not listed here
   - ◯ [4] Prefer not to say

Question Type: Choose only 1

---

6. Within the past two weeks, have you been diagnosed with or suspect that you have a respiratory illness?
   - ◯ [1] Yes
   - ◯ [0] No

Question Type: Choose only 1
Branching: if [0]=checked, then go to Section 4) Re-contact

---

7. What **date** did you **first notice symptoms** of your recent respiratory illness? Provide your best guess or leave blank if you do not remember. Click the box below to display a calendar.

Question Type: Numeric

---

8. Have you been diagnosed with **COVID-19**?
   - ◯ [1] Yes-diagnosed based on symptoms only
   - ◯ [2] Yes-diagnosed with viral swab
   - ◯ [3] Yes-diagnosed with another lab test
   - ◯ [4] No-I was not diagnosed, but I have symptoms
   - ◯ [5] No-I had a negative test, but I have symptoms
   - ◯ [6] No-I do not have any symptoms
   - ◯ [7] Don't Know
   - ◯ [8] Other

Question Type: Choose only 1

---

9. Were you diagnosed with any **other** respiratory illnesses (**not COVID-19**) in the **last two weeks**?

(Select all that apply)

- ☐ [1] Strep throat (Streptococcal bacteria)
- ☐ [2] Another bacterial illness
- ☐ [3] Flu (influenza)
- ☐ [4] Another viral illness
- ☐ [5] Other
- ☐ [6] None

Question Type: Choose n

10. Have you had any of the following symptoms with **your recent respiratory illness or diagnosis**? (Select all that apply)

- ☐ [1] Fever
- ☐ [2] Dry cough
- ☐ [3] Cough with mucus
- ☐ [4] Difficulty breathing/shortness of breath
- ☐ [5] Chest tightness
- ☐ [6] Runny nose
- ☐ [7] Sore throat
- ☐ [8] Changes in food flavor
- ☐ [9] Changes in smell
- ☐ [10] Loss of appetite
- ☐ [11] Headache
- ☐ [12] Muscle aches
- ☐ [13] Fatigue
- ☐ [14] Diarrhea
- ☐ [15] Abdominal pain
- ☐ [16] Nausea
- ☐ [17] No symptoms

Question Type: Choose n

---

11. Optional: Please describe the progression or order you noticed your symptoms

_____

Question Type: Comment

---

12. Optional: What treatment(s) or medication(s) have you received for your recent **respiratory illness or diagnosis**?

_____

Question Type: Comment

The next section of this survey is focused on your experience of smell, taste, and food flavor during your recent respiratory illness or diagnosis.

These questions relate to your <u>sense of smell</u> (for example, sniffing flowers or soap, or smelling garbage) but <u>not the flavor of food</u> in your mouth.

---

13. Rate your ability to **<u>smell</u>** BEFORE your **recent respiratory illness or diagnosis**

No sense of smell — Excellent sense of smell

(Place a mark on the scale above)

Question Type: Line Scale

---

14. Rate your ability to **<u>smell</u>** DURING your **recent respiratory illness or diagnosis**

No sense of smell — Excellent sense of smell

(Place a mark on the scale above)

Question Type: Line Scale

---

15. Have you experienced any of the following changes in **<u>smell</u>** with your **recent respiratory illness or diagnosis**? (Select all that apply)

- ☐ [1] I cannot smell at all / Smells smell less strong than they did before
- ☐ [2] Smells smell different than they did before (the quality of smell has changed)
- ☐ [3] I can smell things that aren't there (e.g, I smell burning when nothing is on fire)
- ☐ [4] Sense of smell fluctuates (e.g. comes and goes)

Question Type: Choose n

---

16. Optional: Please describe any changes in smell

_____

Question Type: Comment

17. How **blocked** was your nose BEFORE your **recent respiratory illness or diagnosis**?

Not at all blocked — Completely blocked

(Place a mark on the scale above)

Question Type: Line Scale

18. How **blocked** was your nose DURING your **recent respiratory illness or diagnosis**?

Not at all blocked — Completely blocked

(Place a mark on the scale above)

Question Type: Line Scale

The following questions are related to your sense of taste. For example sweetness, sourness, saltiness, bitterness experienced in the mouth

19. Rate your ability to **taste** BEFORE your **recent respiratory illness or diagnosis**

No sense of taste — Excellent sense of taste

(Place a mark on the scale above)

Question Type: Line Scale

20. Rate your ability to **taste** DURING your **recent respiratory illness or diagnosis**

No sense of taste — Excellent sense of taste

(Place a mark on the scale above)

Question Type: Line Scale

21. OPTIONAL: Have you experienced changes to **specific tastes** with your **recent respiratory illness or diagnosis**? (Select all that apply)

- ☐ [1]Sweet
- ☐ [2]Salty
- ☐ [3]Sour
- ☐ [4]Bitter
- ☐ [5]Savory/Umami

Question Type: Choose n

22. Optional: Describe any **changes in taste** during your **recent respiratory illness or diagnosis**.

Question Type: Comment

The following questions are related to other sensations in your mouth, like burning, cooling, or tingling. For example chili peppers, mint gum or candy, or carbonation.

23. Rate your **ability to feel these other sensations** BEFORE your **recent respiratory illness or diagnosis**.

Not sensitive at all — Very sensitive

(Place a mark on the scale above)

Question Type: Line Scale

24. Rate your **ability to feel these other sensations** DURING your **recent respiratory illness or diagnosis**

Not sensitive at all — Very sensitive

(Place a mark on the scale above)

Question Type: Line Scale

25. Optional: Describe any **changes in these other sensations** during your **recent respiratory illness or diagnosis**.

Question Type: Comment

---

26. Optional: Think about a food or beverage you consume regularly - for example, your morning coffee or tea or a piece of fruit you have each day. Has the taste, smell, or flavor changed with your recent respiratory illness or diagnosis? If so, **please describe how and be sure to indicate which food or beverage you are describing**.

Question Type: Comment

---

27. Optional: Is there anything else you would like to tell us about how your recent respiratory illness or diagnosis has affected your sense of smell, taste, and flavor?

Question Type: Comment

---

28. Have you recovered from your **recent respiratory illness or diagnosis**? (For example you no longer have a cough, fever, or shortness of breath.)

- ◯ No
- ◯ Yes - partly
- ◯ Yes - fully
- ◯ Don't know

Question Type: Choose only 1
Branching: if [0]=checked, then go to Section 3) General Health Information

---

The next section of this survey is focused on your experiences of smell, taste, and food flavor after your recovery from your recent respiratory illness or diagnosis.

---

29. Rate your ability to **smell** AFTER your recovery

No sense of smell — Excellent sense of smell

(Place a mark on the scale above)

Question Type: Line Scale

---

30. How **blocked** was your nose AFTER your recovery

Not at all blocked — Completely blocked

(Place a mark on the scale above)

Question Type: Line Scale

---

31. Rate your ability to **taste** AFTER your recovery

No sense of taste — Excellent sense of taste

(Place a mark on the scale above)

Question Type: Line Scale

32. Rate your **ability to feel these other sensations like burning, cooling, and tingling** AFTER your recovery

Not sensitive at all — Very sensitive

(Place a mark on the scale above)

Question Type: Line Scale

33. How were you directed to this survey?

- ☐ [1] Clinician or healthcare professional
- ☐ [2] Media (social media, print, radio, tv, etc)
- ☐ [3] Word of mouth
- ☐ [4] Other

Question Type: Choose only 1

The next section of this survey will ask some optional questions about your habits and general health.

General Health Information

34. Optional: Have you smoked at least 100 combustible cigarettes or cigars in your entire life?

- ◯ [1] No
- ◯ [2] Yes
- ◯ [3] Prefer not to say
- ◯ [4] Don't know

Question Type: Choose only 1

35. Optional: During the past 30 days, on how many days did you smoke combustible cigarettes or cigars?

_____

Question Type: Numeric

36. Optional: Have you ever used an e-cigarette ('vaped'/'Juuled') even one time? (E-cigarettes are battery-powered devices that usually contain liquid nicotine, and do not produce smoke.)

- ◯ [1] No
- ◯ [2] Yes
- ◯ [3] Prefer not to say
- ◯ [4] Don't know

Question Type: Choose only 1

37. Optional: During the past 30 days, on how many days did you use an e-cigarette?

_____

Question Type: Numeric (range 0-30; integer)

38. Did you have any of the following **in the 6 months prior** to your recent respiratory illness or diagnosis? (Select all that apply)

- ☐ [1] High blood pressure
- ☐ [2] Heart disease (heart attack or stroke)
- ☐ [3] Diabetes (high blood sugar)
- ☐ [4] Obesity
- ☐ [5] Lung disease (asthma/COPD)
- ☐ [6] Head trauma
- ☐ [7] Neurological disease
- ☐ [8] Cancer that required chemotherapy or radiation
- ☐ [9] Cancer that did NOT require chemotherapy or radiation
- ☐ [10] Chronic sinus problems
- ☐ [11] Seasonal allergies/hay fever
- ☐ [12] None

Question Type: Choose n

39. Optional: Any other medical conditions that you would like to mention?

_____

Question Type: Comment

40. Optional: Which medication(s) do you take regularly? For example, medications for pain, blood pressure, thyroid function, anti-viral, etc.

_____

Question Type: Comment

---

41. Optional: Is there anything we didn't ask about that you would like to share with us?

_____

Question Type: Comment

Re-contact

---

42. We may want to re-contact you for follow up research on this topic. **Is it okay if our team or other researchers re-contact you to participate in future research**? By saying yes, you agree that we can share your email address with other researchers for this purpose.

◯ [1] Yes
◯ [0] No

Question Type: Choose only 1

Branching logic: if [0]=checked, then go to: Section 5)End of test

---

43. Please provide your full email address, so you can be contacted for future studies by our team or other researchers.

_____

Question Type: Comment

End of Test

You have now completed the survey and may close your browser

Thank you for your time!

Notes

"In which year (YYYY) were you born?
-- value must be 1900 or greater
'What **date** did you **first notice symptoms** of your recent respiratory illness? Provide your best guess or leave blank if you do not remember. Click the box below to display a calendar"
-- format (mm/dd/yyyy)
'Have you been diagnosed with COVID-19"
-- if [8] Other was selected, a comment is required
'Were you diagnosed with any other respiratory illnesses (not COVID-19) in the last two weeks? (Select all that apply)"
-- if [6] None was selected, no other options can be selected.
'Have you had any of the following symptoms with your **recent respiratory illness or diagnosis**? (Select all that apply)"
-- if [17] No symptoms was selected, no other options can be selected.
'Rate your ability to smell BEFORE your **recent respiratory illness or diagnosis**"
-- Line Scale Range 0-100, intervals of 1. All following line scales formatted similarly
All line scales had anchors indented at ~10% and 90% of scale range.
'**OPTIONAL**: During the past 30 days, on how many days did you smoke combustible cigarettes or cigars?" and "**OPTIONAL**: During the past
-- value must be between 0-30
Did you have any of the following in the 6 months prior to your **recent respiratory illness or diagnosis**? (Select all that apply)
-- if [12] None was selected, no other options can be selected.