HHS Public Access

Author manuscript

Rhinology. Author manuscript; available in PMC 2024 April 14.

Published in final edited form as:

Rhinology. 2022 June 01; 60(3): 207–217. doi:10.4193/Rhin21.415.

A follow-up on quantitative and qualitative olfactory dysfunction and other symptoms in patients recovering from COVID-19 smell loss

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Conflict of interest

Prof. Hayes is a co-founder of Redolynt LLC. Prof. Philpott is a trustee of the charity Fifth Sense. None of the other authors have any conflicts to disclose.

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Abstract

Background: Sudden smell loss is a specific early symptom of COVID-19, which, prior to the emergence of Omicron, had estimated prevalence of ~40% to 75%. Chemosensory impairments affect physical and mental health, and dietary behavior. Thus, it is critical to understand the rate and time course of smell recovery. The aim of this cohort study was to characterize smell function and recovery up to 11 months post COVID-19 infection.

Methods: This longitudinal survey of individuals suffering COVID-19-related smell loss assessed disease symptoms and gustatory and olfactory function. Participants (n=12,313) who completed an initial survey (S1) about respiratory symptoms, chemosensory function and COVID-19 diagnosis between April and September 2020, were invited to complete a follow-up survey (S2). Between September 2020 and February 2021, 27.5% participants responded (n=3,386), with 1,468 being diagnosed with COVID-19 and suffering co-occurring smell and taste loss at the beginning of their illness.

Results: At follow-up (median time since COVID-19 onset ~200 days), ~60% of women and ~48% of men reported less than 80% of their pre-illness smell ability. Taste typically recovered faster than smell, and taste loss rarely persisted if smell recovered. Prevalence of parosmia and

phantosmia was ~10% of participants in S1 and increased substantially in S2: ~47% for parosmia and ~25% for phantosmia. Persistent smell impairment was associated with more symptoms overall, suggesting it may be a key marker of long-COVID illness. The ability to smell during COVID-19 was rated slightly lower by those who did not eventually recover their pre-illness ability to smell at S2.

Conclusions: While smell ability improves for many individuals who lost it during acute COVID-19, the prevalence of parosmia and phantosmia increases substantially over time. Olfactory dysfunction is associated with broader persistent symptoms of COVID-19, and may last for many months following acute COVID-19. Taste loss in the absence of smell loss is rare. Persistent qualitative smell symptoms are emerging as common long-term sequelae; more research into treatment options is strongly warranted given that even conservative estimates suggest millions of individuals may experience parosmia following COVID-19. Healthcare providers worldwide need to be prepared to treat post COVID-19 secondary effects on physical and mental health.

Trial registration: This project was pre-registered at OSF 1.

Keywords

parosmia; phantosmia; olfaction disorders; long COVID; post-COVID; public health; smell

Introduction

In March 2020, the World Health Organization (WHO) declared that Coronavirus Disease 19 (COVID-19), caused by SARS-CoV-2 infection, had reached pandemic levels [(1)]. Although the symptoms of COVID-19 are highly variable across infected individuals [(2)], sudden loss of taste and smell was quickly identified as a hallmark symptom [(3–5)]. Self-reported smell loss was shown to be useful for both diagnosis [(6–8)] and population surveillance [(9)], at least for SARS-CoV-2 variants common in 2020.

Classically, patient complaints of smell loss with the common cold arise from a blocked or stuffy nose that prevents volatile odorants from reaching olfactory receptors near the top of the nasal cavity, while gustation is not affected [(10)]. However, with COVID-19, sudden smell loss was commonly observed without nasal blockage [(11–13)], and prototypical tastes were also impaired [(6,7)] as supported by direct assessment with odor-free tastants (e.g., sugar) [(14)].

Most individuals (>75–80%) reporting taste and smell impairments due to COVID-19 tend to recover these senses within a few months, but smell impairment is still reported by 25–40% of patients after one or two months [(6,15)] and by 15%−28% patients at 6 months [(15,16)]. Given the widespread confusion between taste, smell and flavor [(17)], data on taste recovery are less clear, although taste qualities may recover more rapidly than smell [(16)]. Some individuals recover from acute smell loss, only to subsequently report other olfactory dysfunction, such as parosmia (smell distortions) and phantosmia (phantom smells or olfactory hallucinations) [(18,19)].

Factors associated with persistent smell and taste dysfunction following acute COVID-19 illness remain unknown. Some early reports suggested COVID-19 smell loss might be

associated with a milder disease course [20,21], although smell and taste impairments were also seen in severely ill patients [22,23]. Pre-COVID, firm data on the incidence of parosmia were generally lacking, but some estimates place it near 4% in the general public and ~12–24% of ENT patients [24]. Data from a clinical sample presenting for specialist assessment suggest parosmia may occur ~4 to 8 weeks after the onset of anosmia or hyposmia, often following an upper respiratory infection [25]. Accordingly, we reasoned a followup survey may capture additional dysfunctions not seen on our initial survey [4,6].

The aim of this preregistered study was to characterize smell impairment and recovery in connection with taste loss and other symptoms, by recontacting respondents of our initial survey [4,6] to collect longitudinal data in a large cohort of participants diagnosed with COVID-19.

Material and Methods

Study design

This longitudinal, observational online cohort study entails a follow-up survey (S2) of respondents between 2 and 10 months after completion of the initial core survey (S1) by the Global Consortium for Chemosensory Research (GCCR) [4,6,26]. Participants self-selected to participate in S1. They were invited via email to participate in S2 if they previously agreed to be re-contacted, provided an email address, completed S1 in English, Spanish, Italian, Dutch, French, and reported a change in smell, taste and/or flavor (via symptom checkbox) in S1. The protocol complies with the revised Declaration of Helsinki and was approved as an exempt study by the Office of Research Protections at The Pennsylvania Study University in the U.S.A. (STUDY00014904). The full questionnaire is provided in the Supplementary Materials.

Participants

Participants (n=12,313) who completed the initial GCCR survey (S1) between April and September 2020 and agreed to be recontacted via email were invited to complete a follow-up survey (S2). Email invitations were sent in five languages (French: n=4,306, English: n=3,422, Dutch: n=1,840, Spanish: n=1,575, Italian: n=1,165) between September and November 2020 to those who consented to be re-contacted. Data were exported in February 2021. We received 3,386 responses (2,448 women, 927 men, 1 non-binary; age range 20 to 85 years) for S2, corresponding to a response rate of ~28%. Of these, 1,918 participants were excluded from further analysis (Figure 1 for details). Thus, the final dataset reported here consisted of 1,468 individuals who reported smell or taste loss at baseline (S1) and consistent positive COVID-19 diagnoses at S1 and S2. The demographics, and overall symptoms of these individuals are reported in Table 1.

To be included in the present analysis, participants had to report a consistent COVID-19 diagnosis on both S1 and S2: i.e., positive COVID-19 diagnosis via clinical presentation (i.e., via symptoms and history), or via viral swab, or another laboratory test. Duplicate entries were removed, and exclusion criteria are summarized in Figure 1. At the request of a reviewer, we reran all analyses after removing all individuals (n=422) who were diagnosed

by a clinician via symptoms (i.e., diagnosed via clinical presentation without a confirmatory test); the major findings did not change, thus we present the results for the larger cohort here. Readers interested in results for the lab-test only group (n=1046) are referred to the Supplemental Materials.

There was no predetermination of the sample size. A pilot inquiry in English (n=100) was used to estimate feasible response rate among S1 completers [(4)], and invitations were sent out in the 5 languages with the greatest number of responses.

Variables, data sources, and measurement

Details of the baseline variables have been described previously [(4)]. The follow-up survey collected ratings of smell and taste function on horizontal 101-point visual analog scales, and self-reporting of parosmia and phantosmia. Other COVID-19 symptoms were collected via checklist and free text comments. Exact presentation and wording of questions are available in the Supplemental Materials.

Bias minimization

The survey was conducted in multiple languages to increase generalizability. Also, because participants self-selected to respond, analysis and conclusions were restricted to individuals with COVID-19 who had chemosensory loss at disease onset. Given the potential bias that may arise from differential response rates (i.e., a possibility that those who had recovered fully might be less likely to participate in S2), we attempted to mitigate this by being highly conservative in the estimation calculations presented in our final conclusions.

Quantitative and binary variables

Here, S2 respondents were grouped according to whether their smell loss persisted or recovered. Participants who returned to less than 80% of their pre-COVID smell ability (as reported in S1) were categorized as smell long-haulers; the rest were classified as non-long-haulers. The cutoff of 80% was specified in the pre-registration (see https://osf.io/3e6zc). It was chosen to account for normal variation of chemosensory ability. This choice reflects the common range between 10th percentile [(27)] to 30th percentile [(28)] for separating normosmics from those with quantitative dysfunction. We also report the prevalence of parosmia and phantosmia for the total sample.

Smell (taste) impairment for the two surveys were calculated for each participant using the following equations:

$$\text{S1}: \frac{\text{taste or smell ability during illness}}{\text{taste or smell ability pre COVID19}} \times 100$$

$$\text{S2}: \frac{\text{current ability to taste or smell}}{\text{taste or smell ability pre COVID19}} \times 100$$

To further assess the type of olfactory dysfunction experienced, we relied on self report using a check-all-that-apply question with four distinct prompts. Positive endorsement of ‘I

cannot smell at all / Smells smell less strong' was considered to be indicative of anosmia or hyposmia, positive endorsement of 'Smells smell different than they did before (the quality of smell has changed)' was taken as being indicative of parosmia, and positive endorsement of 'I can smell things that aren't there (e.g, I smell burning when nothing is on fire)' was considered indicative of phantosmia. See Supplement Materials for complete wording and formatting.

Statistical analysis

Demographics—To report demographics across the whole sample and to assess potential confounding variables, we calculated proportions of the presence of each of the following comorbidities: high blood pressure, heart disease, diabetes, obesity, lung disease (asthma/COPD), head trauma, neurological disease, cancer (treated with chemotherapy), cancer (no chemotherapy), chronic sinus problems, seasonal allergies/hay fever, and no condition. We also calculated the probability in each of the smell long-hauler groups. We tested distributional differences with Pearson's chi-square tests with the R base function "prop.test". We used an alpha of 0.0042 to determine significance (i.e., a Bonferroni corrected alpha of 0.05 for 12 conditions). We repeated this for language and gender distributions. For age we calculated the average and performed an independent sample t-test with an alpha of 0.05.

Differences in probability of smell distortions and other COVID-19 symptoms between participants with persistent versus recovered smell loss—To test differences in smell distortions at the time of S2 between smell long-haulers and non long-haulers, we calculated probability tables of presence and absence of parosmia and phantosmia in each of the smell long-hauler groups. We tested distributional differences with Pearson's chi-square tests with the R base function "prop.test". We used an alpha of 0.025 to determine significance (i.e., a Bonferroni corrected alpha of 0.05 for two types of distortion). We repeated this analysis for the symptoms at the time of S1 to check for any pre-existing differences prior to developing persistent smell long-hauler status.

Differences in symptom counts—To assess effects of smell long-hauler-status on illness severity, we summed the presence of each of commonly listed COVID-19 symptoms (fever, dry cough, cough with mucus, difficulty breathing / shortness of breath, chest tightness, runny nose, sore throat, loss of appetite, headache, muscle aches, fatigue, diarrhea, abdominal pain, nausea, excluding smell and taste symptoms under "changes in food flavor" and "changes in smell"), leading to scores ranging from 0–14. Since this "count" variable was not continuous or categorical (i.e., the total number of symptoms), we used logistic regression with a Poisson distribution for the dependent variable. This was implemented via the "glm" function in R, using the "poisson" option. The assumption of equality between variance and mean of each category of the independent variable was checked [(29)] and a "quasi-Poisson" family variant was applied if overdispersion was observed. To estimate relative risk, a Poisson regression with a robust error variance was calculated with the package Sandwich [(30–32)].

To further characterize rare symptoms not provided in the COVID-19 symptoms checklist, additional symptoms, such as “brain fog”, “memory loss”, were extracted from free text comments. Comments in Spanish, Italian, Dutch, and French were translated into English by scientists who were native speakers of each language, and pooled. In total, 559 comments containing symptoms were analyzed [214 French (74 men, 140 women), 195 English (54 men, 141 women), 65 Spanish (22 men, 43 women), 54 Dutch (14 men, 40 women), and 31 Italian (13 men, 18 women)].

To test for differences in overall symptoms between smell long-haulers and non long-haulers at S2, we calculated probabilities for each of the 16 symptoms (headache, fatigue, difficulty breathing/shortness of breath, diarrhea, nausea, fever, abdominal pain, changes in food flavour, changes in smell, chest tightness, cough with mucus, dry cough, loss of appetite, muscle aches, runny nose, sore throat) in each group. As above, we tested for distribution differences, with a Bonferroni corrected alpha of 0.003125 (0.05/16 tests, one for each symptom). We repeated this analysis for S1 symptoms to check for preexisting differences prior to developing smell long-hauler status.

Smell ability during COVID-19 infection (measured at S1) was compared between smell long-haulers and non long-haulers (defined from S2) using a Welch’s test.

Results

Descriptive data for all 1,468 participants are summarized in Table 1. The mean age was ~44 years, fewer men than women took part, and more responses were collected in English and French, as expected from the relative distribution of email invitations sent. The time elapsed between S1 and S2 ranged from 23 to 291 days (median: 200 days), corresponding to 36 to 326 days (median: 225 days) since disease onset (Supplementary Figure S1). This timing enabled the calculation of cumulative rate of recovery (Table 2).

During the first months after onset of COVID-19 symptoms, less than 10% of participants reported full smell recovery, gradually increasing to 39% in women and 52% in men by up to 11 months (Table 2). Comparatively, the reports for taste recovery were greater (~56 to ~65% by 11 months).

58% of those in the final S2 dataset were classified as smell long-haulers (see methods), with ~39% also reporting persistent taste impairment and ~20% reporting recovered taste (Figure 2A). Only ~3% reported impaired taste with recovered smell. This suggests smell and taste recover separately, and these different sensory modalities can be distinguished by the respondents. Qualitative disorders of smell, specifically parosmia and phantosmia, were more frequently observed at S2 (46.8% and 24.7%, respectively) than S1 (10.2% and 10.1%, respectively; Figure 2B). Parosmia was significantly more common at S2 than S1 (χ^2 = 480.12, 95% CI = 0.41–0.48, p <0.001, OR = 7.73). Phantosmia also was significantly more common at S2 than S1 (χ^2 =110.2, 95% CI = 0.21–0.30, p <0.001, OR =2.95). Further, such dysfunction was significantly more common in smell long-haulers compared to non-long-haulers, as 63.6% of smell long-haulers reported parosmia versus 23.9% of non-long-haulers (χ^2 = 225.0, 95% CI = 0.34–0.44, p <0.001, OR = 5.56) and 33.5% of

smell long-haulers reported phantosmia versus 13.1% of non-long-haulers (χ^2 = 78.9, 95% CI = 0.21–0.32, p <0.001, OR = 3.35). Among smell long-haulers, the incidence of parosmia was not significantly different between women and men (64% versus 58%). Qualitative terms from open-ended text responses were also captured. Typical participant reports for parosmia were “Some things now smell different and unpleasant” or “like chemicals”; reports for phantosmia include responses like “Sometimes I can smell burning but no one else around me can.”

The total number of symptoms decreased at S2 (Figure 3). However, smell long-haulers reported more overall symptoms (median = 1) at S2 compared to non-long-haulers (median = 0). This was confirmed via quasi-Poisson regression (β1 = 0.48, 95% CI = 0.32–0.64, T = 5.66, p < 0.0001). Notably, these groups were not different at S1 (both medians = 6).

When we examined each of the symptoms, including smell and taste symptoms, we observed changes in flavor (χ^2 = 224.9, 95% CI = 0.37–0.46, p <0.001, OR = 7.30) and in smell (χ^2 = 340.17, 95% CI = 0.44–0.53, p <0.001, OR = 10.02) as expected, in addition to other symptoms like fatigue (χ^2 = 22.09, 95% CI = 0.08–0.20, p <0.001, OR = 1.80), headache (χ^2 = 23.99, 95% CI = 0.11–0.25, p <0.001, OR = 2.24), and loss of appetite (χ^2 = 33.58, 95% CI = 0.25–0.40, p <0.001, OR = 5.98), all of which were more frequent in smell long-haulers than in non-long-haulers (Figure 3B). This suggests smell long-haulers had greater overall morbidity. Analysis of spontaneous mentions of rare symptoms in free text responses also supports the notion that smell long-haulers experience more symptoms: spontaneous comments included brain fog, hair loss, hallucination, and memory loss. Formal statistics were not applied due to low incidence of these reports (Figure 3C).

To identify variables with potential prognostic value in predicting who would eventually become a smell long-hauler, we looked for differences in multiple S1 measures across the smell long-hauler and non-long-hauler groups from S2. None of these were significant, save one: the self-rated ability to smell during COVID-19 illness was slightly lower (Welch’s t-test, statistic = −4.33, p <0.0001) in smell long-haulers (n=848) than in non-long-haulers (n=620), with means of 2.96 (± 7.64, 95% CI = 2.45–3.48) and 5.11 (±10.49, 95% CI = 4.28–5.94), respectively. This was confirmed when the distributions of smell ability at S1 were compared by status at S2 (Kolmogorov–Smirnov test statistic = 0.12; p<0.0001). As shown in Figure 4, a greater number of smell long-haulers rated their smell ability during illness below 5 (on a 101-point scale), relative to non-long-haulers, although the prognostic value of this small difference still needs to be confirmed.

Given other work on long-COVID [15,33], we performed an exploratory analysis (see supplement) to compare fully recovered individuals (N=153) with those still experiencing 1 or more long-term symptoms (N=202). The number of overall symptoms experienced during acute COVID-19 was predictive of long-term symptoms. Consistent with Sudre et al. [33], the greater the number of symptoms experienced by the participants during the first 2 weeks of the disease, the more likely they were to have long-term symptoms more than 2 months later. This is also in line with more severe outcomes of hospitalized vs non-hospitalized COVID-19 patients [34].

Discussion

Our follow-up of 1,462 participants suggests that ~60% of women and ~48% of men recover less than 80% of their pre-illness olfactory ability multiple months (200 days median) since COVID-19 onset. Using a much more conservative cutoff (i.e., recovery to just 50% of pre-illness ability, rather than 80%) results in a lower incidence, but ~30% of participants are still classified as smell long-haulers. Such percentages are similar to those recently reported elsewhere for long-term follow-up of COVID-19 patients [35]. Here, taste recovered more quickly and rarely persisted if smell recovered. Prevalence of parosmia and phantosmia rose from 10% during the baseline survey to ~47% and ~25% at the follow-up. These olfactory dysfunctions were more common for smell long-haulers than non long-haulers. Persistent smell loss also coincided with more COVID-19 symptoms at follow-up and a higher incidence of follow-up symptoms, such as headache.

Qualitative olfactory disorders are common, comprising up to half of smell impairment complaints, at least prior to COVID-19; critically, these qualitative disorders show distinct patterns of demographics, medical history, and perceptual experiences [36–38]. Parosmia often occurs during recovery from prior viral olfactory loss [38–41]. Mechanistically, this may arise from a mismatch in rewiring in the olfactory bulb during neurogenesis [42], differences across olfactory sensory neurons (OSNs) in time to recover [43], or changes in receptor expression [44]. Specific to COVID-19, patients experiencing parosmia tend to be younger and report a lower quality of life than those with simple loss [45]. Phantosmia is also common following viral smell loss; however, its co-occurrence with recovery is less clear [38,46].

Previously, some speculated smell loss might indicate milder COVID-19 morbidity [21]. Our data fail to support this; instead, we found smell long-haulers had more symptoms than recovered participants. This suggests under-reporting of smell dysfunction among severely ill patients elsewhere may reflect a sampling bias; it seems highly likely (and understandable) that clinicians treating critically ill patients were less focused on anosmia or parosmia as symptoms, and such patients were presumably unavailable for acute chemosensory testing.

There is important practical value in being able to predict which patients may develop long term smell loss. We found a greater reduction in ability to smell during COVID-19 among those who later became smell long-haulers compared to those who recovered smell ability, although this difference was numerically small. Despite the small relative effect size seen here, such a difference may still be prognostically useful, as pre-COVID data suggest residual olfactory function at initial assessment was predictive of future recovery [47]. Tentatively, this suggests early assessment with a validated smell test during acute COVID-19 may be prognostically useful in predicting recovery, although additional data would be needed to confirm this.

While some studies suggest self-reports may underestimate smell loss prevalence relative to direct assessment [19,48,49], others found correlations between self-reporting and direct assessments [50,51]. Furthermore, although direct assessments have been proposed very

recently [52], self-report remains the current standard of care for assessment of parosmia and phantosmia [53], at least until newly proposed methods can be further validated. The presence of parosmia in nearly half of the smell long-haulers in our sample is not surprising for post-viral olfactory dysfunction [54], and in other recent datasets (i.e., healthcare workers in the UK [55] and Sweden [56], and social media scraping [18,57], parosmia is also emerging as a common sequela of COVID-19.

Limitations of this web-based study include recruitment of participants for S1 via social media (with additional coverage in traditional media), which may explain why participants under 60 years of age and women are overrepresented in our sample. The ~28% response rate for S2 may reflect that many S1 participants had spontaneously recovered olfactory and/or gustatory function and were therefore no longer interested in responding. The time lapse between disease onset and follow-up survey varies between participants.

Here, we included 422 COVID-19 positive participants based on clinical diagnosis via symptoms and history, because early in the pandemic, PCR or antigen-based testing was often unavailable. Previously, we found very similar chemosensory profiles in individuals with COVID-19 diagnosis based on lab tests such as PCR versus clinical examination [4]. After excluding those diagnosed via clinical assessment and retaining only those diagnosed via testing (see Supplemental Materials), we observed no meaningful changes in the proportions of smell long-haulers and non-smell long-haulers compared to the data from the full sample reported here (n=1,046 versus n=1,468). Age and gender were also similarly distributed in both samples.

Furthermore, launch dates and pandemic situations varied between different countries, and time between surveys S1 and S2 differed by individuals. Last, we should caution that our participants were not formally tested with a validated smell test – rather, they self-reported perceived smell ability using a visual analog scale, which may lack sufficient precision for diagnosis and follow up of individual patients; still, it is notable that the crowdsourced approach used here reveals similar proportions of parosmic and phantosmic individuals as other longterm studies that did use clinical assessment [56]. Collectively, despite these limitations, our findings characterize profiles of smell and taste loss recovery, with important downstream implications for public health.

As of November 2021, there are over 245 million people worldwide recovering from COVID-19 [58]. According to meta-analysis [48], 77% of those with COVID-19 have acute smell loss when smell function is measured directly or 44% if based on self-reports. If we conservatively assume half of those with COVID-19 experience acute smell loss, this suggests ~18 million Americans may have experienced acute anosmia. If we are highly conservative and assume all of the individuals who did not respond to our follow-up survey recovered, we calculate 50% (smell long haulers) of 30% (response rate), resulting in ~2.7 million Americans and ~15 millions worldwide may be smell long-haulers. Present data suggest ~47% of smell long-haulers report parosmia, which would translate to over a million Americans (and over 7 million worldwide) with parosmia as a result of COVID-19. While olfactory symptoms may be formally classified as mild outcomes by some health authorities, the possibility that millions of individuals may experience long term anosmia and parosmia

as a consequence of prior COVID-19 infection is highly concerning, given the downstream impacts this will likely have on dietary habits [59], quality of life [38], and mental health [60]. We also find that smell long-haulers report other post-acute sequelae of COVID-19.

Conclusion

Our study provides insights into the symptoms of many individuals diagnosed with COVID-19, who experienced persistent smell and taste loss, up to 11 months (6–7 months median) since disease onset. Prevalence of parosmia before the pandemic was estimated as 4% in adults. We find that parosmia increases from ~10% at baseline of COVID-19 patients suffering smell loss to almost 50% at follow-up, suggesting parosmia as a common symptom post-COVID-19, consistent with other recent reports [56,61,62]; whether parosmia might associate with less anosmia over the long run [47] is unknown. Here, we find a small but significant difference in the amount of smell loss in smell long-haulers versus those who do not become long-haulers. Further studies are needed to determine if objective smell tests have prognostic value in predicting persistent smell loss. It is important that health providers, patients, and their families are aware of the potential for quantitative and qualitative smell dysfunction following viral infection, and that they are educated about the course of disease and management [54]. Millions of people worldwide are likely affected and additional research as well as development of new treatment options are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank all members of the Global Consortium for Chemosensory Research (GCCR) for the core survey and for help with translations. We thank Danielle R. Reed and Thomas Hummel for their valuable contributions in the initial stages of this work.

Funding

This work was supported by the following grants: NIH T32 (DC000014) and F32 (DC020100) to M.E. Hannum; NSF DGE1839285 to K.W. Cooper; EXTREM-O (CNRS, CNES) to D. Pierron, A.M. Martinez Peneda, and V. Pereda-Loth; NIH NIAAA Z01AA000135, NIH Distinguished Scholar program, and Rockefeller University Heilbrunn Nurse Scholar Award to P.V. Joseph; NIH T32 DC000014-40 and F32 (DC020380) to R. Pellegrino; Edmond de Rothschild Foundation grant to M.Y. Niv; 2232 International Fellowship for Outstanding Researchers Program of TÜBİTAK 118C299 to M.G. Veldhuizen; Deployment of both surveys by the Penn State Sensory Evaluation Center was supported by discretionary funds controlled by Prof. Hayes, including an unrestricted gift from James and Helen Zallie in support of Sensory Science.

Data availability

The data will be made available in an Open Science Framework (OSF) registry upon publication.

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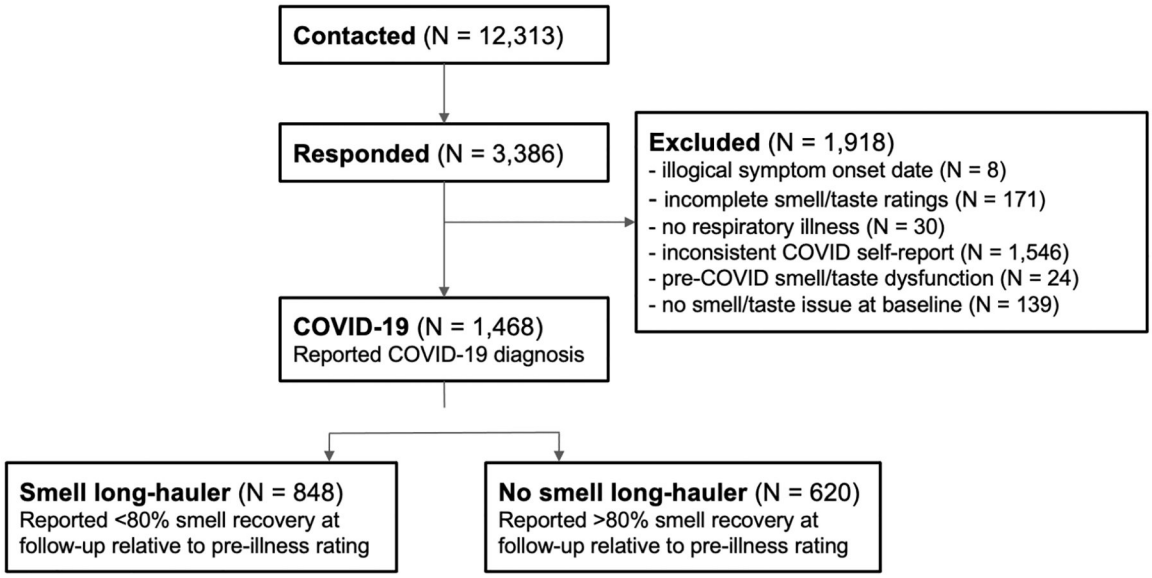

Figure 1.

Summary of participants described in the current study. As shown in the exclusion box, the majority of S2 respondents were excluded from present analyses due to inconsistent reports of their COVID-19 diagnosis between S1 and S2. Participants were also excluded for missing or inconsistent data, chemosensory dysfunction prior to COVID-19.

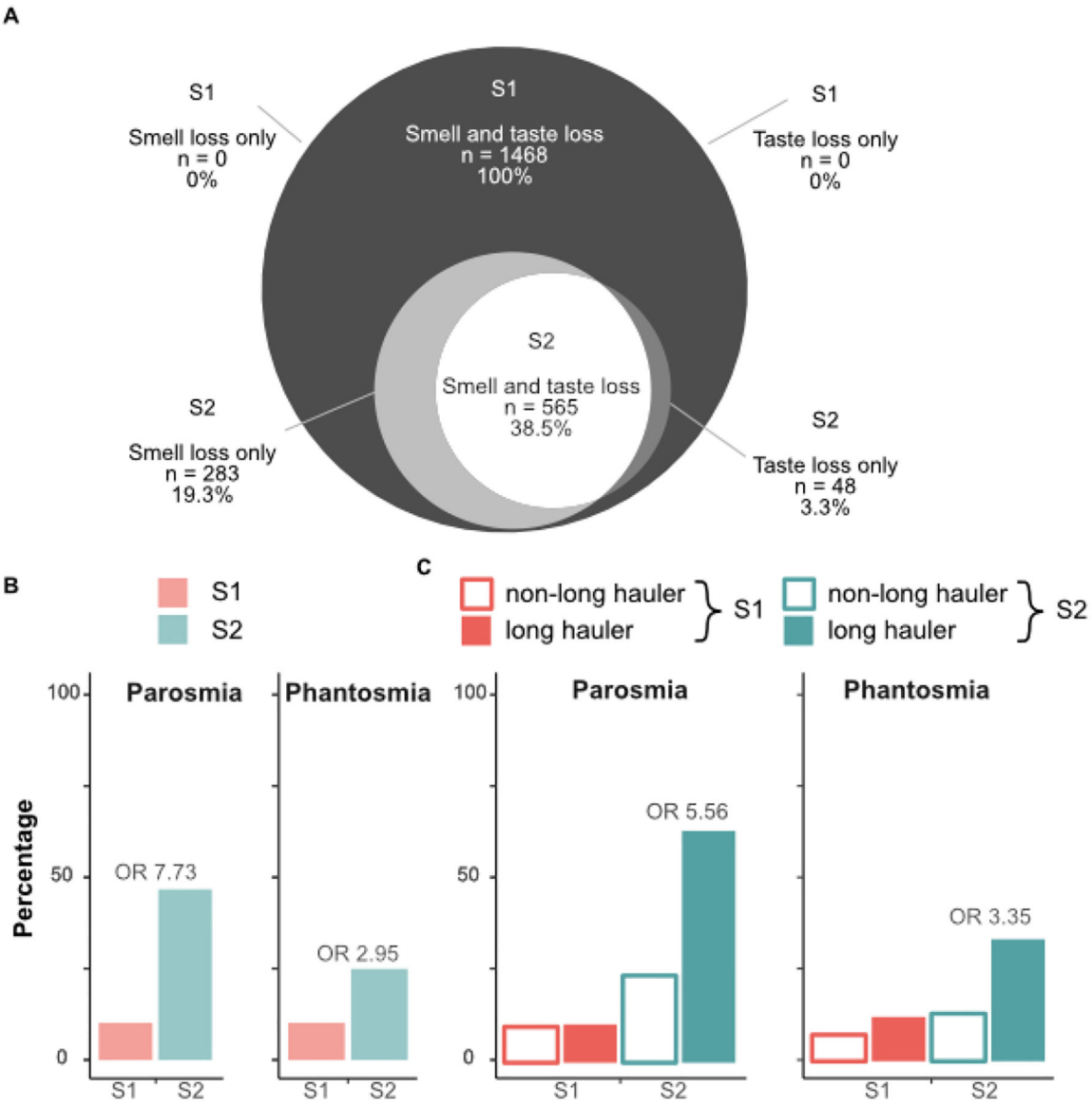

Figure 2.

A: Proportions of participants with smell, taste, and combined smell and taste impairments during baseline (S1, dark gray) and follow-up (S2, lighter grays and white). B: Proportions of qualitative smell changes at S1 (pink) and S2 (green), across all participants. C: Same analysis as B but stratified by individuals who later regained smell ability (white fill) or exhibited smell long-hauling (solid fill).

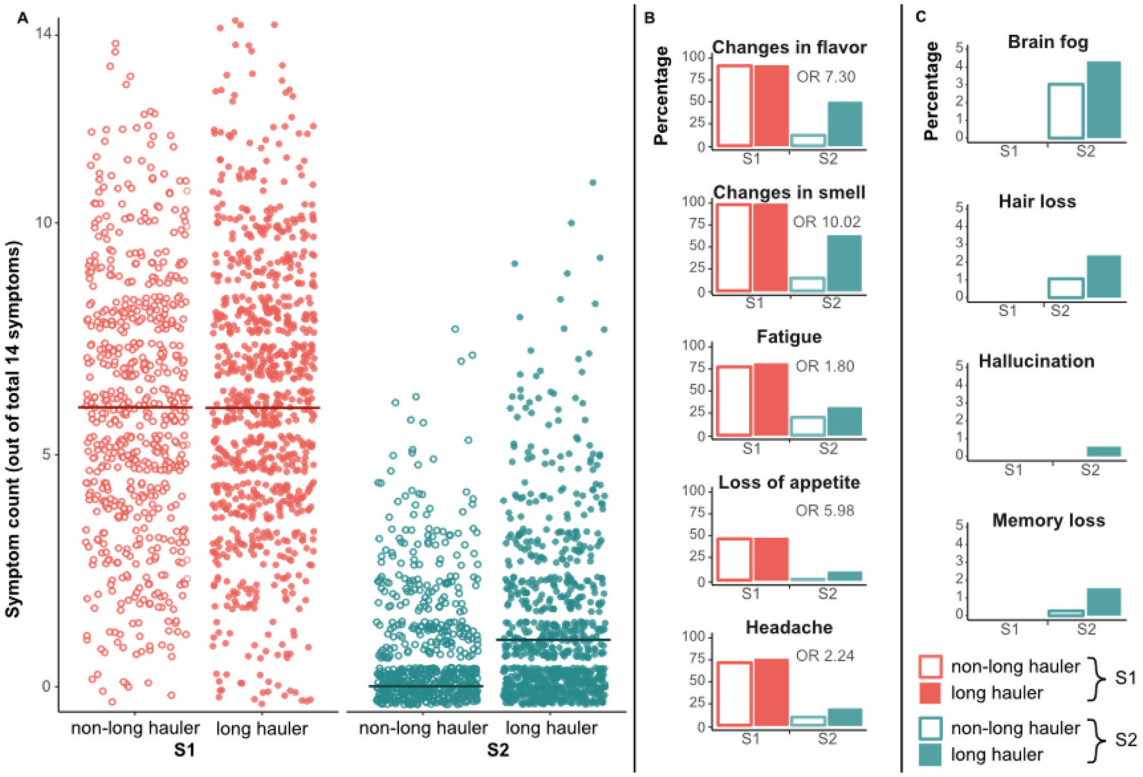

Figure 3.

A: Comparison of overall number of non-chemosensory symptoms at baseline (S1, pink) and follow-up (S2, green), stratified by smell long-hauler (LH) status at S2 with white fill indicating non-long haulers and solid fill indicating long-haulers. B: Comparison of selected symptoms at S1 and S2 stratified by smell long-haulers status at S2. C: Percentage of rare symptoms spontaneously mentioned in free text responses in English, Spanish, Dutch, Italian, and French.

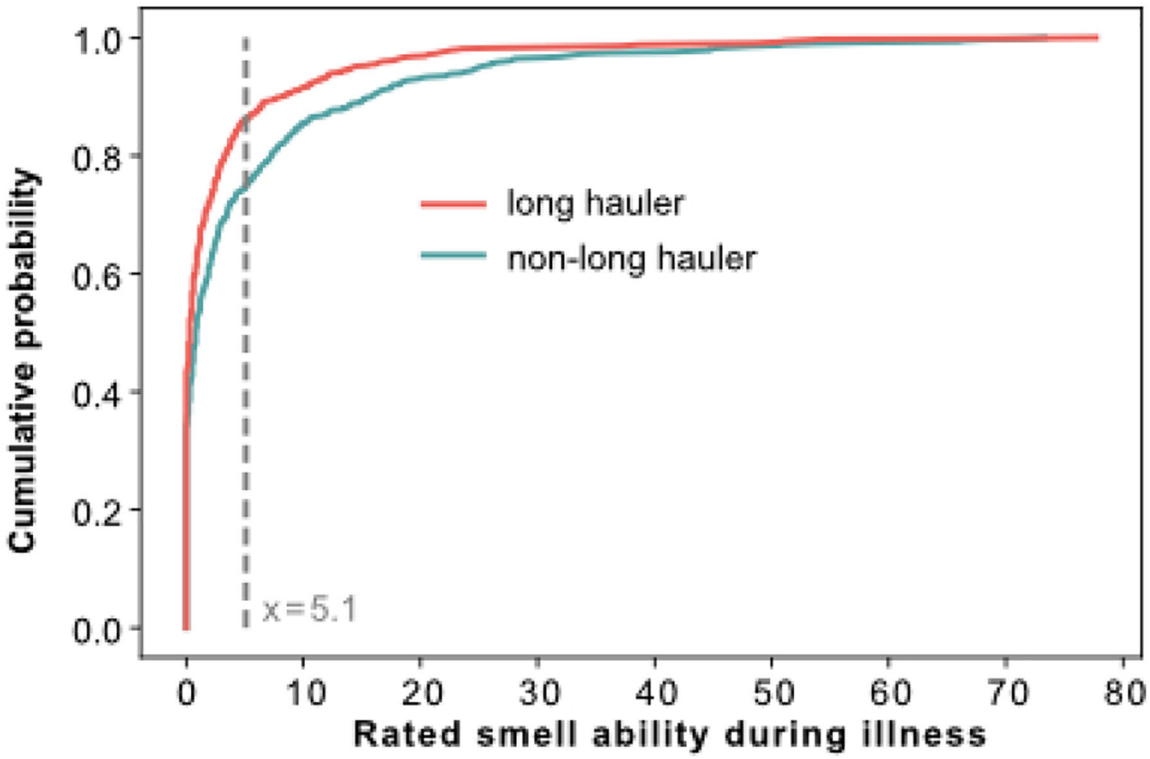

Figure 4.

Distribution of ratings for smell ability at baseline (S1), stratified by whether a participant was classified as a smell long-hauler (pink) or non long-hauler (green) at follow-up (S2). In the original survey (i.e., baseline), the majority of both groups (i.e., more than 50%) reported complete smell loss (a score of zero on a VAS, shown on the x-axis); however, a greater proportion of those who would later become long haulers reported almost complete loss at S1, and fewer of the non long haulers reported near total loss at S1. The dashed vertical line indicates the smell ability rating (on a VAS from 0–100) where the two groups differ maximally.

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Table 1.

Descriptive data of all participants and the smell long-hauler (LH) and no smell long-hauler (nLH) groups.

Categorical variables	All		LH		nLH		statistics				
	%	n	%	n	%	n	Chi2	p	OR	CI low	CI high
Prior conditions											
High blood pressure	8.24	121	7.67	65	9.03	56	0.71	0.398	0.84	−0.14	0.05
Heart disease	0.41	6	0.59	5	0.16	1	0.73	0.392	3.67	−0.13	0.64
Diabetes	2.04	30	1.89	16	2.26	14	0.10	0.757	0.83	−0.24	0.15
Obesity	8.99	132	9.79	83	7.90	49	1.33	0.248	1.26	−0.03	0.15
Lung disease (asthma / copd)	5.11	75	5.31	45	4.84	30	0.08	0.778	1.10	−0.10	0.14
Head trauma	0.14	2	0.24	2	0.00	0	0.24	0.621	Inf	0.15	0.70
Neurological disease	0.68	10	0.94	8	0.32	2	1.23	0.268	2.94	−0.08	0.52
Cancer (chemo-therapy)	0.14	2	0.12	1	0.16	1	0.00	1.000	0.73	−0.85	0.69
Cancer (no chemo-therapy)	0.14	2	0.24	2	0.00	0	0.24	0.621	Inf	0.15	0.70
Chronic sinus problems	4.02	59	3.42	29	4.84	30	1.52	0.218	0.70	−0.23	0.05
Seasonal allergies/hay fever	16.42	241	16.27	138	16.61	103	0.01	0.919	0.98	−0.08	0.06
No conditions	60.15	883	59.79	507	60.65	376	0.08	0.781	0.96	−0.06	0.04
Gender							18.87	7.98E-05			
Women	75.68	1111	60.85	676	39.15	435					
Men	24.25	356	48.03	171	51.97	185					
Non-binary	0.07	1	100.00	1	0.00	0					
Language							30.30	4.26E-06			
Dutch		9.13	134	64.93	87	35.07	47				
English		37.74	554	62.27	345	37.73	209				
French		33.65	494	47.98	237	52.02	257				
Italian		6.81	100	66.00	66	34.00	34				
Spanish		12.67	186	60.75	113	39.25	73				
	mean	SD	mean	SD	mean	SD	t-test	p		CI lo	CI hi
Age in years	43.89	12.17	44.37	12.16	43.23	12.18	−1.76	0.078		−2.40	0.13

Table 2.

Cumulative percentage of participants who recovered their pre-illness ability to smell or taste by months from the onset of disease.

Time in months	2	3	4	5	6	7	8	9	10	11
Smell										
Women	0.18	1.26	2.43	4.05	6.66	12.69	27.27	29.43	35.37	39.15
Men	0.28	1.68	3.93	6.17	9.26	14.88	35.95	37.92	45.22	51.96
Taste										
Women	0.27	1.89	3.87	5.94	10.08	18.72	39.33	43.20	51.93	56.07
Men	0.56	2.24	4.77	7.30	11.23	18.53	45.78	48.31	58.70	64.88