Clinical factors associated with lower health scores in COVID-19–related persistent olfactory dysfunction

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Abstract
Background: Patients with persistent COVID-19 olfactory dysfunction (OD) commonly report parosmia. Understanding the impact of COVID-19 OD and parosmia is critical to prioritizing research and interventions. In this study we investigate the impact of parosmia and other clinical and disease characteristics on health state utility values (HUVs) for those with persistent COVID-19 OD.

Methods: Patients with a history of COVID-19 diagnosis and persistent OD were recruited from a tertiary medical center and a social media support forum for chemosensory dysfunction. Clinical characteristics and disease-specific symptoms were obtained along with self-reported history of smell function and presence of parosmia. HUVs were calculated using indirect (EuroQol 5-Dimension [EQ-5D]) and direct (VAS) measures.

Results: Our study included 286 subjects (75.52% women) with persistent COVID-19–related OD. Results (mean ± standard deviation) of HUVs based on EQ-5D and VAS were 0.81 ± 0.14 and 0.73 ± 0.21, respectively. Mean self-reported smell function (on a 0-10 scale) was 9.67 ± 1.25 pre–COVID-19, 0.93 ± 2.34 at diagnosis, and 3.39 ± 2.32 at most current assessment. A total of 89.16% of the subjects reported parosmia and 24.13% sought medical care for anosmia. Seeing an MD for OD (p < 0.001), female gender (EQ-5D only, p = 0.002), a history of chronic pain (p < 0.05) and depression/anxiety (EQ-5D only, p < 0.001) predicted worse health. Parosmia and persistent symptoms, such as shortness of breath, were associated with lower EQ-5D and VAS scores, but did not independently predict poorer health scores on multivariable analysis.

Conclusion: Persistent COVID-19 OD results in health states comparable to other chronic diseases.

Keywords COVID-19, health utility values, parosmia, persistent olfactory dysfunction, quality of life

Persistent olfactory dysfunction (OD) has become a common COVID-19 “long-hauler” symptom affecting nearly 25% of patients who presented with olfactory loss during their COVID-19 infection.1–4 Parosmia, a qualitative form of OD characterized by the distortion of odors,5 has become a frequent characteristic of post–COVID-19 OD and is typically associated with an unpleasant scent that can be described as foul, rotten, sewage, or
The prevalence of temporary parosmia was found to be 4% in the general population, and 56% following postviral etiologies of olfactory loss. After COVID-19, the prevalence of parosmia may be even higher, as reported by some groups to be 43.1% to 74.9%, presenting at a median interval of 2.5 months from the onset of OD.

Parosmia is thought to be a sign of active but impaired reinnervation of the olfactory bulb by peripheral olfactory neurons. However, its value as a prognosticator of recovery of OD is controversial, with some suggesting it carries a positive prognostic sign and others finding no impact on gradual chemosensory recovery. Therapeutic options for parosmia remain scarce, with some preliminary evidence favoring olfactory training and the use of intranasal sodium citrate.

Given our paucity of knowledge on parosmia despite its high prevalence, there is a need for understanding the valuation of parosmia and persistent OD in a person’s overall health. Studies have demonstrated that parosmia has a negative impact on quality of life (QOL) resulting in social problems and dietary disorders, and COVID-19–related parosmia has been recently found to be associated with poor QOL, as measured by an olfactory-specific QOL assessment (QOD-NS). However, the health state utility values (HUVs) related to parosmia have not been determined. HUVs are individually assessed, health-related QOL measurements, which quantitatively represent a patient’s value on their current health status. HUVs are important general QOL parameters used to compare different disease states and determine resource allocation in health care. This study investigates the clinical and disease characteristics associated with lower HUVs in subjects with persistent COVID-19 OD with a focus on parosmia.

1 | PATIENTS AND METHODS

1.1 | Patient recruitment

University of California San Diego institutional review board approval (IRB #200485X) was obtained for this cross-sectional study conducted from April to May 2021. Participants were identified by either laboratory test–confirmed COVID-19 patients from a single institution consecutively diagnosed between June 2020 and April 2021 or by a social media online support forum for COVID-19–related chemosensory loss (Facebook). Inclusion criteria were: English-speaking adults (>18 years of age) with a history of COVID-19 infection and self-reported persistent OD. Subjects with chemosensory dysfunction due to reasons other than COVID-19 were excluded. Electronic invitations were sent to all subjects to complete an online survey (Qualtrics, Provo, Utah) and informed consent was obtained before the start of the survey. Data including demographics, COVID-19 diagnosis and symptoms, and past medical history were collected along with subjective self-reported smell function at 3 time-points (pre–COVID-19, time of diagnosis, and current) using a visual analog scale (VAS; with 0-10 scoring, where 0 = anosmia and 10 = normal smell). In addition to self-reported persistent OD, subjects were surveyed about their parosmia with the question: “Do you currently have an altered sense of smell due to COVID-19 (aka parosmia)?” HUVs were obtained using indirect (EuroQol 5-Dimension [EQ-5D]) and direct (VAS 0-100 scale) measures.

1.2 | Health utility value assessments

1.2.1 | EuroQol 5-Dimension

The EQ-5D is a generic, standardized measure of health-related QOL consisting of 5 domains: motility, self-care, usual activities, pain/discomfort, and anxiety/depression. Subjects rank the 5 domains as no problem, slight problems, moderate problems, severe problems, and either unable to perform activities or extreme problems. These answer choices correspond to different levels of health status, with the best health level in each domain coded as 1 and the worst health level coded as 5. Survey responses were converted into a single index value using the “EQ-5D-5L Crosswalk Index Value Calculator,” which normalizes the response to a United States–based database ranging from 0 (death) to 1 (best health possible).

1.2.2 | Visual analog scale

Participants were asked to subjectively rate their own health status using a sliding scale ranging from 0 to 100, in which 0 corresponds to worst imaginable health and 100 corresponds to best health. Each VAS-based HUS was determined by dividing the selected value by 100.

1.3 | Statistical analysis

Statistical analysis was performed with SPSS (Version 27, IBM Corp, Armonk, NY). Chi-square analysis and Kruskal-Wallis test were performed. Univariate linear regression analysis was performed to determine predictors of HUVs. Multivariate linear regression analysis was conducted for predictors of HUVs identified by univariate analysis with $p < 0.1$. $p < 0.05$ was considered statistically significant.
TABLE 1
Demographics and clinical characteristics of participants with persistent COVID-19–associated olfactory dysfunction

| Variable                                | N   | %    |
|-----------------------------------------|-----|------|
| Age (mean, SD)                          | 37.1| 13.08|
| Group                                   |     |      |
| Medical center                          | 101 | 35.32|
| Social media                            | 185 | 64.69|
| Gender                                  |     |      |
| Male                                    | 52  | 18.18|
| Female                                  | 216 | 75.52|
| Gender diverse                          | 1   | 0.35 |
| Ethnicity                               |     |      |
| Hispanic                                | 37  | 12.94|
| White, non-Hispanic                     | 194 | 67.83|
| Black, non-Hispanic                     | 6   | 2.10 |
| 2 or more races                         | 17  | 5.94 |
| Asian or Pacific Islander               | 17  | 5.94 |
| American Indian or Alaskan Native       | 1   | 0.35 |
| PMH                                     |     |      |
| Diabetes                                | 8   | 2.80 |
| Heart disease                           | 1   | 0.35 |
| High blood pressure                     | 30  | 10.49|
| Chronic lung disease                    | 6   | 2.10 |
| Chronic kidney disease                  | —   | —    |
| Cancer                                  | 2   | 0.70 |
| Chronic pain                            | 12  | 4.20 |
| Bleeding disorder                       | 2   | 0.70 |
| Liver disease                           | 3   | 1.05 |
| Sinus disease                           | 3   | 1.05 |
| Allergies                               | 70  | 24.48|
| Other immunosuppressed conditions       | 6   | 2.10 |
| History of head trauma                  | 4   | 1.40 |
| Neurologic disease                      | 4   | 1.40 |
| Depression/anxiety                      | 67  | 23.43|
| Parosmia                                |     |      |
| No                                      | 31  | 10.84|
| Yes                                     | 255 | 89.16|
| Duration of parosmia                    |     |      |
| <1 month                                | 46  | 16.1 |
| 1-3 months                              | 114 | 39.9 |
| 4-6 months                              | 96  | 33.6 |
| 6-9 months                              | 11  | 3.85 |
| 9-12 months                             | 5   | 1.75 |
| >12 months                              | 3   | 1.05 |
| VAS smell (mean, SD)                    |     |      |
| Before COVID                            | 9.67| 1.25 |
| During COVID                            | 0.934| 2.34 |

SD - standard deviation; PMH - past medical history; VAS - visual analog scale; HUV- health utility value. MD - Medical Doctor.

2 | RESULTS

A total of 286 participants with persistent OD related to COVID-19 were enrolled in this study: 185 (64.69%) from a COVID-19 anosmia/parosmia social media group and the remaining subjects from an academic institution’s COVID-19 registry. Table 1 summarizes the demographics and clinical characteristics of the participants in the study. Age (mean ± standard deviation [SD]) was 37.15 ± 13.08 and women accounted for 75.52% of the respondents. Most participants in this study were not hospitalized for their COVID-19 infection (94.41%) and did not seek medical care for their chemosensory dysfunction (75.18%). Parosmia was reported by 89.16% of the participants. Self-reported smell function (VAS) before, during, and after COVID-19 infection was 9.67, 0.93, and 3.39, respectively (Table 1). HUV scores (mean ± SD), as measured by the VAS and EQ-5D, were 0.73 ± 0.21 and 0.81 ± 0.14, respectively.

We evaluated the impact of demographic and clinical factors on self-reported health in those with persistent COVID-19 OD (Table 2). Women reported worse health-related QOL compared with men (EQ-5D: 0.79 vs 0.88,
**TABLE 2** EQ-5D and VAS health values based on demographic and clinical variables (univariate linear regression)

| Variable                          | EQ-5D Mean | SD    | p Value   | VAS Mean | SD    | p Value |
|-----------------------------------|------------|-------|-----------|----------|-------|---------|
| **Group**                         |            |       | <0.001a   |          |       | <0.001a |
| Medical center                    | 0.867      | 0.127 | 0.796     | 0.139    |       |         |
| Social media                      | 0.778      | 0.144 | 0.690     | 0.232    |       |         |
| **Time of diagnosis**             |            |       |           |          |       |         |
| <1 month ago                      | 0.864      | 0.117 | 0.801     | 0.130    |       |         |
| 1-3 months ago                    | 0.826      | 0.141 | 0.759     | 0.177    |       |         |
| 4-6 months ago                    | 0.796      | 0.155 | 0.705     | 0.225    |       |         |
| 6-9 months ago                    | 0.808      | 0.117 | 0.733     | 0.217    |       |         |
| 9-12 months ago                   | 0.724      | 0.097 | 0.673     | 0.303    |       |         |
| >12 months ago                    | 0.787      | 0.103 | 0.700     | 0.252    |       |         |
| **Hospitalized**                  |            |       | 0.359     | 0.134    |       |         |
| No                                | 0.812      | 0.142 | 0.735     | 0.204    |       |         |
| Yes                               | 0.767      | 0.194 | 0.624     | 0.227    |       |         |
| **Symptoms**                      |            |       |           |          |       |         |
| Cough                             | 0.794      | 0.159 | 0.387     | 0.694    | 0.223 | 0.232   |
| Fever                             | 0.775      | 0.149 | 0.115     | 0.704    | 0.198 | 0.489   |
| Fatigue                           | 0.775      | 0.141 | <0.001a   | 0.677    | 0.223 | <0.001a |
| Shortness of breath               | 0.740      | 0.146 | <0.001a   | 0.629    | 0.212 | <0.001a |
| Diarrhea                          | 0.762      | 0.144 | 0.056     | 0.674    | 0.249 | 0.139   |
| Headaches                         | 0.760      | 0.155 | <0.001a   | 0.694    | 0.231 | 0.108   |
| Nasal congestion                  | 0.788      | 0.156 | 0.144     | 0.714    | 0.216 | 0.571   |
| “Brain fog”/confusion             | 0.754      | 0.147 | <0.001a   | 0.653    | 0.237 | <0.001a |
| Muscle aches/Joint pain           | 0.766      | 0.151 | 0.001a    | 0.676    | 0.259 | 0.017a  |
| Runny nose                        | 0.812      | 0.145 | 0.869     | 0.723    | 0.213 | 0.904   |
| Sore throat                       | 0.772      | 0.142 | 0.060     | 0.667    | 0.225 | 0.038a  |
| Nausea or vomiting                | 0.735      | 0.169 | 0.004a    | 0.620    | 0.252 | 0.009a  |
| Seen MD for anosmia               |            |       | <0.001a   |          |       | <0.001a |
| No                                | 0.830      | 0.141 | 0.756     | 0.184    |       |         |
| Yes                               | 0.744      | 0.135 | 0.632     | 0.257    |       |         |
| **Parosmia**                      |            |       | 0.028a    | 0.016a   |       |         |
| No                                | 0.865      | 0.119 | 0.826     | 0.078    |       |         |
| Yes                               | 0.802      | 0.146 | 0.716     | 0.218    |       |         |
| **Duration of parosmia**          | 0.490      |       | 0.530     |          |       |         |
| <1 month                          | 0.839      | 0.132 | 0.772     | 0.144    |       |         |
| 1-3 months                        | 0.806      | 0.145 | 0.714     | 0.208    |       |         |
| 4-6 months                        | 0.800      | 0.155 | 0.724     | 0.231    |       |         |
| 6-9 months                        | 0.819      | 0.123 | 0.709     | 0.246    |       |         |
| 9-12 months                       | 0.730      | 0.077 | 0.630     | 0.277    |       |         |
| >12 months                        | 0.755      | 0.077 | 0.875     | 0.035    |       |         |
| **Gender**                        |            |       | <0.001a   | 0.013a   |       |         |
| Male                              | 0.879      | 0.140 | 0.802     | 0.130    |       |         |
| Female                            | 0.792      | 0.142 | 0.715     | 0.219    |       |         |
| Gender diverse                    | 0.720      |       |           |          |       |         |
| **Age**                           |            |       | 0.039a    | 0.925    |       |         |
| 80-89                             | 0.809      | 0.146 | 0.726     | 0.209    |       |         |

(Continues)
TABLE 2 (Continued)

| Variable                                      | EQ-SD Mean | SD  | p Value | VAS Mean | SD  | p Value |
|-----------------------------------------------|------------|-----|---------|----------|-----|---------|
| Hispanic                                      | 0.853      | 0.128 |         | 0.739    | 0.196 |         |
| White, non-Hispanic                           | 0.807      | 0.148 |         | 0.731    | 0.209 |         |
| Black, non-Hispanic                           | 0.755      | 0.090 |         | 0.690    | 0.288 |         |
| 2 or more races                               | 0.781      | 0.132 |         | 0.751    | 0.197 |         |
| Asian or Pacific Islander                     | 0.781      | 0.164 |         | 0.672    | 0.232 |         |
| American Indian or Alaskan Native             | 0.861      | 0.710 |         |          |      |         |

PMH*:  

| Diabetes                                      | 0.733      | 0.170 | 0.133   | 0.683     | 0.099 | 0.552 |
|-----------------------------------------------|------------|-------|---------|-----------|-------|-------|
| Heart disease                                 | 0.880      | 0.621 | 0.750   | 0.133     | 0.683 | 0.099 |
| High blood pressure                          | 0.796      | 0.124 | 0.616   | 0.714     | 0.172 | 0.751 |
| Chronic lung disease                         | 0.684      | 0.118 | 0.032a  | 0.742     | 0.143 | 0.866 |
| Chronic kidney disease                       | –          | –     | –       | –         | –     | –     |
| Cancer                                       | 0.821      | 0.057 | 0.907   | 0.765     | 0.049 | 0.794 |
| Chronic pain                                 | 0.620      | 0.189 | <0.001a | 0.531     | 0.295 | 0.013a|
| Bleeding disorder                            | 0.869      | 0.011 | 0.557   | 0.700     | 0.141 | 0.860 |
| Liver disease                                | 0.721      | 0.272 | 0.292   | 0.650     | 0.409 | 0.530 |
| Sinus disease                                | 0.759      | 0.076 | 0.548   | 0.673     | 0.127 | 0.663 |
| Allergies                                    | 0.786      | 0.156 | 0.138   | 0.732     | 0.209 | 0.803 |
| Other immunosuppressed conditions            | 0.701      | 0.241 | 0.064   | 0.500     | 0.374 | 0.015a|
| History of head trauma                       | 0.698      | 0.022 | 0.123   | 0.750     | 0.087 | 0.844 |
| Neurologic disease                           | 0.734      | 0.139 | 0.296   | 0.688     | 0.118 | 0.712 |
| Depression/anxiety                           | 0.711      | 0.141 | <0.001a | 0.649     | 0.209 | <0.001a|

*Variables considered binary.

EQ-SD- EuroQol 5-dimension; VAS- visual analog scale; SD- standard deviation; PMH- past medical history; MD- Medical Doctor.

p < 0.01; VAS: 0.72 vs 0.80, p = 0.013). EQ-5D and VAS health values were significantly lower in those who reported having fatigue (p < 0.001, p < 0.001), shortness of breath (p < 0.001, p < 0.001), “brain fog”/confusion (p < 0.001, p < 0.001), and muscle ache/joint pain (p < 0.001, p = 0.017). A history of depression and anxiety was also a predictor of poor self-reported health. Those who sought medical care for their chemosensory dysfunction reported significantly lower HUVs compared with those who did not seek medical advice (EQ-5D: 0.74 vs 0.83, p < 0.001; VAS: 0.63 vs 0.76, p < 0.001). Similarly, belonging to a social media support group for OD was a predictor of lower HUV (p < 0.001).

On multivariate analysis (Table 3), seeing an MD for OD (p < 0.001), female gender (EQ-5D only, p = 0.002), a history of chronic pain (p < 0.05), and depression/anxiety (EQ-5D only, p < 0.001) predicted worse health. The presence of parosmia continued to be associated with worse health, but it failed to reach statistical significance (VAS: p = 0.09; EQ-5D: p = 0.34). Similarly, other persistent symptoms, such as shortness of breath and fatigue, were not independent predictors of lower health scores.

A subgroup analysis of the 2 recruitment groups was also performed (Table 4). Those recruited from the social media group were more likely to have parosmia, seen an MD for OD, experienced longer duration OD, and more likely to be female, compared with those recruited from the medical institution (p < 0.001). The cohort recruited from medical centers were more likely to report other COVID-19 symptoms, including nasal congestion (p = 0.028) and rhinorrhea (p = 0.008). Overall, the social media recruitment group had lower health scores compared with the medical center group (EQ-5D: 0.809 vs 0.867, p < 0.001; VAS: 0.726 vs 0.796, p = 0.002).

In our study population with persistent COVID-19-related OD, 89.9% of participants reported parosmia (Table 5), which was more commonly reported by those recruited from the social media group. Parosmia more commonly affected women (92.1%) than men (80.1%, p = 0.047), but there was no significant difference in
### TABLE 3  Multivariate analysis of demographic and clinical variables that contribute to EQ-5D and VAS scores

|                     | EQ-5D |                      | VAS |                      |
|---------------------|-------|----------------------|-----|----------------------|
|                     |       | 95% CI               |     | 95% CI               |
|                     | B     | SE       | t    | p Value | Lower bound | Upper bound | B     | SE       | t    | p Value | Lower bound | Upper bound |
| **Intercept**       | 0.953 | 0.027    | 35.01| 0.000   | 0.899       | 1.006       | 0.850 | 0.084    | 10.16| 0.000   | 0.685       | 1.015       |
| **Symptoms**        |       |          |      |         |             |             |       |          |      |         |             |             |
| Fatigue             | 0.000 | 0.019    | 0.004| 0.997   | −0.038      | 0.038       | −0.045 | 0.032    | −1.388| 0.167   | −0.108      | 0.019       |
| Shortness of breath | −0.040| 0.021    | −1.915| 0.057   | −0.082      | 0.001       | −0.046 | 0.035    | −1.306| 0.193   | −0.115      | 0.023       |
| Diarrhea            | 0.022 | 0.029    | 0.742| 0.459   | −0.036      | 0.079       | −0.051 | 0.031    | −1.652| 0.100   | −0.113      | 0.010       |
| Headaches           | 0.004 | 0.020    | 0.196| 0.845   | −0.036      | 0.044       | 0.019  | 0.035    | 0.539 | 0.590   | −0.050      | 0.088       |
| “Brain fog”/confusion | −0.033| 0.018    | −1.782| 0.076   | −0.069      | 0.003       | −0.037 | 0.037    | −1.023| 0.307   | −0.109      | 0.035       |
| Muscle aches/joint pain | −0.017| 0.021    | −0.778| 0.438   | −0.059      | 0.026       | −0.021 | 0.045    | −0.462| 0.645   | −0.109      | 0.068       |
| Sore throat         | −0.021| 0.023    | −0.905| 0.367   | −0.066      | 0.025       |       |          |      |         |             |             |
| Nausea or vomiting  | −0.029| 0.028    | −1.037| 0.301   | −0.083      | 0.026       |       |          |      |         |             |             |
| **Seen MD for anosmia** | | | | | | | | | | | | |
| No                  | Ref.  |          |      |         |             |             | Yes   | 0.029    | 3.899 | <0.001*| −0.169      | −0.056       |
| Yes                | −0.074| 0.017    | −4.236| <0.001* | −0.109      | −0.040      | −0.073 | 0.043    | −1.706| 0.090   | −0.157      | 0.011       |
| **Parosmia**        |       |          |      |         |             |             |       |          |      |         |             |             |
| No                  | Ref.  |          |      |         |             |             | Yes   | Ref.     |      |         |             |             |
| Yes                | −0.024| 0.025    | −0.954| 0.341   | −0.074      | 0.026       | −0.051 | 0.033    | −1.565| 0.119   | −0.116      | 0.013       |
| **Gender**          |       |          |      |         |             |             |       |          |      |         |             |             |
| Male                | Ref.  |          |      |         |             |             | Yes   | Ref.     |      |         |             |             |
| Female             | −0.060| 0.019    | −3.078| 0.002** | −0.098      | −0.021      | −0.170 | 0.081    | −2.107| 0.036* | −0.329      | −0.011       |
| Gender diverse      | 0.037 | 0.131    | 0.282| 0.778   | −0.221      | 0.295       | −0.164 | 0.098    | −1.669| 0.097   | −0.357      | 0.030       |
| **PMH**             |       |          |      |         |             |             |       |          |      |         |             |             |
| Chronic lung disease | 0.009 | 0.059    | 0.144| 0.886   | −0.108      | 0.125       |       |          |      |         |             |             |
| Chronic pain        | −0.173| 0.042    | −4.117| <0.001* | −0.255      | −0.090      |       |          |      |         |             |             |
| Other immunosuppressed conditions | −0.020| 0.052    | −0.390| 0.697   | −0.123      | 0.082       | −0.048 | 0.030    | −1.617| 0.107   | −0.107      | 0.011       |
| Depression/anxiety  | −0.092| 0.018    | −5.018| <0.001* | −0.128      | −0.056      |       |          |      |         |             |             |

*Variables with $p < 0.1$ on univariate linear regression were utilized.

* $p < 0.05$, ** $p < 0.01$.

EQ-5D- EuroQol 5-dimension; VAS- visual analog scale; PMH- past medical history; MD- Medical Doctor.
### TABLE 4  Clinical characteristics and demographics of patients by recruitment group

| Variable                      | Medical center (n = 101) | Social media (n = 185) | Total (n = 286) | Pearson chi-square (p value) |
|-------------------------------|--------------------------|------------------------|-----------------|-----------------------------|
| Time of diagnosis             |                          |                        |                 |                             |
| <1 month ago                  | 24                       | 3                      | 27              | <0.001**                    |
| 1-3 months ago                | 37                       | 27                     | 64              |                             |
| 4-6 months ago                | 38                       | 116                    | 154             |                             |
| 6-9 months ago                | 38                       | 28                     | 154             |                             |
| 9-12 months ago               | 0                        | 4                      | 4               |                             |
| >12 months ago                | 1                        | 7                      | 8               |                             |
| Hospitalized                  |                          |                        |                 | 0.398                       |
| No                            | 97                       | 173                    | 270             |                             |
| Yes                           | 2                        | 7                      | 9               |                             |
| Symptoms                      |                          |                        |                 |                             |
| Cough                         | 27                       | 32                     | 59              | 0.059                       |
| Fever                         | 15                       | 26                     | 41              | 0.854                       |
| Fatigue                       | 43                       | 88                     | 131             | 0.418                       |
| Shortness of breath           | 24                       | 33                     | 57              | 0.231                       |
| Diarrhea                      | 16                       | 18                     | 34              | 0.127                       |
| Headaches                     | 31                       | 57                     | 88              | 0.984                       |
| Nasal congestion              | 37                       | 45                     | 82              | 0.028**                     |
| “Brain fog”/confusion         | 37                       | 58                     | 95              | 0.365                       |
| Muscle aches/joint pain       | 30                       | 53                     | 83              | 0.851                       |
| Runny nose                    | 25                       | 23                     | 48              | 0.008**                     |
| Sore throat                   | 17                       | 30                     | 47              | 0.893                       |
| Nausea or vomiting            | 12                       | 18                     | 30              | 0.570                       |
| Seen MD for anosmia           |                          |                        |                 | <0.001**                    |
| No                            | 94                       | 121                    | 215             |                             |
| Yes                           | 6                        | 63                     | 69              |                             |
| Parosmia                      |                          |                        |                 | <0.001**                    |
| No                            | 21                       | 10                     | 31              |                             |
| Yes                           | 80                       | 175                    | 255             |                             |
| Duration of parosmia          |                          |                        |                 | 0.01*                       |
| <1 month                      | 23                       | 23                     | 46              |                             |
| 1-3 months                    | 42                       | 72                     | 114             |                             |
| 4-6 months                    | 30                       | 66                     | 96              |                             |
| 6-9 months                    | 0                        | 11                     | 11              |                             |
| 9-12 months                   | 0                        | 5                      | 5               |                             |
| >12 months                    | 1                        | 2                      | 3               |                             |
| Gender                        |                          |                        |                 | <0.001**                    |
| Male                          | 31                       | 21                     | 52              |                             |
| Female                        | 63                       | 153                    | 216             |                             |
| Gender diverse                | 0                        | 1                      | 1               |                             |
| Race                          |                          |                        |                 | <0.001**                    |
| Hispanic                      | 23                       | 14                     | 37              |                             |
| White, non-Hispanic           | 53                       | 141                    | 194             |                             |
| Black, non-Hispanic           | 2                        | 4                      | 6               |                             |
| 2 or more races               | 9                        | 8                      | 17              |                             |

(Continues)
TABLE 4 (Continued)

| Variable                             | Medical center (n = 101) | Social media (n = 185) | Total (n = 286) | Pearson chi-square (p value) |
|--------------------------------------|--------------------------|------------------------|----------------|-----------------------------|
| Asian or Pacific Islander            | 8                        | 9                      | 17             |                             |
| American Indian or Alaskan Native    | 0                        | 1                      | 1              |                             |
| PMH                                  |                          |                        |                |                             |
| Diabetes                             | 5                        | 3                      | 8              | 0.103                       |
| Heart disease                        | 0                        | 1                      | 1              | 0.459                       |
| High blood pressure                  | 15                       | 15                     | 30             | 0.075                       |
| Chronic lung disease                 | 5                        | 1                      | 6              | 0.013*                      |
| Chronic kidney disease               | —                        | —                      | —              | —                           |
| Cancer                               | 1                        | 1                      | 2              | 0.663                       |
| Chronic pain                         | 6                        | 6                      | 12             | 0.277                       |
| Bleeding disorder                    | 1                        | 1                      | 2              | 0.663                       |
| Liver disease                        | 1                        | 2                      | 3              | 0.942                       |
| Sinus disease                        | 2                        | 1                      | 3              | 0.253                       |
| Allergies                            | 24                       | 46                     | 70             | 0.836                       |
| Other immunosuppressed conditions    | 2                        | 4                      | 6              | 0.918                       |
| History of head trauma               | 2                        | 2                      | 4              | 0.536                       |
| Neurologic disease                   | 2                        | 2                      | 4              | 0.536                       |
| Depression/anxiety                   | 22                       | 45                     | 67             | 0.628                       |

*p < 0.05. **p < 0.01.
MD-Medical Doctor; PMH - past medical history.

race or age distribution or other clinical characteristics between the 2 groups. Individuals with parosmia reported lower HUVs vs those without parosmia (Table 6) (EQ-5D: 0.802 vs 0.865, p = 0.028; VAS: 0.716 vs 0.826, p = 0.016). However, the duration of the parosmia did not have an impact on health scores. Parosmia impacted health, especially through the EQ-5D subdomains of pain/discomfort (p = 0.021) and anxiety/depression (p = 0.012). The average respondent with parosmia reported that anxiety was a slight to moderate problem (EQ-5D anxiety score [mean ± SD]: 2.433 ± 1.098).

3 | DISCUSSION

In this study we have assessed characteristics associated with lower health scores in those with COVID-19–persistent OD. We have previously shown that those with persistent OD reported lower health-related QOL scores compared with their age-matched population norm.20,21 The health scores of those of with COVID-19–related OD are equivalent to those with chronic rhinosinusitis (CRS) and worse than patients with mild to moderate symptoms of COPD, angina, and asthma.22

In this work we have also investigated the impact of parosmia on HUVs post–COVID-19 infection. Thus far, few studies have characterized the association between COVID-19 OD and parosmia.10,17,23–25 The lack of parosmia literature may be due to the subjective nature of the condition and the difficulty in objective measurement its the severity. Thus, assessing general health utility measures such as EQ-5D and VAS can help shed light on the impact of parosmia on COVID-19 “long-haulers.” Of the 5 EQ-5D domains, subjects in our study with parosmia indicated heightened sensitivity to pain and anxiety. Although parosmia predicted worse health scores on univariate analysis, statistical significance was not achieved in the multivariate analysis (VAS: p = 0.09; EQ-5D: p = 0.34), whereas other variables, including a history of chronic pain, depression, and anxiety, continued to predict poor health. These findings suggest that there are multiple factors that contribute to poor health aside from parosmia, and an understanding of past medical history, in particular mental health status, may be helpful in evaluating overall post–COVID-19 health. On the other hand, there may also be aspects of collinearity across variables that create a challenge in differentiating parosmia from other factors. Given that 94.6% of the social media group reported parosmia, our multivariate model excluded this method of recruitment as a variable due to its collinearity with parosmia. Further studies that employ recruitment from heterogeneous populations, including those with large non-parosmic COVID-19
TABLE 5  Demographic and clinical characteristics associated with parosmia

| Variable                          | Parosmia | No parosmia | Total     | p Value |
|----------------------------------|----------|-------------|-----------|---------|
| Gender                           |          |             |           | 0.047*  |
| Male                             | 42       | 10          | 52        |         |
| Female                           | 199      | 17          | 216       |         |
| Gender diverse                   | 1        | 0           | 1         |         |
| Age, mean                        | 37.2 (13.1) | 37.1 (13.5) | 37.1 (13.1) | 0.994   |
| Race                             |          |             |           | 0.751   |
| Hispanic                         | 35       | 2           | 37        |         |
| White, non-Hispanic              | 171      | 23          | 194       |         |
| Black, non-Hispanic              | 6        | 0           | 6         |         |
| 2 or more races                  | 16       | 1           | 17        |         |
| Asian or Pacific Islander        | 15       | 2           | 17        |         |
| American Indian or Alaskan Native| 1        | 0           | 1         |         |
| PMH                              |          |             |           |         |
| Diabetes                         | 8        | 0           | 8         | 0.317   |
| Heart disease                    | 1        | 0           | 1         | 0.727   |
| High blood pressure              | 28       | 2           | 30        | 0.437   |
| Chronic lung disease             | 5        | 1           | 6         | 0.643   |
| Chronic kidney disease           | 0        | 0           | 0         | NA      |
| Cancer                           | 2        | 0           | 2         | 0.621   |
| Chronic pain                     | 12       | 0           | 12        | 0.217   |
| Bleeding disorder                | 2        | 0           | 2         | 0.621   |
| Liver disease                    | 3        | 0           | 3         | 0.544   |
| Sinus disease                    | 3        | 0           | 3         | 0.544   |
| Allergies                        | 62       | 8           | 70        | 0.855   |
| Other immunosuppressed conditions| 6        | 0           | 6         | 0.388   |
| History of head trauma           | 4        | 0           | 4         | 0.483   |
| Neurologic disease               | 3        | 1           | 4         | 0.359   |
| Depression/anxiety               | 64       | 3           | 67        | 0.056   |
| Time of diagnosis                |          |             |           | <0.001**|
| <1 month ago                     | 14       | 13          | 27        |         |
| 1-3 months ago                   | 60       | 4           | 64        |         |
| 4-6 months ago                   | 141      | 13          | 154       |         |
| 6-9 months ago                   | 28       | 1           | 29        |         |
| 9-12 months ago                  | 4        | 0           | 4         |         |
| >12 months ago                   | 8        | 0           | 8         |         |
| Recruitment group                |          |             |           | <0.001**|
| Medical center                   | 80       | 21          | 101       |         |
| Social media                     | 175      | 10          | 185       |         |
| Hospitalized                     |          |             |           | 0.281   |
| Yes                              | 239      | 31          | 270       |         |
| No                               | 9        | 0           | 9         |         |
| Symptoms                         |          |             |           |         |
| Cough                            | 51       | 8           | 59        | 0.451   |
| Fever                            | 37       | 4           | 41        | 0.810   |

(Continues)
TABLE 5 (Continued)

| Variable                        | Parosmia | No parosmia | Total | \( p \) Value |
|--------------------------------|----------|-------------|-------|---------------|
| Fatigue                        | 120      | 11          | 131   | 0.222         |
| Shortness of breath            | 51       | 6           | 57    | 0.932         |
| Diarrhea                       | 30       | 4           | 34    | 0.853         |
| Headaches                      | 81       | 7           | 88    | 0.295         |
| Nasal congestion               | 71       | 11          | 82    | 0.374         |
| “Brain fog”/confusion          | 85       | 10          | 95    | 0.904         |
| Muscle aches/joint pain         | 72       | 11          | 83    | 0.401         |
| Runny nose                     | 44       | 4           | 48    | 0.540         |
| Sore throat                    | 41       | 6           | 47    | 0.642         |
| Nausea or vomiting             | 26       | 4           | 30    | 0.642         |

Abbreviation: NA, not applicable.

* \( p < 0.05 \), ** \( p < 0.01 \).

PMH- past medical history.

TABLE 6 Distribution of health assessment among EQ-5D dimensions

| EQ-5D total | No parosmia | Parosmia | \( p \) Value |
|-------------|-------------|----------|---------------|
| Mobility    | 1.071 (0.262) | 1.150 (0.475) | 0.481         |
| Self-care   | 1.036 (0.189) | 1.101 (0.385) | 0.419         |
| Usual activities | 1.429 (0.690) | 1.688 (0.935) | 0.212         |
| Pain        | 1.286 (0.535) | 1.721 (0.945) | 0.021*        |
| Anxiety     | 1.929 (1.086) | 2.433 (1.098) | 0.012*        |

Note: Data expressed as mean (standard deviation). Health state utility values are presented for EQ-5D and VAS total, with lower scores indicative of worse health. Conversely, raw scores are presented for the 5 EQ-5D domains (range, 1-5) with higher scores indicative of worse health.

* \( p < 0.05 \).

EQ-5D- EuroQol 5-dimension; VAS- Visual analog scale.

OD control groups, will be useful to better delineate the impact of parosmia on health scores.

Duration of parosmia did not impact health scores despite evidence that COVID-19–related parosmia improves over time. Although the average duration of parosmia is unknown, 2 cross-sectional studies performed showed that most of subjects reported parosmia lasting >3 months.\(^{17,25}\) The prevalence of parosmia was previously reported to be 40% in postviral anosmic/hyposmia patients before COVID-19,\(^{14}\) yet distortion of smell is particularly common after SARS-COV-2 infection and is associated with persistent post–COVID-19 OD.\(^{25}\) In our study, 89.2% of participants with persistent OD reported having parosmia. Among subjects recruited from our medical center’s COVID-19 registry, parosmia was present in 79.2% of those with persistent OD. This percentage is similar to the 74.9%\(^{10}\) reported in another study and may represent a more accurate prevalence of COVID-19–related parosmia. The higher prevalence of parosmia from the social media support group for OD (94.6%) suggests patients with distortion of smell are more likely to seek support and further reflects the elevated QOL disturbance. Our study has shown that, despite most participants reporting parosmia, only 24.1% sought medical attention for their chemosensory dysfunction. Other studies reported that patients with parosmia found it difficult to find medical providers familiar with this condition and struggled to articulate their symptoms and obtain adequate counseling.\(^{26}\) Future research in this area is warranted given its significant impact on health and QOL.

Limitations of this study include its recruitment strategy from a single-institution study and an online social support forum that may reflect a selection bias with those with worse OD electing to participate in the study. There may be recall bias for participants with a longer duration from diagnosis and for survey questions that involved scoring the health status of before and during the COVID-19 infection. The data were obtained from a self-report questionnaire and may include inaccurate reporting. Although only patients with onset of OD at time of COVID-19 infection
were included in the study, the presence of pre-existing medical problems are associated with OD, and unrecognized baseline olfactory loss may be a confounding factor. The 2 methods of recruitment also contributed to a potential sampling bias but were important for us to incorporate the range of impact of COVID-19 on QOL. Our study assessed general health impact utilizing HUVs rather than olfactory-specific QOL impact, as used in previous work.\textsuperscript{17} Future studies with objective olfactory testing and heterogeneous populations may better characterize the contributors to lower health scores in those with COVID-19–associated OD.

In conclusion, individuals with persistent COVID-19 OD report worse health compared with age-matched general population norms. Although approximately three quarters of those with persistent OD related to COVID-19 report parosmia, only a quarter seek medical care for their OD. We identified a higher prevalence of parosmia in those with a history of anxiety and depression. Future studies evaluating the health impact of COVID-19 persistent OD and parosmia and its pathophysiology are essential to promote attention and treatment for this patient population.

**POTENTIAL CONFLICT OF INTEREST**

A.S.D.: consultant for Stryker Endoscopy, speaker’s fees for GSK.

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**How to cite this article:** Said M, Luong T, Jang SS, Davis ME, DeConde AS, Yan CH. Clinical factors associated with lower health scores in COVID-19–related persistent olfactory dysfunction. *Int Forum Allergy Rhinol*. 2022;12:1242–1253. [https://doi.org/10.1002/alr.22978](https://doi.org/10.1002/alr.22978)