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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

burnt.[6] The prevalence of temporary parosmia was found to be 4% in the general population,[7] and 56% following postviral etiologies of olfactory loss.[8] After COVID-19, the prevalence of parosmia may be even higher, as reported by some groups to be 43.1% to 74.9%,[9,10] presenting at a median interval of 2.5 months from the onset of OD.[9]

Parosmia is thought to be a sign of active but impaired reinnervation of the olfactory bulb by peripheral olfactory neurons.[11,12] However, its value as a prognosticator of recovery of OD is controversial, with some suggesting it carries a positive prognostic sign[13] and others finding no impact on gradual chemosensory recovery.[8] Therapeutic options for parosmia remain scarce, with some preliminary evidence favoring olfactory training[14] and the use of intranasal sodium citrate.[15]

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,[6,16] 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).[17] 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.[18] 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).[19]

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.[19]

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
Current	3.39	2.32
HUV (mean, SD)		
VAS	0.726	0.21
EQ-5D	0.809	0.14
Seen MD for olfactory dysfunction		
No	215	75.2
Yes	69	24.1
Hospitalized		
No	270	94.4
Yes	9	3.15
Symptoms		
Cough	59	20.6
Fever	41	14.3
Fatigue	131	45.8
Shortness of breath	57	19.9
Diarrhea	34	11.9
Headaches	88	30.8
Nasal congestion	82	28.7
"Brain fog"/confusion	95	33.2
Muscle aches/joint pain	83	29.0
Runny nose	48	16.8
Sore throat	47	16.4
Nausea or vomiting	30	10.5

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)

	EQ-5D			VAS		
Variable	**Mean**	**SD**	***p* Value**	**Mean**	**SD**	***p* Value**
Group			<0.001[a]			<0.001[a]
Medical center	0.867	0.127		0.796	0.139	
Social media	0.778	0.144		0.690	0.232	
Time of diagnosis			0.215			0.373
<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[a]						
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	<0.001[a]	0.677	0.223	<0.001[a]
Shortness of breath	0.740	0.146	<0.001[a]	0.629	0.212	<0.001[a]
Diarrhea	0.762	0.144	0.056	0.674	0.249	0.139
Headaches	0.760	0.155	<0.001[a]	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	<0.001[a]	0.653	0.237	<0.001[a]
Muscle aches/Joint pain	0.766	0.151	0.001[a]	0.676	0.259	0.017[a]
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	0.038[a]
Nausea or vomiting	0.735	0.169	0.004[a]	0.620	0.252	0.009[a]
Seen MD for anosmia			<0.001[a]			<0.001[a]
No	0.830	0.141		0.756	0.184	
Yes	0.744	0.135		0.632	0.257	
Parosmia			0.028[a]			0.016[a]
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			<0.001[a]			0.013[a]
Male	0.879	0.140		0.802	0.130	
Female	0.792	0.142		0.715	0.219	
Gender diverse	0.720			—	—	
Age	0.809	0.146	0.224	0.726	0.209	0.039[a]
Race			0.340			0.925

(Continues)

TABLE 2 (Continued)

Variable	EQ-5D Mean	EQ-5D SD	EQ-5D *p* Value	VAS Mean	VAS SD	VAS *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[a]						
Diabetes	0.733	0.170	0.133	0.683	0.099	0.552
Heart disease	0.880		0.621	0.750		0.910
High blood pressure	0.796	0.124	0.616	0.714	0.172	0.751
Chronic lung disease	0.684	0.118	0.032[a]	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	<0.001[a]	0.531	0.295	0.013[a]
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	0.015[a]
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	<0.001[a]	0.649	0.209	<0.001[a]

[a]Variables considered binary.

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

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

$p < 0.001$; 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 medial 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[a]

	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	**Intercept**	0.850	0.084	10.16	0.000	0.685	1.015
Symptoms							**Symptoms**						
Fatigue	0.000	0.019	0.004	0.997	−0.038	0.038	Fatigue	−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	Shortness of breath	-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	"Brain fog"/confusion	-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	Muscle aches/joint pain	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	Sore throat	−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	Nausea or vomiting	−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	**Seen MD for anosmia**						
Nausea or vomiting	−0.029	0.028	−1.037	0.301	−0.083	0.026	No	Ref.					
Seen MD for anosmia							Yes	−0.112	0.029	−3.899	<0.001**	−0.169	−0.056
No	Ref.						**Parosmia**						
Yes	−0.074	0.017	−4.236	<0.001**	-0.109	−0.040	No	Ref.					
Parosmia							Yes	−0.073	0.043	−1.706	0.090	−0.157	0.011
No	Ref.						**Gender**						
Yes	−0.024	0.025	−0.954	0.341	−0.074	0.026	Male	Ref.					
Gender							Female	-0.051	0.033	−1.565	0.119	−0.116	0.013
Male	Ref.						**PMH**						
Female	−0.060	0.019	−3.078	0.002**	−0.098	−0.021	Chronic pain	−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	Depression/anxiety	−0.164	0.098	−1.669	0.097	−0.357	0.030
PMH							Other immunosuppressed conditions	−0.048	0.030	−1.617	0.107	−0.107	0.011
Chronic lung disease	0.009	0.059	0.144	0.886	-0.108	0.125	**Age**	0.002	0.001	2.411	0.017*	0.000	0.004
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	$^{*}p < 0.05$, $^{**}p < 0.01$						
Depression/anxiety	−0.092	0.018	−5.018	<0.001**	−0.128	−0.056							

[a]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				<0.001**
<1 month ago	24	3	27	
1-3 months ago	37	27	64	
4-6 months ago	38	116	154	
6-9 months ago	1	28	29	
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

	No parosmia	Parosmia	*p* Value
EQ-5D total			
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.[23] 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 workd.[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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