



# Long-standing gustatory and olfactory dysfunction in COVID-19 patients: a prospective study

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## Abstract

**Purpose** Our study aimed to describe recovery of gustatory dysfunction (GD) and olfactory dysfunction (OD) in COVID-19 patients, and to analyze variables associated with early or late recovery.

**Methods** Telephone surveys were administered during an 18-month follow-up after COVID-19 diagnosis. One hundred and thirty-two included patients rated olfactory and gustatory function at each follow-up.

**Results** One hundred and twenty-nine patients reported GD, of whom 91 (70.5%) reported severe GD, and 99 patients reported OD, of whom 84 (84.9%) reported severe OD. Seventy-two/129 (55.8%) and 52/99 (52.5%) patients reported an improvement in GD and in OD during the first 7 days from the onset, respectively. At 3-month follow-up, 110/120 patients (85.3%) recovered from GD, while 80/99 patients (80.8%) recovered from OD. At 18-month follow-up, a total of 120/129 patients (93.0%) recovered from GD and 86/99 patients (86.9%) recovered from OD; while 10 patients (7.0%) still reported GD and 13 patients (13.1%) still reported OD. Severe GD/OD at presentation were associated with late complete recovery of taste/smell ( $p = 0.019$  and  $p = 0.034$ , respectively). Improvement over the first 7 days from onset was significantly associated with faster recovery ( $p < 0.001$ ).

**Conclusions** More than 80% of patients reported complete recovery of olfactory/gustatory function in the first 3 months after symptom onset. At 18-month follow-up, patients reporting complete recovery of gustatory and olfactory function were 93% and 87%, respectively. Severity of chemosensory dysfunction at the onset was negatively correlated to recovery, and improvement of taste and/or smell function within the first 7 days from symptom onset was significantly associated with early resolution.

**Keywords** COVID-19 · Taste · Smell gustatory dysfunction · Olfactory dysfunction

## Introduction

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, the scientific community has dedicated to studying the effects and mortality rate of

SARS-CoV-2 infection in the population and their consequences on public health issues [1–5]. Among minor symptoms of COVID-19, the prevalence of gustatory dysfunction (GD) and olfactory dysfunction (OD) was estimated to be around 50% [6–8]. Given the global burden of COVID-19 in the last 2 years, this translates into a considerable number of patients seeking medical attention for GD and OD. The pathogenesis of chemosensory dysfunction in COVID-19 has been explained by the neurotropism of coronaviruses and is consistent with the presence of additional mild neurological symptoms in COVID-19 [9]. A few studies exist on the evolution and recovery of COVID-19-related chemosensory dysfunction in the intermediate and long term. Due to the impact of GD and OD on the quality of life of patients, it is mandatory to better define the characteristics, clinical course, and recovery times of chemosensory dysfunctions

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in COVID-19, to properly counsel patients during medical visits as well as to conceive new therapeutic strategies to address the problem.

The aim of this study was to describe the recovery pattern of GD and OD in a cohort of COVID-19 patients with an 18-month follow-up and to analyze the possible variables associated with spontaneous early or late recovery.

## Methods

### Study population

This is a prospective observational cohort study on COVID-19 patients admitted to a single Academic Institution in the North of Italy from March 5 to March 23, 2020. Inclusion criteria were the presence of SARS-CoV-2 infection on nasopharyngeal swab polymerase chain reaction [10], and GD and/or OD related to COVID-19.

Patients were interviewed on the evolution of SARS-CoV-2 related GD and OD over time. All interviews were carried out by telephone. The surveys were administered at the time of COVID-19 diagnosis and then 1, 3, 6, 9, 12, and 18 months from the onset of COVID-related OD/GD. The dates on which patients reported their gustatory and/or olfactory function to be returned to the baseline were recorded, when applicable. Patients who were either unable to answer (intubated, receiving noninvasive ventilatory assistance, or deceased) or unreachable by telephone were excluded from the study. Informed consent was obtained before enrollment. The study was approved by our local ethics committee (Protocol Number: 1363).

Medical history and general symptoms related to SARS-CoV-2 infection were collected for each patient. No patient reported any history of chronic or recurrent sinusitis. Olfactory and gustatory function were investigated. All interviewed patients were asked to rate the quality of their sense of taste and smell as “good”, “average”, “mildly impaired”, “moderately impaired”, “severely impaired”, or “totally absent” (which corresponded to a score of 5, 4, 3, 2, 1, or 0 points, respectively). Such score was recorded at the first survey and then at 1, 3, 6, 9, 12, and 18 months from the onset of the dysfunction. Patients were also asked to assess their gustatory and olfactory function at the baseline (i.e., before the COVID-19 outbreak) with the same method and to describe whether they experienced any improvement in gustatory and/or olfactory function within the first 7 days from the onset of the symptom. Scores 5–4 were considered normal. GD and/or OD were defined as “mild to moderate” (scores 3–2) or “severe to complete” (scores 1–0). Patients were asked to report the presence of parosmia. Loss/

reduction of taste was investigated for the five basic tastes: sweet, salty, bitter, sour, and umami. In the evaluation of the gustatory function, patients were also interviewed about the trigeminal sensations, defined as spiciness, fizzy feeling, cooling, or tingling sensation in the oral cavity. No specific therapy for OD/GD was administered to any patient. SARS-CoV-2 positivity duration was described as the number of days elapsing from the SARS-CoV-2-positive nasopharyngeal swab to the date of the first of two consecutive negative swabs.

### Statistical analysis

Categorical variables were expressed as numbers and percentages, and continuous variables were expressed as means and standard deviations (SD) or medians and ranges, as appropriate. Kaplan–Meier curves were used to estimate the time to recovery for olfactory and/or gustatory functions, considering complete recovery as an endpoint. The variables used to carry out univariate logistic regression analysis to explore the presence of possible associations with the duration of the OD/GD were the following: gender, age, BMI, smoking history, presence of nasal obstruction, OD and/or GD, and their severity at the time of the recruitment, SARS-CoV-2 positivity duration, and improvement in smell and/or taste within the first 7 days from the onset. A *p* less than 0.05 was considered as significant. All analyses were done with Stata software, version 16 (StataCorp, LLC, TX, USA).

## Results

Out of 135 eligible patients, 132 were included in the study, while 3 were excluded because lost to follow-up. The study population included 74 female (56.1%) and 58 male (43.9%) patients. Mean age was 49.2 years (SD 13.8). All patients developed COVID-19 in a mild-to-moderate form and have subsequently recovered completely. Patient characteristics are summarized in Table 1. Ninety-six patients (72.7%) reported both OD and GD during COVID-19, while 33 (25%) and 3 (2.3%) reported only GD and only OD, respectively. Among the 129 patients who suffered from GD, 110 (85.3%) reported a reduction in the perception of all five basic tastes (sweet, salty, bitter, sour, and umami), and 39 (30.2%) patients reported dysgeusia, while 123 (95.3%) reported reduction in trigeminal sensations also. Among the 99 who suffered from OD, 4 (4.04%) reported the presence of parosmia. Nasal obstruction was reported by 60 out of 132 patients (45.6%), including 18 (13.6%) with severe nasal obstruction. The median SARS-CoV-2 positivity in our sample was 29 days (range 7–84).

**Table 1** Patients' demographics and clinical characteristics

	Mean	SD
Age (years)	49.2	13.8
BMI (kg/m <sup>2</sup> )	25.9	4.2
	No. of patients ( <i>N</i> = 132)	%
Sex		
Female	74	56.1
Male	58	43.9
Smoking history		
Never smokers	87	65.9
Former smokers	36	27.3
Current smokers	8	6.1
Comorbidities		
Hypertension	24	18.2
Allergies	24	18.2
Allergy to inhalants	18	13.6
Diabetes	9	6.8
Cancer	8	6.1
Dyslipidemia	8	6.1
Asthma	7	5.3
Cardiovascular disease	6	4.5
Chronic obstructive pulmonary disease	5	3.8
COVID-19 general symptoms		
Fever	110	83.3
Dry cough	89	67.4
Myalgia or arthralgia	70	53.0
Headache	38	28.8
Dyspnea	29	22.0
Diarrhea	17	12.9
Fatigue	13	9.8
Nausea or vomiting	8	6.1
Pharyngodynia	2	1.5
COVID-19 specific symptoms		
Taste dysfunction	129	97.7
Smell dysfunction	99	75.0
Both taste and smell dysfunction	96	72.7
Nasal obstruction	60	45.6
Severe nasal obstruction	18	13.6
Taste dysfunction	No. of patients ( <i>N</i> = 129)	%
Severe taste dysfunction	91	70.5
Reduction in all 5 basic tastes	110	85.3
Reduction in sweet sensation	114	88.4
Reduction in salty sensation	108	83.7
Reduction in bitter sensation	116	89.9
Reduction in sour sensation	113	87.6
Reduction in umami sensation	116	89.9
Dysgeusia	39	30.2
Reduction in trigeminal sensations	123	95.3
Smell dysfunction	No. of patients ( <i>N</i> = 99)	%
Severe smell dysfunction	84	63.6

**Table 1** (continued)

Smell dysfunction	No. of patients ( <i>N</i> =99)	%
Parosmia	4	4.0
	Median (days)	Range
Taste dysfunction onset with respect to general symptoms	+2	–3 to +15
Taste dysfunction onset with respect to COVID-19 diagnosis	–4	–18 to +7
Smell dysfunction onset with respect to general symptoms	+2	–3 to +10
Smell dysfunction onset with respect to COVID-19 diagnosis	–3	–18 to +7
SARS-CoV-2 positivity at nasopharyngeal swab	29	7 to 84

Among the 129 patients with GD, the average taste score during COVID-19 was 0.8 (SD 1.0); in particular, 91 (70.5%) out of those 129 patients reported severe-to-complete loss of taste (scores 0–1). Among the 99 patients with OD, the average smell score during COVID-19 was 0.4 (SD 0.8); in particular, 84 (84.9%) out of those 99 patients reported severe-to-complete loss of smell (scores 0–1). Patients who suffered from GD scored their pre-COVID-19 baseline taste with an average score of 5.0 (SD 0.2), while the average smell score in patients who suffered from OD during COVID-19 was 4.9 (SD 0.3) at baseline. Among the 129 patients who reported GD, 72 (55.8%) reported an improvement in gustatory function within the first 7 days from the onset of the symptom, while among the 99 patients who reported OD, 52 (52.5%) reported an improvement in olfactory function within the first 7 days from the onset. At 1-month follow-up, 79 out of 129 (61.2%) reported normal gustatory function, while 53 out of 99 patients (53.5%) reported normal olfactory function. At 3-month follow-up, further 31 (24.0%) reported normal gustatory function, while further 27 (27.3%) reported normal olfactory function. Therefore, after 3 months, a total of 110 patients out of 120 (85.3%) recovered from GD, while 80 patients out of 99 (80.8%) recovered from OD. At 18-month follow-up, further 10 patients (7.8%) reported normal gustatory function, while further 6 patients (6.1%) reported normal olfactory function. Therefore, after 18 months, a total of 120 patients out of 129 (93.0%) recovered from GD, while 86 patients out of 99 (86.9%) recovered from OD. At 18-month follow-up, 10 patients (7.0%) still reported GD, while 13 patients (13.1%) still reported OD. The average taste score at 18-month follow-up was 4.8 (SD 0.7), while the average smell score at 18-month follow-up was 4.6 (SD 0.9). Table 2 shows recovery rates of gustatory and olfactory function and taste/smell scores at different time points. Among the 13 patients who reported OD at 18-month follow-up, 3 patients reported parosmia (23.1%). Kaplan–Meier curves reporting the recovery pattern of olfactory and gustatory function are shown in Fig. 1. At univariate analysis, a late complete recovery in gustatory function was associated with the presence of

severe GD ( $p=0.019$ ), while a late complete recovery in olfactory function was associated with the presence of severe OD at presentation ( $p=0.034$ ). The presence of OD, and in particular severe OD, was significantly associated with a longer time to complete recovery of gustatory function ( $p=0.020$  and  $p=0.006$ , respectively). An improvement in gustatory/olfactory function over the first 7 days from the onset of the dysfunction was significantly associated with a faster recovery of taste/smell ( $p<0.001$ ). The presence of nasal obstruction, to any degree, was associated with neither a fast nor a late recovery from GD and/or OD ( $p=0.246$  and  $p=0.226$ , respectively). SARS-CoV-2 positivity duration, age, sex, BMI, and smoking status did not influence the recovery pattern of gustatory/olfactory function (Table 3).

## Discussion

In this study, we presented 18-month follow-up data in a cohort of COVID-19 patients who reported GD and/or OD. The primary objectives were to evaluate the rate and timing of resolution of chemosensory dysfunction, including both taste and smell, and to investigate those factors associated with an early or late recovery. As previously reported, severe nasal obstruction was only present in a minority of COVID-19 patients presenting with GD and/or OD and, furthermore, GD and OD were early symptoms, frequently appearing among the first COVID-19 manifestations [6]. Most patients also reported a decrease in trigeminal sensations, which may constitute a negative predictive factor for the recovery of olfactory and gustatory function, as demonstrated in a previous study, where self-reported severe impairment of trigeminal nasal sensation at was associated with a lower rate of olfactory recovery at 6-month follow-up [11]. About 50% of patients reported improvement in taste and/or smell function within the first 7 days. Kaplan–Meier curves relative to GD and OD in the study population showed a rapid recovery during the first weeks, with a flattening of the curve between the second and third month from the symptom onset, both

**Table 2** Recovery rate of gustatory and olfactory function with taste and smell scores at different time points

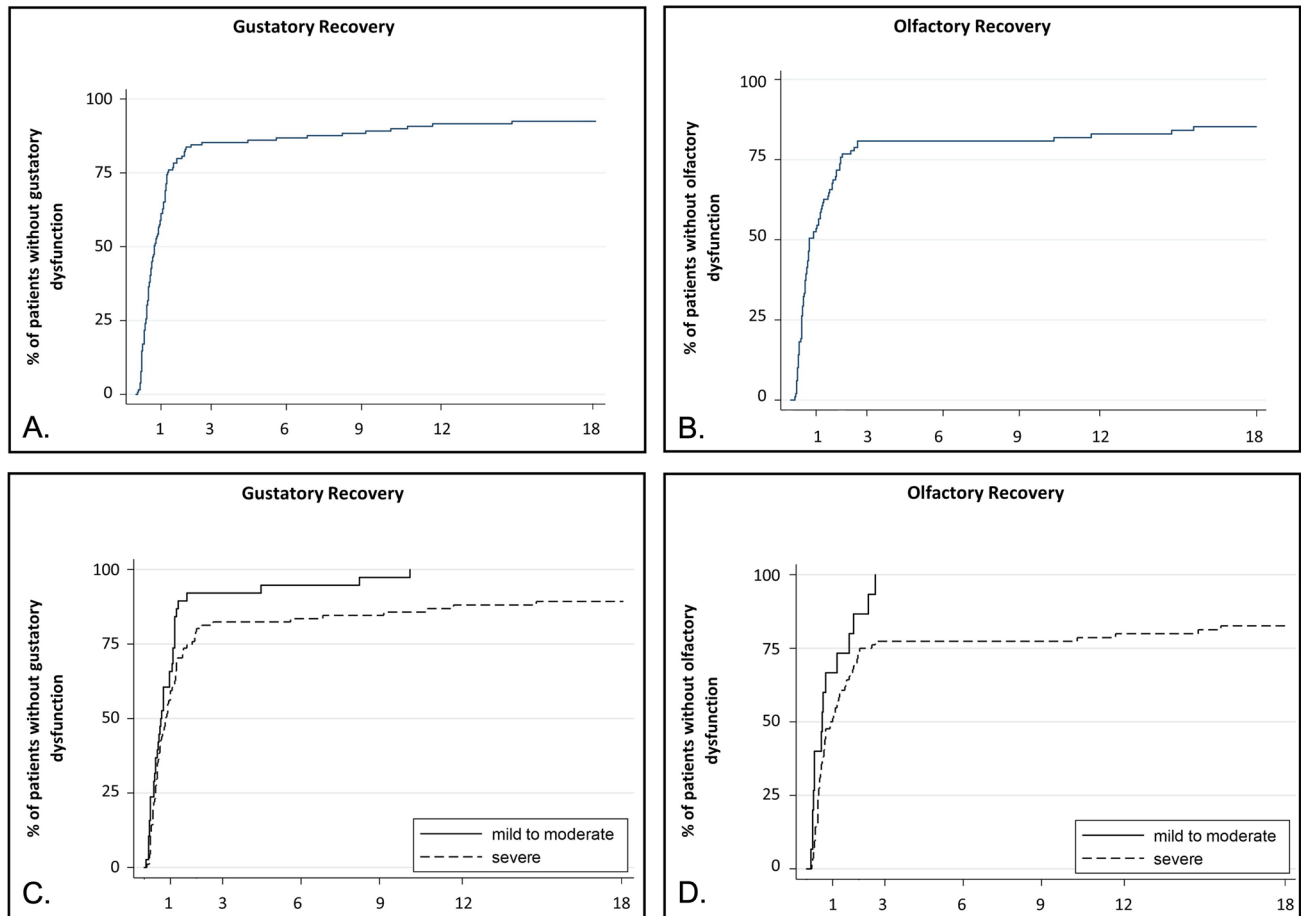
Gustatory dysfunction (GD)							
	No. of patients (N= 129)	%		Average	SD	Median	Range
			Pre-COVID-19 taste score	5.0	0.2	5	4–5
			Taste score during COVID-19	0.8	1.0	0	0–4
Taste improvement in the first 7 days from the onset	72	55.8					
Taste recovery at 1-month follow-up	79	61.2	Taste score at 1-month follow-up	4.0	1.5	5	0–5
Taste recovery at 3-month follow-up	31	24.0	Taste score at 3-month follow-up	4.7	1.0	5	0–5
Taste recovery at 6-month follow-up	2	1.6	Taste score at 6-month follow-up	4.8	0.8	5	0–5
Taste recovery at 9-month follow-up	2	1.6	Taste score at 9-month follow-up	4.8	0.6	5	1–5
Taste recovery at 12-month follow-up	5	3.9	Taste score at 12-month follow-up	4.8	0.8	5	1–5
Taste dysfunction present at 12-month follow-up	10	7.8					
Olfactory dysfunction (OD)							
	No. of patients (N= 99)	%		Average	SD	Median	Range
			Pre-COVID-19 smell score	4.9	0.3	5	4–5
			Smell score during COVID-19	0.4	0.8	0	0–3
Smell improvement in the first 7 days from the onset	52	52.5					
Smell recovery at 1-month follow-up	53	53.5	Smell score at 1-month follow-up	3.6	1.8	5	0–5
Smell recovery at 3-month follow-up	27	27.2	Smell score at 3-month follow-up	4.4	1.3	5	0–5
Smell recovery at 6-month follow-up	0	0.0	Smell score at 6-month follow-up	4.3	1.3	5	0–5
Smell recovery at 9-month follow-up	0	0.0	Smell score at 9-month follow-up	4.5	1.0	5	0–5
Smell recovery at 12-month follow-up	4	4.0	Smell score at 12-month follow-up	4.5	1.1	5	0–5
Smell dysfunction present at 12-month follow-up	15	15.2					

for GD and OD. By the third month of follow-up, more than 80% of patients recovered their sense of taste and smell, while at 18-month follow-up, 93% of patients recovered their sense of taste and 87% recovered their sense of smell. Recent papers observed rates of olfactory recovery of around 40% at 6 months [12, 13]. These differences in recovery rates could be explained by the inter-individual variations in self-reported smell scores.

The grade of dysfunction at the onset was associated with the timing of resolution in our sample. In fact, patients presenting with a severe chemosensory dysfunction had significantly longer recovery times or incomplete recovery at 18 months. Furthermore, the presence of severe OD was associated with a longer recovery of gustatory function; this may be explained by the fact that the sense of smell is involved in the perception and experience of food, through retronasal olfaction [14]. In contrast, an improvement in taste and/or smell within 7 days from the onset of GD and/or OD was associated with a faster recovery. These aspects should be considered during counseling with patients, as they may allow to anticipate the possible evolution of the symptom and the relative recovery pattern. At univariate analysis, the duration of SARS-CoV-2 positivity was not

associated neither with taste nor smell recovery, and neither was age. Even BMI and current smoking status were not associated with the recovery of smell and/or taste, just like they were not correlated with the prevalence of COVID-19-related GD and OD, as previously described [6, 15]. The role of gender in the recovery of COVID-19-related GD and OD is debated. Some authors reported how females showed a slower recovery of both taste and smell in a recent study [16]; however, this study was limited by a short follow-up. Other authors did not find any statistically significant differences between males and females [12, 17]. In our study, despite the higher prevalence of both GD and OD in female patients, no significant differences with males were observed in smell and taste recovery at 18-month follow-up.

The main limitation of our study was that analyses were based on subjective evaluation, with the possibility of under- or overestimation of GD and OD in our patient sample. Another bias was the exclusion of more severe COVID-19 cases from the study, including intubated patients, patients receiving noninvasive ventilation, or deceased at the moment of recruitment. Our data are difficult to interpret at the moment due to the lack of available studies with long-term follow-up of post-COVID-19 chemosensory dysfunction in



**Fig. 1** Kaplan–Meier curves showing the recovery pattern of gustatory (A) and olfactory (B) dysfunction in the entire series, as well as according to the severity of gustatory (C) and olfactory (D) dysfunction at presentation

the literature. Studies based on objective evaluation of taste and smell are needed. It was previously demonstrated that patients with post-viral olfactory dysfunction may achieve recovery beyond 2 years from the acute phase [18], and therefore, it is essential to extend the follow-up for these patients.

## Conclusions

Our study confirmed that the majority of patients with SARS-CoV-2-related GD and OD report complete recovery of gustatory and olfactory function in the first 3 months after symptom onset. Overall, 93% of patients recovered

their sense of taste and 87% of patients recovered their sense of smell at 18-month follow-up in our study. The severity of chemosensory dysfunction at the onset was negatively correlated to recovery, while an improvement of taste and/or smell function within the first 7 days from symptom onset was significantly associated with an early resolution. Therefore, it is necessary to identify the presence of GD/OD early in the course of SARS-CoV-2 infection, to act promptly on it once evidence of an effective treatment is identified.

**Table 3** Univariate logistic regression analysis of factors associated with the timing of recovery of gustatory and olfactory function

Gustatory dysfunction (GD)			
Independent variables	HR (95% CI)	<i>p</i>	
Age	0.99 (0.97–1.00)	0.081	
BMI	1.02 (0.98–1.07)	0.287	
Sex (M)	1.39 (0.96–2.02)	0.083	
Smoker (current)	1.07 (0.52–2.21)	0.844	
Gustatory dysfunction (GD) at presentation	0.79 (0.66–0.94)	0.008*	
Severe GD at presentation	0.67 (0.45–0.99)	0.044*	
Olfactory dysfunction (OD) at presentation	0.91 (0.84–0.99)	0.028*	
Severe OD dysfunction at presentation	0.60 (0.41–0.88)	0.010*	
Nasal obstruction at presentation	0.92 (0.83–1.02)	0.129	
Severe nasal obstruction at presentation	0.67 (0.39–1.15)	0.151	
SARS-CoV-2 positivity at nasopharyngeal swab duration	1.00 (0.98–1.01)	0.473	
Taste improvement in the first 7 days from the onset	4.32 (2.66–7.00)	< 0.001°	
Smell improvement in the first 7 days from the onset	4.30 (2.67–6.92)	< 0.001°	
Olfactory dysfunction (OD)			
Independent variables	HR (95% CI)	<i>p</i>	
Age	0.99 (0.97–1.00)	0.093	
BMI	1.02 (0.97–1.09)	0.398	
Sex (male)	1.46 (0.94–2.27)	0.095	
Smoker (current)	1.22 (0.53–2.80)	0.642	
Gustatory dysfunction (GD) at presentation	0.89 (0.74–1.06)	0.189	
Severe GD at presentation	0.80 (0.49–1.31)	0.376	
Olfactory dysfunction (OD) at presentation	0.76 (0.59–0.99)	0.041*	
Severe OD dysfunction at presentation	0.54 (0.31–0.96)	0.034*	
Nasal obstruction at presentation	0.93 (0.82–1.05)	0.219	
Severe nasal obstruction at presentation	0.73 (0.39–1.34)	0.309	
SARS-CoV-2 positivity at nasopharyngeal swab duration	1.00 (0.98–1.01)	0.659	
Taste improvement in the first 7 days from the onset	3.27 (2.07–5.18)	< 0.001°	
Smell improvement in the first 7 days from the onset	5.03 (3.09–8.17)	< 0.001°	

HR hazard ratio, 95% CI 95% confidence interval

\**p* value negatively correlated with the recovery of gustatory/olfactory function

°*p* value positively correlated with the recovery of gustatory/olfactory function

## Declarations

**Conflict of interest** The authors have no relevant financial or non-financial interests to disclose.

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