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# Prolonged complaints of chemosensory loss after COVID-19

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## ABSTRACT

Introduction: Chemosensory loss is a common symptom of coronavirus disease 2019 (COVID-19) and has been associated with a milder clinical course in younger patients. Whereas several studies have confirmed this association, knowledge about the improvement and recovery of olfactory and gustatory loss is lacking. The aim of this study was to investigate the temporal dynamics of improvement and recovery from sudden olfactory and gustatory loss in patients with confirmed and suspected COVID-19.

Methods: Subjective chemosensory function, symptoms of COVID-19, COVID-19 tests results, demographics and medical history were collected through a questionnaire.

Results: Among the 109 study participants, 95 had a combined olfactory and gustatory loss, five participants had isolated olfactory loss and nine participants has isolated taste loss. The mean age of participants was 39.4 years and 25% of participants were under the age of 30 years. Young age was not associated with a higher recovery rate. After a mean time of > 30 days since the chemosensory loss, participants reported relatively low recovery and improvement rates. For participants with olfactory loss, only 44% had fully recovered, whereas 28% had not yet experienced any improvement of symptoms. After gustatory loss, 50% had fully recovered, whereas 20% had not yet experienced any improvement. Olfactory and gustatory deficits were predominantly quantitative and mainly included complete loss of both olfactory and gustatory function.

Conclusions: Chemosensory loss was frequent in young individuals and persisted beyond a month after symptom onset, often without any improvement during this time.

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Trial registration: not relevant.

Chemosensory loss is as a common symptom of coronavirus disease 2019 (COVID-19), with a

prevalence of up to 88% [1, 2]. This association between COVID-19 and chemosensory loss has been documented in reports on COVID-19 symptoms [3] and by chemosensory testing of COVID-19 patients [4, 5]. Interestingly, both olfaction, gustation and trigeminal sensation are often affected [6]. This runs contrary to the common clinical characteristics of patients with chemosensory loss prior to COVID-19, where olfactory loss was the dominating chemosensory deficit [7, 8].

Chemosensory deficits are not an uncommon or a novel phenomenon. 15-20% of the general population are affected by smell loss, 1% to 5% of whom suffer from complete smell loss [9, 10]. However, before the COVID-19 pandemic, age was a key risk factor for post-viral chemosensory loss where most patients were in their 50s or 60s [8, 11, 12]. Conversely, in COVID-19 patients, sudden chemosensory loss is often reported as a symptom in younger patients [2, 4]. Furthermore, chemosensory loss in COVID-19 seems to be associated with a milder disease severity [13, 14]. As such, there is currently a new group of patients with chemosensory loss that differs from other patients with chemosensory loss in terms of both demographics and the multisensory nature of chemosensory deficits.

Whereas several studies have focused on the potential use of chemosensory loss as a diagnostic marker for COVID-19 [14-16], information on the expected duration of the chemosensory loss and the chances for recovery is lacking.

The aim of the present study was to map the rate of subjective improvement and recovery of chemosensory function in the weeks following confirmed or suspected COVID-19.

## METHODS

### Study design and population

A retrospective questionnaire was designed in REDCap [17] and distributed online on social media, through radio and flyers placed in the waiting rooms of general practitioners and outpatient clinics.

Patients were eligible for participation if they were above 18 years of age and had experienced a sudden chemosensory loss in 2020. Data were included in this study for patients with symptom onset after 27 February when the first case of COVID-19 was confirmed in Denmark.

The questionnaire included demographics, information on olfactory, gustatory and trigeminal sensory loss. Furthermore, data were collected about the occurrence and timing of other COVID-19 symptoms, medical history, smoking, alcohol, demographics and previous episodes of chemosensory loss after respiratory infections.

Data collection started on 22 April and concluded on 4 May when data on 100 participants with subjective complaints of smell loss for more than two weeks had been collected. The

decision to focus on smell loss was made as this has historically been the main chemosensory patient complaint after viral infections.

Olfactory and gustatory loss was not acknowledged as a symptom of COVID-19 by the Danish healthcare authorities until 4 May 2020 [18]. As the data collection in the present study ended on this date, participants with isolated chemosensory loss or only mild secondary symptoms did not meet the requirements for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing at the time. Consequently, participants without SARS-CoV-2 testing were included in the study. Data were collected after regional approval from the Danish Data Protection Agency. The questionnaire-based design did not require ethics approval (Danish Committee Act, Section 14, Subsection 2), which was confirmed by the Regional Ethics Committee.

### Statistics

All data were registered in a REDCap database and analysed using JMP 14.0. Pearson $\chi^2$-test was used for evaluating differences in categorical variables between groups. For parametric data, mean values were calculated and displayed along with 95% confidence intervals (CI). For non-parametric data, averages were calculated as median values, and interquartile ranges were added to ensure an adequate representation of the underlying distributions. Differences between groups for parametric data were calculated with a two tailed t-test, whereas Mann-Whitney was used for non-parametric data.

## RESULTS

In total, 109 non-hospitalised participants completed the questionnaire. Of these, 95 participants had a combined olfactory and gustatory loss, five participants had isolated olfactory loss, and nine participants had isolated gustatory loss. Two additional participants reported onset of chemosensory loss before February 27 and were excluded from the study. The mean age was 39.4 years with 25% of participants being under the age of 30 years.

Of the 95 patients with olfactory loss, 45 had undergone SARS-CoV-2 testing, and 40 had tested positive. Among the five participants with isolated olfactory loss, two had been tested and both were positive for SARS-CoV-2. Of the nine participants with isolated gustatory loss, five had been tested and one was positive for SARS-CoV-2. Some participants (28%) tried to get tested for SARS-CoV-2, but did not meet the formal requirements for testing, as chemosensory loss was not acknowledged as a symptom of COVID-19 at the time. Of the 58 participants without SARS-CoV-2 testing, 40 suspected that their sensory loss was due to COVID-19 (**Table 1**).

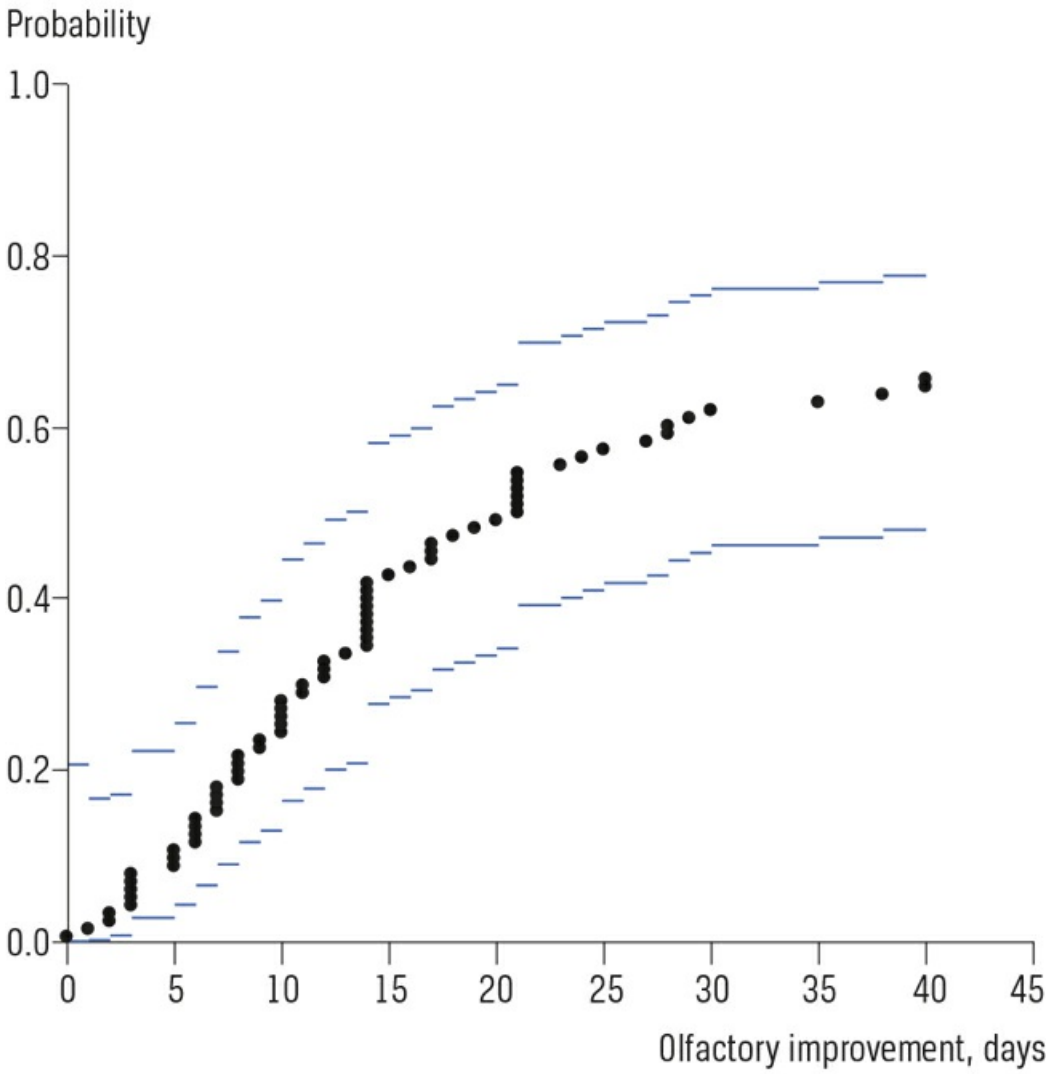
**TABLE 1 /** Olfactory and gustatory loss for patients with and without confirmed coronavirus disease 2019.

| | Olfactory loss | | | | Gustatory loss | | | |
|---|---|---|---|---|---|---|---|---|
| | total | confirmed COVID-19 | unknown COVID-19 | p-value (test) | total | confirmed COVID-19 | unknown COVID-19 | p-value (test) |
| *Patients, n* | | | | | | | | |
| Total | 100 | 42 | 58 | - | 104 | 41 | 63 | - |
| Females | 79 | 32 | 47 | 0.5572 ($\chi^2$) | 83 | 33 | 50 | 0.8891 ($\chi^2$) |
| Age, mean (IQR), yrs | 39.4 (37.0-41.8) | 37.4 (34.0-40.8) | 40.8 (37.4-44.2) | 0.1584 (t) | 40.3 (37.8-42.8) | 37.7 (34.2-41.3) | 42.0 (38.6-45.5) | 0.0423 (t) |
| Sensory loss delay, median (IQR), days[a] | 3 (1.3-5) | 3 (2-4.3) | 4 (1-6.3) | 0.6321 (MW) | 3 (1.25-5) | 3 (2-4.5) | 4 (1-6) | 0.6678 (MW)[b] |
| *Sensory abilities, median (IQR), n* | | | | | | | | |
| Before loss | 93 (84-100) | 93.5 (84.8-100) | 91 (81.5-100) | 0.5673 (MW) | 91 (81-100) | 91 (80.5-100) | 91 (80.8-100) | 0.9810 (MW) |
| After loss | 3 (0-23) | 0 (0-10) | 6 (0-24) | 0.0392 (MW)[b] | 10 (0-30) | 3 (0-24) | 12 (1.8-34.5) | 0.0805 (MW)[b] |
| Days to improvement, mean (95% CI) [n][c] | 14.1 (11.9-16.3) [72] | 12.4 (9.7-15.2) [34] | 15.6 (12.1-19.1) [38] | 0.1524 (t) | 10.9 (11.7-16.1) [83] | 9.8 (7.7-11.8) [36] | 11.8 (9.5-14.1) [47] | 0.1838 (t) |
| Days to recovery, mean (95% CI) [n][c] | 15.0 (12.2-17.7) [44] | 15.1 (10.0-20.2) [19] | 14.9 (11.7-18.1) [25] | 0.9382 (t) | 15.4 (12.1-18.8) [52] | 14.9 (9.5-20.2) [21] | 15.8 (11.2-20.5) [31] | 0.7754 (t) |
| *Days of follow-up, mean (95%CI) [n][c]* | | | | | | | | |
| Total | 33.5 (31.0-35.9) [100] | 29.8 (25.6-34.1) [42] | 36.1 (33.4-38.8) [58] | 0.0150 (t) | 34.4 (31.9-36.9) [104] | 30.0 (25.9-34.7) [41] | 37.1 (34.1-40.0) [63] | 0.0116 (t) |
| No improvement | 30.5 (25.2-35.8) [28] | 18.4 (8.0-28.7) [8] | 35.4 (30.2-40.5) [20] | 0.1520 (t) | 34.0 (27.6-40.5) [21] | 27.6 (5.0-50.2) [5] | 36.0 (29.4-42.8) [16] | 0.3741 (t) |
| No recovery | 33.0 (29.6-36.4) [56] | 29.8 (23.4-36.3) [23] | 35.2 (31.6-38.8) [33] | 0.1420 (t) | 33.8 (30.0-37.6) [52] | 29.2 (21.9-36.4) [20] | 36.7 (32.6-40.8) [32] | 0.0353 (t) |

CI = confidence interval; COVID-19 = coronavirus disease 2019; IQR = interquartile range; MW = Mann-Whitney.
a) The number of days sensory loss occurred after initial symptom of disease.
b) Due to low numbers, these statistical comparisons should be interpreted with caution.
c) Notice that not all patients had improved or recovered after the sensory loss at the time of data collection.

After mean of > 30 days after symptom debut, 28% of participants had not yet experienced any improvement of their olfactory function, whereas 44% had fully recovered from their olfactory loss, see **Figure 1**. Participants who had improved their sense of smell were not significantly younger (mean difference: –3.5 years (95% CI: –9.6-2.7), p = 0.2611), and no age difference was found for recovery (mean difference: 0.03 years (95% CI: –4.8-4.8), p = 0.9888).

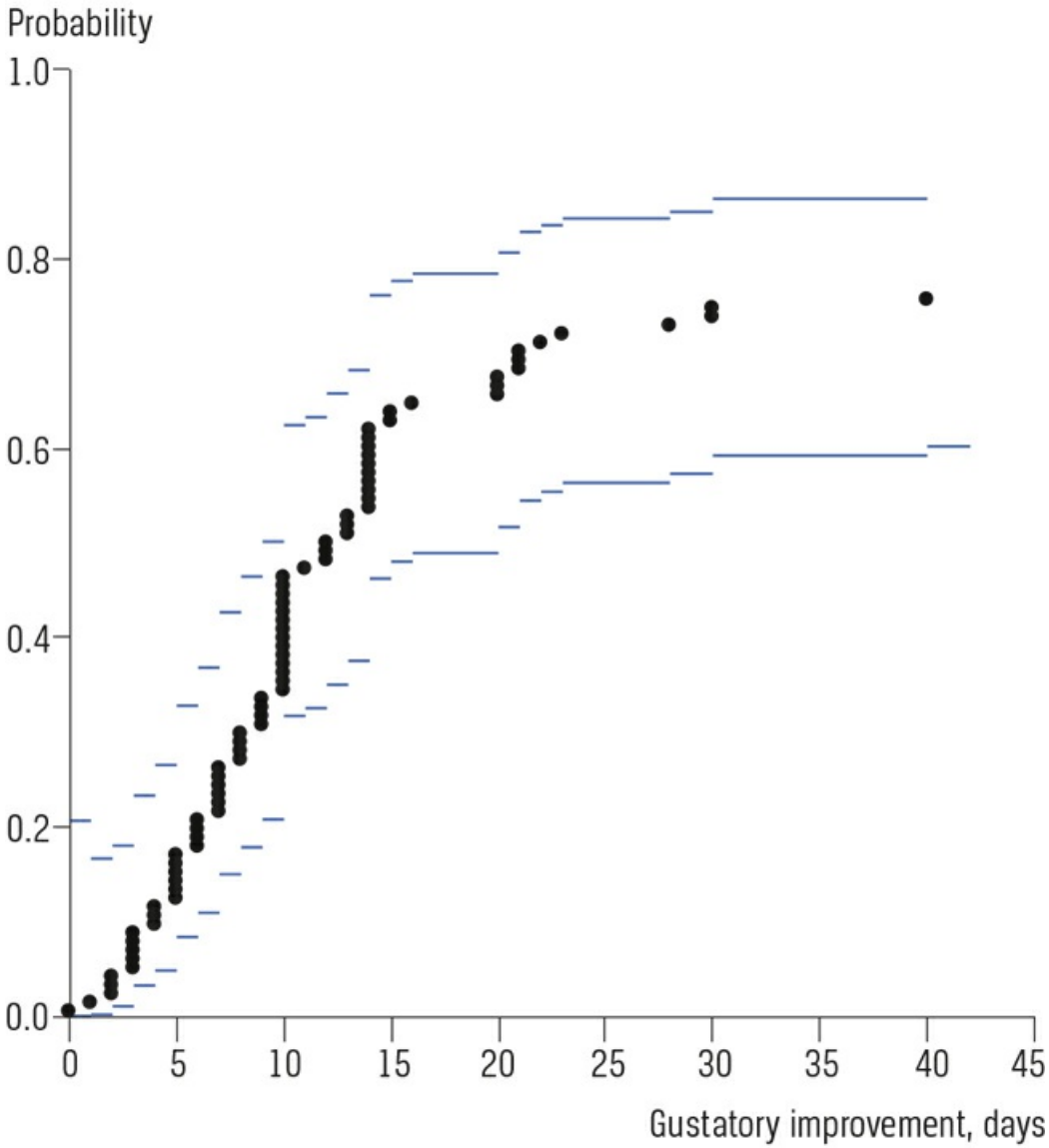
**FIGURE 1 /** Kaplan-Meyer plot of days until olfactory improvement.




After a mean of > 30 days after symptom debut, 20% of participants still had had not experienced any improvement of their gustatory function, whereas 50% had fully recovered from their olfactory loss, see **Figure 2**. Participants who had improved their sense of smell

were younger (mean difference: –8.0 years (95% CI: –14.9-–1.1), p = 0.0248), whereas no age difference was found for recovery (mean difference: 0.62 years (95% CI: –4.4-5.7), p = 0.8090)

**FIGURE 2 /** Kaplan-Meyer plot presenting days until gustatory improvement.




**Categorisation of qualitative and quantitative sensory deficits**

Among participants with olfactory deficits (n = 100), most reported complete olfactory loss (anosmia, n = 82), whereas 15 participants reported a reduction of olfactory intensity (hyposmia). Four participants reported that odours were distorted (parosmia), of whom two also had hyposmia. One participant had hyposmia and phantom smells (phantosmia).

Among participants with gustatory complains (n = 104), complete taste loss was most common (ageusia, n = 72), whereas 24 participants reported having a reduced taste intensity (hypogeusia). Fifteen participants complained of distorted taste, among whom seven also had hypogeusia. No participants complained of phantom taste sensations.

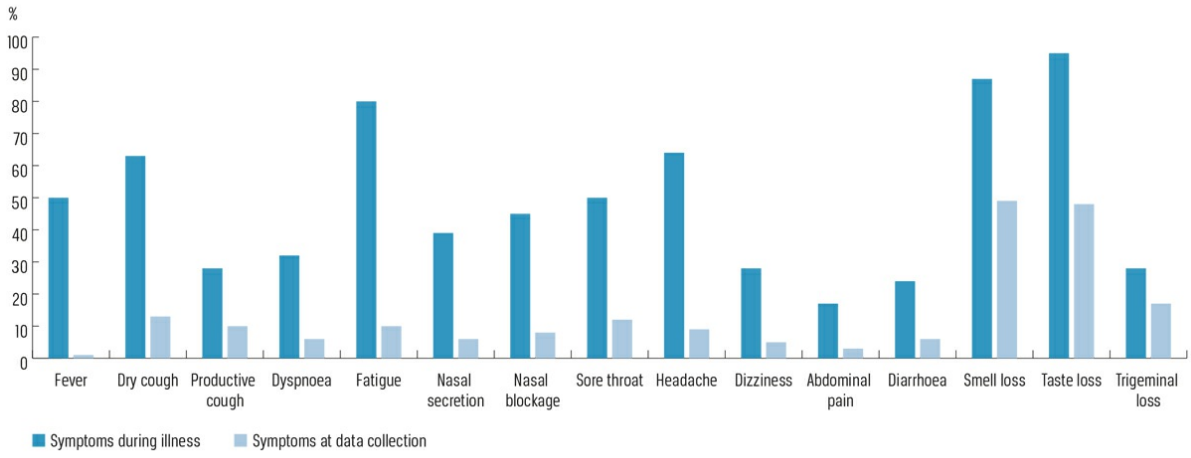
Trigeminal deficits were defined as alterations of other oral sensations like burning, cooling or tingling (e.g., chili peppers, carbonated water, peppermint or ginger). The degree of trigeminal function was rated on a 0-100 scale (before/after symptom onset and current function). Two of the four participants with complete loss had experienced no improvement at the time of data collection. The 27 participants with reduced trigeminal sensation had a significant reduction immediately after symptom onset (difference –24.7 (95% CI: –38.8-–10.5), p = 0.0014 (paired t-test)), but not at the time of data collection (–9.3 (95% CI: –23.5-4.9), p = 0.1915 (paired t-test)).

### Symptoms

Nine of the 109 participants experienced smell loss as the primary symptom, among whom seven reported a combined smell and taste loss (three had been COVID-19 tested, all of whom were SARS-CoV-2-positive). For delay in chemosensory symptoms, see Table 1.

Half of the patients with olfactory deficits (n = 50) had no nasal secretion or blockage. Among the participants with olfactory deficits and nasal blockage (n = 48), 56% were in the "unknown COVID-19" group, indicating that this symptom did not differ between groups. For the frequency of other COVID-19 symptoms, see **Figure 3**.

**FIGURE 3 /** Frequency of other symptoms in 109 participants with olfactory and gustatory deficits. Symptoms were included if they occurred at any time during the perceived illness or during the sensory deficits.



### Risk factors for sensory loss

Only a few participants had other risk factors for olfactory or gustatory loss. Prior to the sensory loss, four participant had run a fever, one had undergone general anaesthesia (orthopaedic surgery), one had a mild concussion and one had recently been prescribed new medication (oral budesonide).

None had a medical history of chronic rhinosinusitis, chronic obstructive pulmonary disorder, cardiac disease, stroke or neurological disease. The medical history of participants included hay fever (n = 10), asthma (n = 9), metabolic disease (n = 6), diabetes (n = 2), arthritis (n = 2), prior cancer (n = 1) and depression (n = 1).

Seven participants had experienced previous chemosensory deficits after respiratory infections, defined as continuous chemosensory loss one week after recovery. The majority were non-smokers (79%) or had a history of smoking (14%), whereas 6% were current smokers.

## DISCUSSION

We found that participants predominantly complained of combined olfactory and gustatory loss (100/109). They reported a high frequency of anosmia (82/100) and/or ageusia (72/104) with a rare occurrence of qualitative deficits. Whereas participants had recovered from most symptoms, the chemosensory deficits often persisted.

Of the 100 participants with olfactory loss (among whom 95 had affected gustatory function), 47 had undergone SARS-CoV-2 testing and 42 had tested positive. This is in line with recent reports where olfactory loss was found to be a good predictor for SARS-CoV-2 in patients [19].

In a study of hospitalised COVID-19 patients, two thirds of the 53 patients with reported chemosensory dysfunction reported complete recovery of symptoms. Half had a duration of chemosensory loss less than five days [5]. In an assessment of 59 clinically cured hospitalised patients, the short-term olfactory recovery rate was 44%, whereas 72.6% recovered olfactory function within the first eight days following the resolution of the disease [1]. However, whereas most COVID-19 hospitalisations are due to lower respiratory symptoms [20], chemosensory loss in COVID-19 is associated with a milder clinical course of COVID-19, indicating a more severe affection of the upper airways. As such, these reports may not be representative of the chemosensory improvement and recovery in the majority of patients with COVID-19 associated chemosensory loss.

The high proportion of relatively young participants with persistent severe chemosensory loss is noteworthy - especially in the absence of nasal blockage. The age group presented here was younger (mean age 39.4 years) than patients previously known to develop post-

viral olfactory loss, as the mean age in previous reports was 56.7-58.5 years [12]. This supports previous reports in which COVID-19-related chemosensory loss seems to be more frequent in the younger population [15]. This younger age was found in both the "confirmed COVID-19" and "unknown COVID-19" group in the current dataset. We found that young age had no impact on time of recovery.

As chemosensory loss is a common symptom of COVID-19, persistent chemosensory loss may become a frequent complaint in years to come. This often results in a severely reduced quality of life as patients with olfactory disorders often complain of anxiety, depression, impairment of eating experiences, isolation and relationship difficulties. Reden et al. previously investigated the improvement rate of olfactory function after post-viral olfactory loss, reporting that only 32% were found to improve over the course of 14 months. However, as the patient demographics and causal virus differ from previous studies, the long-term effects of COVID-19-associated chemosensory loss may prove to be very different.

### Limitations

The chemosensory deficits reported in this study are based on subjective assessments. There is a risk of misclassifying the nature of chemosensory deficits when subjective assessments are used. However, the participants in this study rated a subjective loss occurring in the course of a short period of time. Furthermore, whereas patients with olfactory deficits have a tendency to classify their sensory loss as a taste loss [8], the high frequency of subjective combined gustatory and olfactory deficits in this population may indicate a more reliable assessment. At least for the olfactory loss, this seems to be the case, as the reliability of subjective olfactory loss is relatively high for patients with anosmia.

Not all participants in this study had undergone SARS-CoV-2 testing. However, as indicated in Table 1, participants without confirmed COVID-19 had a similar age and improvement rate as the confirmed COVID-19 participants.

The design of the study carries an inherent risk of recall bias. Nonetheless, a large proportion of patients had continuous chemosensory impairment at the time of data collection, which indicates that the prolonged time of improvement and recovery are reliable estimates. As patients with long-lasting chemosensory deficits may have been more inclined to respond to the questionnaire, the current data may overestimate the average time for improvement and recovery.

## CONCLUSIONS

Olfactory and gustatory deficits after COVID-19 often persist for more than a month and are predominantly quantitative. At a mean of > 30 days after their chemosensory loss, only 44% and 50% had fully recovered from their olfactory and gustatory loss, respectively. Moreover, at this time, 28% and 20% had not experienced any subjective improvement of

their olfactory and gustatory loss, respectively. Patients were young compared with the typical clinical population with post-viral chemosensory loss and young age was not found to be predictor for faster recovery.

With the rapid spread of COVID-19 and the high frequency of chemosensory loss, more longitudinal studies are needed to enhance our knowledge and support patients' suffering from chemosensory disorders.

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**Conflicts of interest**: Disclosure form provided by the author is available with the full text of this article at Ugeskriftet.dk/dmj

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