# Exploring Trajectory Curves from Loss of Smell and Taste in Previously Hospitalized COVID-19 Survivors: the LONG-COVID-EXP-CM Multicenter Study

## INTRODUCTION

Self-reported loss of smell (anosmia) and taste (ageusia) have a prevalence of 19% and 23% in COVID-19 patients at the acute phase[1] and a prevalence of 15% in a post-COVID phase[2, 3]. Altered taste and smell may lead to disruption to basic daily living activities; nevertheless, almost 80% of patients may expect spontaneous recovery after 6 months[4]. Most studies investigating loss of smell/taste have used cross-sectional designs assessing their presence just once. Understanding longitudinal patterns of loss of smell/taste could have significant implications for determining comprehensive plans for prevention and management of these post-COVID complications.[5] This study explores the recovery trajectory of loss of smell/taste symptom in previously hospitalized COVID-19 survivors by using mosaic and exponential model bar plots for showing the long-term evolution of these symptoms.

## METHODS

The LONG-COVID-EXP-CM is a multicenter cohort study including patients with a positive diagnosis of SARS-CoV-2 hospitalized during the first wave of the pandemic in five urban hospitals of Madrid (Spain). From all hospitalized patients, a sample of 400 individuals from each hospital was randomly selected. The study was approved by all the Ethics Committees (HUF/EC1517, HCSC20/495E, HSO25112020, HUIL/092-20, HUFA 20/126). Informed consent was obtained from all participants.

Patients were scheduled for two telephone interviews at two follow-ups with a 5-month period in between. We used the AAO–HNS Anosmia Reporting Tool[6] for collecting data about smell/taste disturbances. Clinical (i.e., age, gender, height, weight, medical comorbidities) and hospitalization (e.g., symptoms at hospital admission, days at the hospital, intensive care unit admission) data were collected from medical records and used as adjusted covariables.

Python's library statsmodels 0.11.1 was used for producing the mosaic plots, while the bar plots were done with Matplotlib 3.3.4. The exponential curves were fitted to the data according to the formula $y = Ke^{ct}$, where $y$ represents the modeled prevalence of a symptom (anosmia or ageusia) at time $t$ (in months), and $K$ and $c$ are the parameters of the model.

## RESULTS

From a total of 2000 randomly selected individuals from the five hospitals, finally 1593 (45% women, age: 61, SD: 16 years) were assessed at T0 (hospital admission), T1 (mean: 8.4, range 6–10 months), and T2 (mean: 13.2, range 11–15 months) after discharge. The mosaic plots revealed that prevalence of loss of smell decreased from 8.1% ($n = 130$) at T0, to 4.0% ($n = 64$) at T1, to 3.1% ($n = 49$) at T2. Looking the figure, 91% of those patients ($n = 119/130$) experiencing anosmia at hospitalization (T0) had recovered 7 months after (T1). Further, 82% (53/64) of those with anosmia at T1 had developed it "de novo" (did not experience anosmia at T0). The prevalence of ageusia decreased from 7.1% ($n = 114$) at T0, to 3.0% ($n = 48$) at T1, to 1.75% ($n = 28$) at T2. Again, 90% of individuals (103/114) experiencing ageusia at hospitalization (T0) had recovered 7 months after (T1), whereas 77% (37/48) patients with ageusia at T1 had developed it "de novo." The trajectory analysis revealed fitted exponential curves with a decreased prevalence trend (Fig. 1).

## DISCUSSION

To the best of the authors' knowledge, this is the first trajectory curve of recovery of post-COVID loss of smell/taste. The mosaic plots revealed that patients with anosmia or ageusia at T0 had mostly recovered by T1. In fact, most cases at T1 corresponded to individuals who had developed the symptoms "de novo." Since there are more individuals recovering than developing loss of smell/taste symptoms, the overall trend is descending. Considering the long regenerate time of olfactory/gustatory neurons, the recovery of loss of smell/taste could be
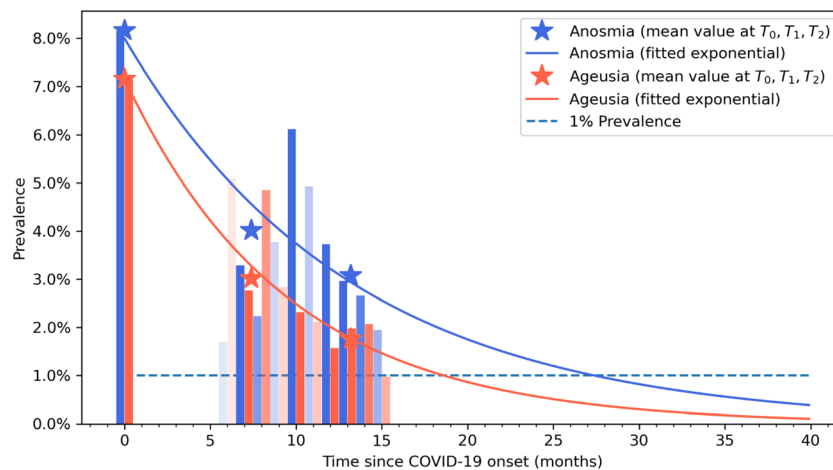
**Figure 1** Trajectory recovery curves of self-reported anosmia (in blue) or ageusia (in red) symptoms at any given time. Opacity indicates the sample size at that follow-up time. Asterisks represent the mean values employed at T0, T1, and T2 follow-up periods.

longer than expected. The exponential recovery trend identified here suggests that these symptoms could be present at least 3 years after the infection. This may be related to the fact that 80% of COVID-19 survivors developed "de novo" loss of smell/taste the following months after hospitalization.

We acknowledge some weaknesses of this study. First, only hospitalized patients aged 60 years old were included. Loss of smell/taste were self-reported. Third, we just focused on these two post-COVID symptoms. Interaction between different post-COVID symptoms is common.

In conclusion, post-COVID loss of smell/taste tends to spontaneously recover during the 3 years after COVID-19 in previously hospitalized survivors. The recovery rate is higher than the rate of "de novo" symptoms.

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**Declarations:**

**Consent to Participate:** *Participants provided informed consent before collecting data.*

**Consent for Publication:** *No personal info of any patient is provided in the text.*

**Conflict of Interest:** *The authors declare that they do not have a conflict of interest.*

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