

# The Long-Term Loss of Smell and Taste in COVID-19 Patients – A Systematic Review and Meta-Analysis

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## ABSTRACT

**Introduction:** Olfactory symptoms have been reported as particular in COVID-19 patients. **Objective:** To synthesize and analyze the existing evidence on the monitoring loss of sense of smell and taste in COVID-19 patients, and for how long symptoms persist after the virus is no longer active in the organism. **Methods:** A search was implemented in PubMed, Embase, Scopus, Science Direct, and Web of Science databases. This systematic review and meta-analysis were conducted according to PRISMA, and the risk of bias was assessed through the Newcastle-Ottawa Scale. The review protocol is registered in PROSPERO. **Results:** Our systematic review included data from 14 articles with a total of 2143 participants. The most reported sensory symptom of COVID-19 was anosmia, which was detected in 1499 patients, being the only symptom to appear in all studies. Ageusia was detected in 595 patients, dysgeusia in 514 patients, and hyposmia in 209 patients. The studies provided the number of 729 patients with sensory symptoms during the acute COVID-19 infection of 15 days, and 1020 patients with lasting sensory symptoms, presenting sensory dysfunctions after the average latent period of 15 days of the acute COVID-19 infection. **Conclusion:** Evidence points to the loss or dysfunction of taste and smell as one of the symptoms of COVID-19 persisting for an average time of 15 days, with 44% of COVID-19 patients with persistent symptoms for more than 15 days. Nevertheless, most studies do not perform a follow-up with those patients. Therefore, further research on sensory symptoms and their follow-up is required.

**Keywords:** anosmia; ageusia; Coronavirus; dysgeusia; sensation disorders.

## INTRODUCTION

On December 31, 2019, the World Health Organization (WHO) reported pneumonia of unknown cause originated in Wuhan, China. Later, it was discovered that this new pneumonia was a type of severe acute respiratory syndrome (SARS), a disease caused by a new type of Coronavirus (SARS-CoV-2). In January 2020, the WHO reported the outbreak of the new disease, and on February 11 of the same year, the disease that was causing the respiratory syndrome was named COVID-19 (Coronavirus Disease 2019), with more than 452 million confirmed cases and more than 6,029 million deaths from the disease worldwide by March 2022<sup>1,2</sup>.

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After several reports about olfactory dysfunction symptoms in COVID-19-positive patients, the American Academy of Otolaryngology-Head and Neck Surgery and the British Association of Otorhinolaryngology added anosmia and dysgeusia to the list of common symptoms during COVID-19 infection<sup>3,4</sup>. The symptoms of sensory dysfunction can be described as dysgeusia (alteration of the sense of taste) and hyposmia (alteration of the sense of smell). The complete absence of sensitivity to sensory stimuli can be described as anosmia (total loss of sense of smell) and ageusia (total loss of sense of taste). In studies evaluating the prevalence of these symptoms, it was found that the prevalence of hyposmia and dysgeusia can reach 86% in the populations analyzed. These sensory symptoms were considered a clinical criterion for COVID-19 prognostic factor<sup>1,5-7</sup>.

There are several well-done and widely viewed systematic reviews with meta-analyses evaluating smell and taste dysfunction associated with COVID-19<sup>8,9</sup>. These studies presented a pool prevalence for smell loss of 77%<sup>8</sup>; an alteration of the sense of smell and taste with 31% in severely symptomatic patients, and 67% in mild-to-moderate symptomatic patients<sup>9</sup>; and a pooled proportion of 41% of patients presenting with olfactory dysfunction, and 38,2% gustatory dysfunction<sup>10</sup>. However, our current study examines beyond the prevalence of smell and taste dysfunction in the setting of COVID-19, adding a novel twist that includes the evaluation of the prevalence of persistent smell and taste symptoms by examining the percentage of COVID-19-positive patients with symptoms lasting beyond 15 days.

This systematic review and meta-analysis aimed to examine the emerging evidence as to the rates of olfactory and gustatory manifestations in COVID-19-positive patients, and for how long symptoms persist after the virus is no longer active in the organism.

## METHODS

This systematic review and meta-analysis were conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement<sup>11</sup>. The review protocol is registered in PROSPERO and is available online (CRD42020216612).

### Research strategy and selection criteria.

Our search strategy was organized and discussed by all researchers in the group and performed by two authors (JDCP and YSB), who conducted the search and identified studies published between January 01, 2020, and August 20, 2021, applying the eligibility criteria, independently. The systematic search was implemented in PubMed, Embase, Scopus, Science Direct, and Web of Science databases. The search strategy and keywords were inserted in the fields of "title and abstract", with the use of the Booleans Operators

"AND" and "OR" to obtain better search results, and was used as follows: ("COVID-19") AND ("brain" OR "nervous system") AND ("human") AND ("anosmia" OR "hyposmia" OR "nerve damage"). The initial search was screened for duplicates. Then, two authors (JDCP and YSB) identified, independently, potential articles that met the established criteria by firstly screening titles and abstracts, and then screening full text for inclusion according to eligibility for the review question "How long do patients with COVID-19 have lasting symptoms of loss of smell and taste?"

### Inclusion and exclusion criteria

This systematic review used the PICO Approach (population, intervention, control, and outcome), which is considered a strategy for framing good research questions for the inclusion criteria of the studies. The study population group consisted of patients diagnosed with COVID-19 with lasting symptoms of smell and taste loss, and the intervention that we observed was about groups that had symptoms of loss of sense of smell and taste after being diagnosed and recovering from acute COVID-19 infection. The comparison was about the number of days that the participants had the lasting effects of loss of sense of smell and taste, and our main outcome is to analyze the olfactory and gustatory rate and how long the symptoms persisted after the virus was no longer active in the body. Articles were excluded in case of no full text available, no available English version, all types of reviews, as well as letters to the editor, perspective, or opinions that do not contain original data of interest.

### Data extraction and quality assessment

Data were extracted from each article and presented in a spreadsheet containing the following information: title, authors, journal, country, study type (i.e., case report or case-control studies), Ethics Committee (if the study was approved by one or not), total number, age, and gender of participants, control group (if presented), anosmia, ageusia, hyposmia, dysgeusia, patients with more than one symptom at once, days with persistent symptoms, and main findings. In case of discrepancies, the scenario to resolve divergences was evaluated.

The Newcastle-Ottawa Scale<sup>12</sup> was used for the quality assessment evaluation of each study performed by independent researchers. This scale assigns a maximum of 9 points to studies of the highest quality according to 3 parameters: selection (4 points), comparability (2 points), and exposure (case-control studies) or outcome (cohort studies; 3 points). Low, moderate, and high-quality studies were assigned scores of 0-3, 4-6, and 7-9, respectively.

### Statistical analysis

The results of the meta-analysis using the random effect were presented graphically as a forest plot, plotting the prevalence of

olfactory and gustatory dysfunctions in COVID-19, and the long-term period of the sensory symptoms of the patients across the studies. The effect sizes were calculated as the difference between the prevalence of anosmia vs total, hyposmia vs total, ageusia vs total, dysgeusia vs total, and the number of patients that had a time of recovery of more than 15 days vs total. Diamonds were used to plot the summary prevalence for all studies, and the individual study estimates were represented as black boxes on the continuous horizontal line, with their center representing the point estimated and their extremes the 95% CI<sup>13</sup>. The meta-analysis was performed with the R language and environment for statistical computing<sup>14</sup>. The main R packages used in this meta-analysis were dplyr<sup>15</sup>, tidyr<sup>16</sup>, stringr<sup>17</sup>, ggplot2<sup>18</sup>, and metafor<sup>19</sup>.

and Meta-Analyses (PRISMA), with a diagram detailing the study retrieval process through the distinct phases of this systematic review. The initial search resulted in a collection of 2,809 records. After the removal of duplicates, 2,426 original articles were left for screening, excluding unrelated articles (n=2,236); review articles (n=56); and articles with no available English version (n=77). The remaining 57 articles were entered into full-text screening using the inclusion and exclusion criteria. After eligibility was assessed, articles with no relation to loss of smell or taste were excluded (n=29); articles that presented data of persistent symptoms of loss of sense of smell and taste for less than 15 days (n=9); and articles with no full text available were also excluded (n=5). The final qualitative and quantitative (meta-analysis) synthesis included 14 articles (Figure 1).

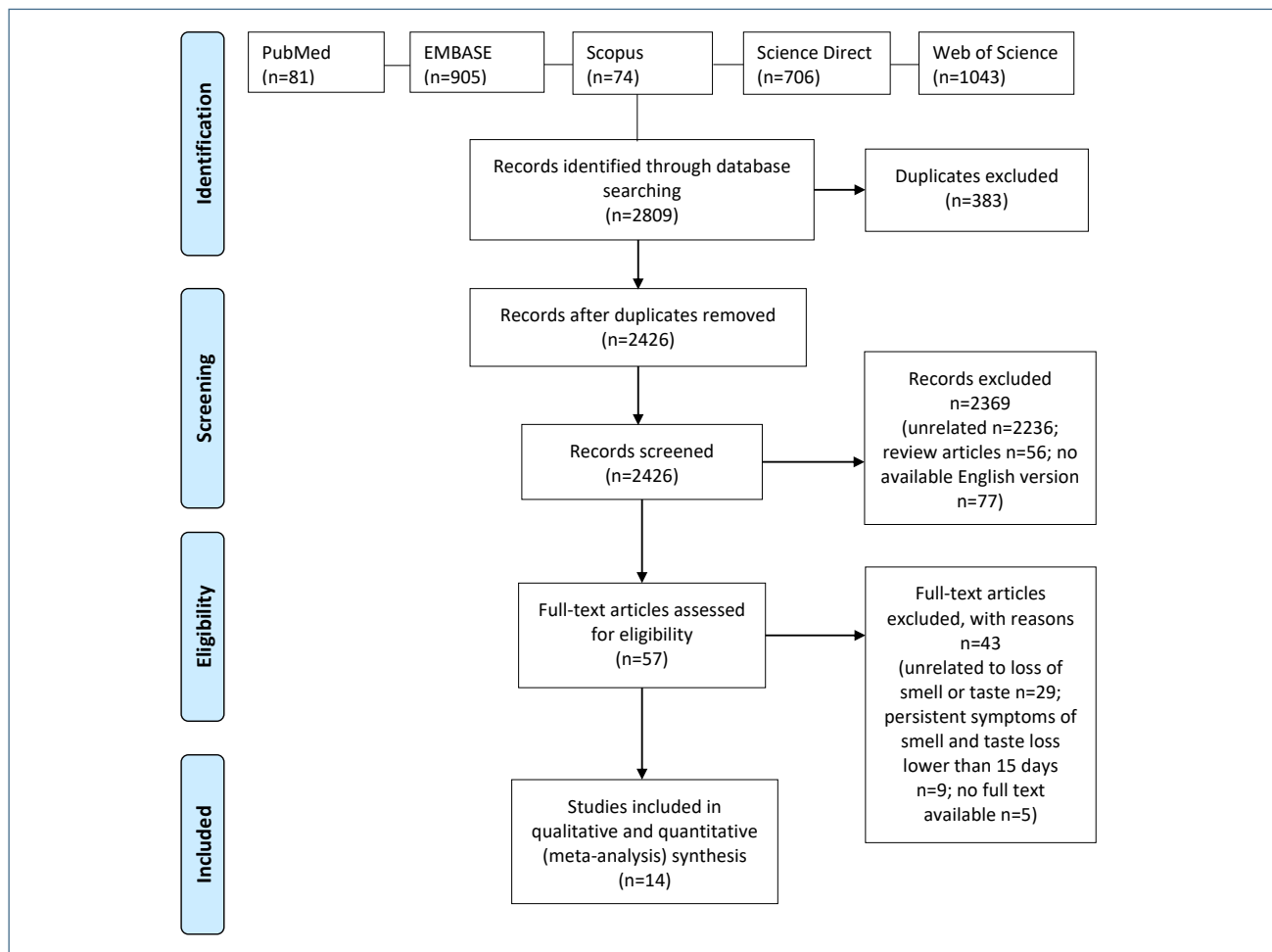
## RESULTS

### Search results

Our search strategy was performed in line with the recommendations of the Preferred Reporting Items for Systematic Reviews

### Study characteristics

After the screening, fourteen studies were eligible<sup>20-33</sup> with a total of 2.143 participants with confirmed COVID-19 infection, which were included in the analysis. All the studies reported on the sensory symptoms of COVID-19, presenting a specified



**Figure 1:** PRISMA flow diagram depicting the flow of information through the distinct phases of this systematic review and meta-analysis.

period of the symptoms. A summary of the main characteristics of each study, including the type of publication, country, publication source, age of the participants from the study, male-to-female ratio, and prevalence of each olfactory and gustatory condition is presented in the supplemental material (SP1).

The results of the quality assessment of the studies were conducted according to the Newcastle-Ottawa Scale shown in the supplemental material (SP2 and SP3). The estimated scores of all the included studies were in the range of 4-9 points.

All the studies reported some dysfunction or loss of smell and taste that surpasses the period of the acute symptomatic window of 15 days<sup>26</sup>. The sex ratio of the individuals per study was 59.92% of females, and 36.58% of males.

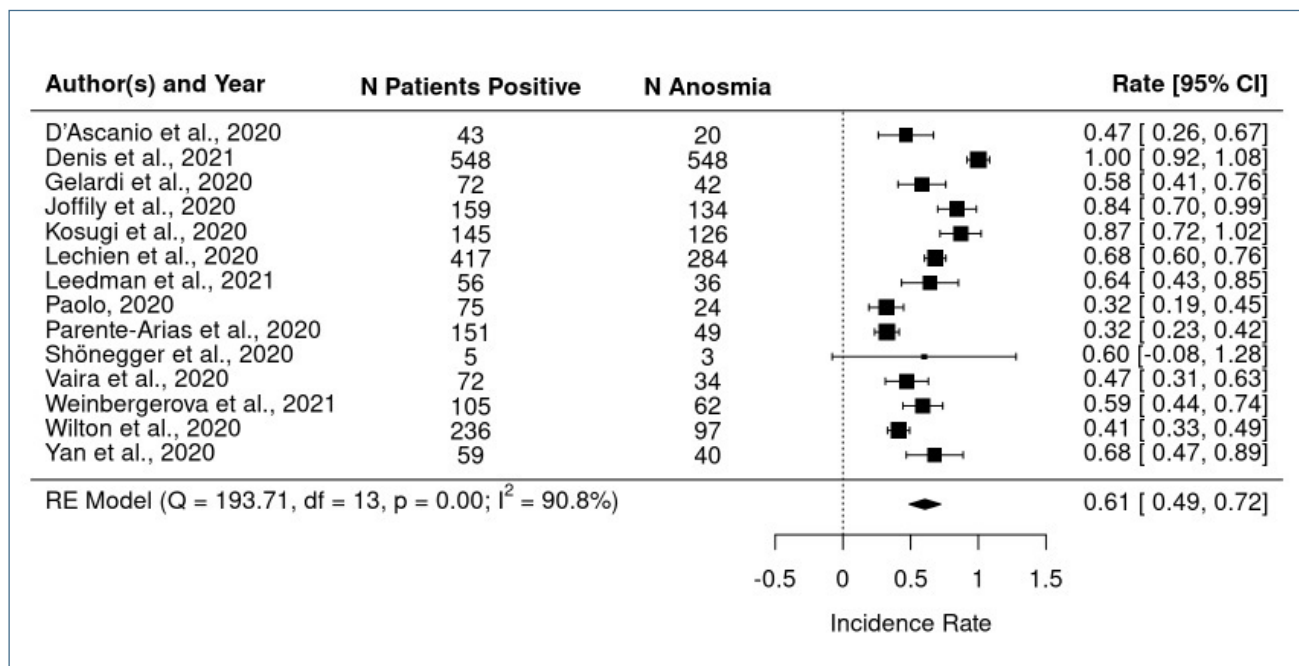
Fourteen studies assessed the complete loss of smell (anosmia), with an overall average of 53% of the general percentage of symptoms taken from the calculated proportion.

Additionally, eight studies assessed the prevalence of a partial sense of smell (hyposmia), with an overall average of 8% of the general percentage of symptoms. With anosmia being the highest ratio of symptoms, and hyposmia being the lowest ratio, ageusia, and dysgeusia have presented a similar percentage, with an overall average of 21% and 18%, respectively. The studies provided the number of 729 patients with sensory symptoms in the average latent period of 15 days, while there are still onset respiratory symptoms. After 15 days, 1020 patients were still presenting symptoms of anosmia, dysgeusia, hyposmia, and ageusia, some of those reaching a long-term period.

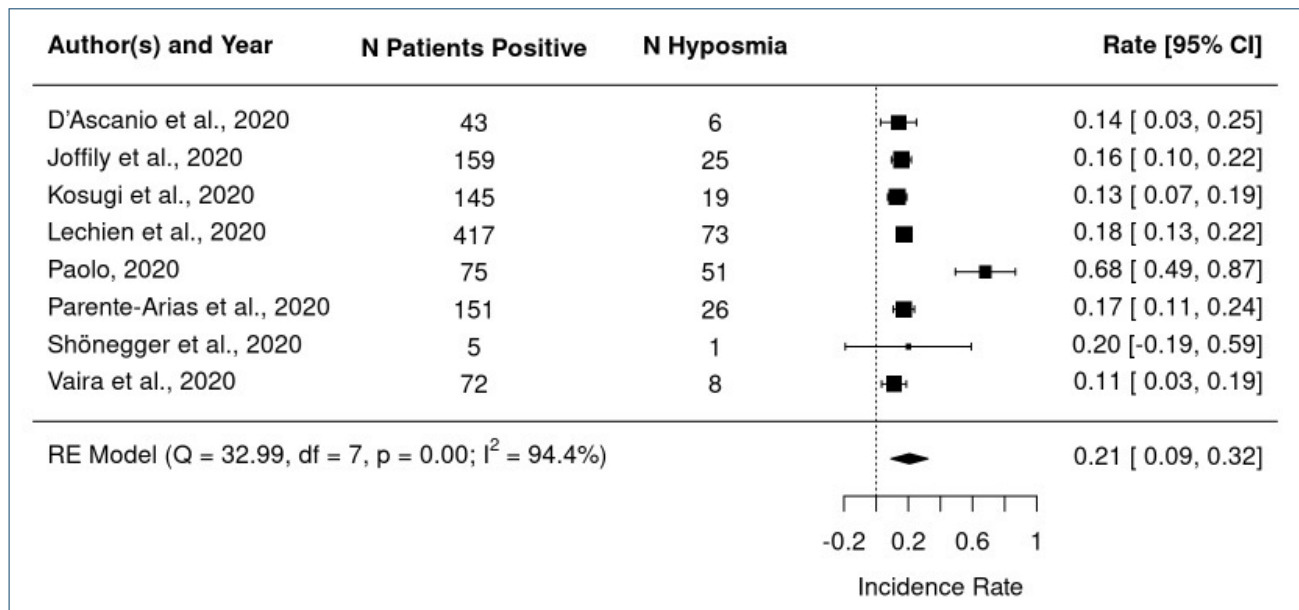
### Concerning olfactory symptoms

Complete loss of smell (anosmia) was detected in 1499/2143 COVID-19 patients, appearing in all 14 studies<sup>20-33</sup>, which were analyzed to investigate the association between anosmia and the occurrence of COVID-19. The number of cases of anosmia per study ranged from 3 to 548, with prevalence estimates ranging from 32% to 100% among COVID-19-positive patients. For this analysis, a mean effect size was statistically significant, with Cochran's Q, approximated from the chi-square distribution ( $Q=193.71$ , degrees of freedom  $[df]=13$ ,  $p<0.001$ ), and the  $I^2$  value of 90.8%, confirming the heterogeneity of the meta-analysis across the subjective studies. The pooled estimate for the prevalence for the overall cohort was 61% with a 95% CI of 49-72% (Figure 2).

A decreased sense of smell (hyposmia) was detected in 209/2143 COVID-19 patients, appearing in eight studies<sup>20,22,23,25,27-29,31-33</sup>, which were analyzed to investigate the association between hyposmia and the occurrence of COVID-19. The number of cases of hyposmia per study ranged from 1 to 73, with prevalence estimates ranging from 11% to 68% among COVID-19-positive patients. For this analysis, a mean effect size was statistically significant, with Cochran's Q, approximated from the chi-square distribution ( $Q=32.99$ , degrees of freedom  $[df]=7$ ,  $p<0.001$ ), and the  $I^2$  value of 94.4%, confirming the heterogeneity of the meta-analysis across the subjective studies. The pooled estimate for the prevalence for the overall cohort was 21% with a 95% CI of 9-32% (Figure 3).



**Figure 2:** Forest plot meta-analysis of the prevalence of anosmia in 1,499 COVID-19 patients. Each study prevalence is displayed as a black square; the horizontal bar represents 95% CI (confidence interval). The diamond represents the summary prevalence for all studies.



**Figure 3:** Forest plot meta-analysis of the prevalence of hyposmia in 209 COVID-19 patients. Each study prevalence is displayed as a black square, the horizontal bar represents 95% CI (confidence interval). The diamond represents the summary prevalence for all studies.

### Concerning gustatory symptoms

Complete loss of taste functions (ageusia) was detected in 595/2143 patients, appearing in eight studies<sup>21-23,25,27,28,32,33</sup>, which were analyzed to investigate the association between ageusia and the occurrence of COVID-19. The number of cases of ageusia per study ranged from 2 to 279, with prevalence estimates ranging from 4% to 92% among COVID-19-positive patients. For this analysis, a mean effect size was statistically significant, with Cochran's Q, approximated from the chi-square distribution (Q=328.23, degrees of freedom [df]=7,  $p < 0.001$ ), and the I<sup>2</sup> value of 97.2%, confirming the heterogeneity of the meta-analysis across the subjective studies. The pooled estimate for the prevalence for the overall cohort was 46% with a 95% CI of 26-66% (Figure 4).

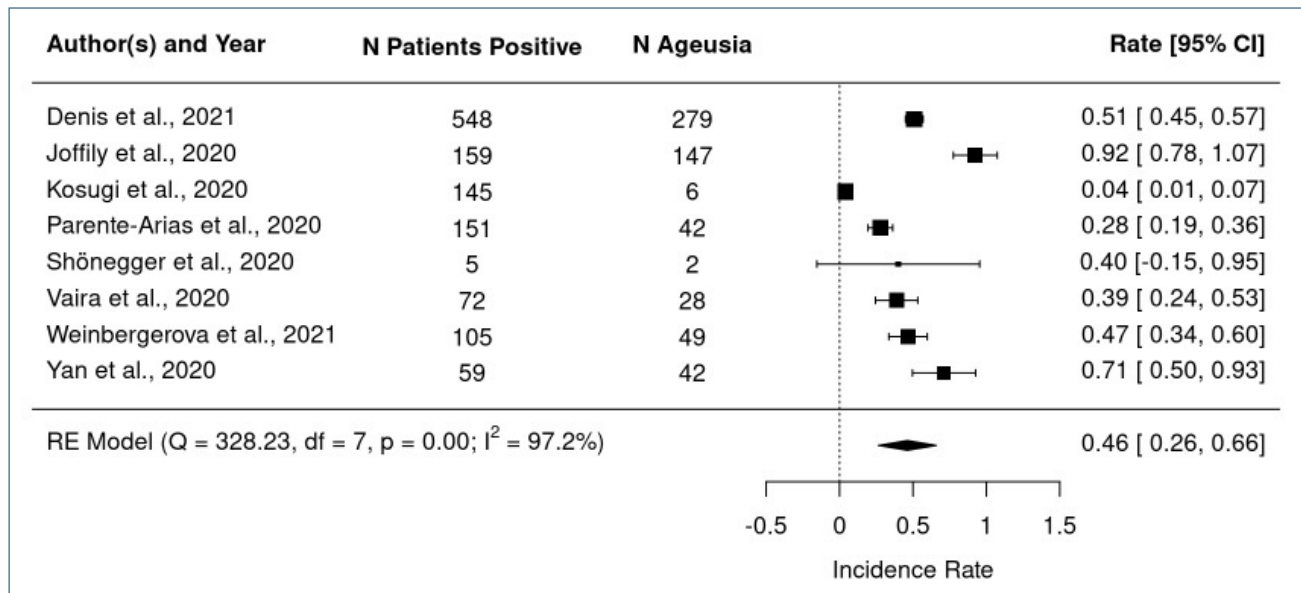
The distortion or alteration of the sense of taste (dysgeusia) was detected in 514/2143 patients, appearing in six studies<sup>22,26,29,31-33</sup>, which were analyzed to investigate the association between dysgeusia and the occurrence of COVID-19. The number of cases of dysgeusia per study ranged from 1 to 342, with prevalence estimates ranging from 17% to 100% among COVID-19-positive patients. For this analysis, a mean effect size was statistically significant, with Cochran's Q, approximated from the chi-square distribution (Q=179.12, degrees of freedom [df]=5,  $p < 0.001$ ), and the I<sup>2</sup> value of 96.8%, confirming the heterogeneity of the meta-analysis across the subjective studies. The pooled estimate for the prevalence for the overall cohort was 53% with a 95% CI of 24-82% (Figure 5).

### Period of the symptoms

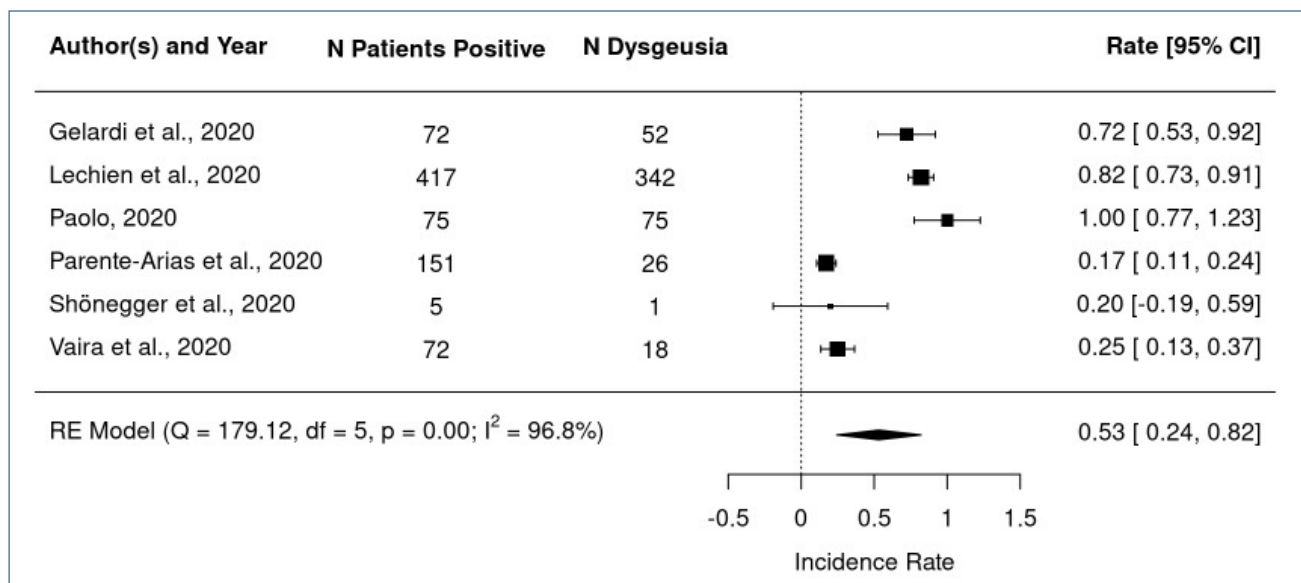
The olfactory and gustatory disorders appeared simultaneously with the general symptoms of COVID-19. Most studies<sup>20,22,24,25,27-29</sup>

acknowledged the time above 15 days with no other follow-up. These studies assessed 1131 patients of which 246 followed the characteristic showing symptoms but with no follow-up. Two studies<sup>26,31</sup> assessed 147 patients, in which 42 patients presented symptoms for over 20 days and no more specific follow-up. One study<sup>33</sup> had a follow-up with five patients, and 3 were symptomatic for more than 30 days. One study<sup>32</sup> had a follow-up with 151 patients, with 11 patients showing symptoms up until 108 days. Two studies<sup>23,30</sup> had a follow-up of 6 months with a total of 161 patients. In one study<sup>30</sup>, the sensory symptoms were presented in 18 patients for the 6-month mark. In another study<sup>23</sup>, one patient had the symptoms for 159 days, and six patients' symptoms lasted up until 194 days. One study<sup>21</sup> conducted in France, had a follow-up of 12 months, with all 548 participants presenting symptoms for more than 30 days, the follow-up was conducted in association with sensory training that showed better outcomes to olfactory function improvement, up until the end of the study at the 12-month mark, 70 patients were still presenting sensory symptoms.

The long-last sensory symptoms were detected in 1020/2143 patients, appearing in all 14 studies<sup>20-33</sup>, which were analyzed to investigate the association between the cases with sensory symptoms after 15 days and the general occurrence of COVID-19. The number of cases that showed sensory symptoms for more than 15 days, per study ranged from 3 to 548, with prevalence estimates ranging from 9% to 100% among COVID-19-positive patients. For this analysis, a mean effect size was statistically significant, with Cochran's Q, approximated from the chi-square distribution (Q=763.63, degrees of freedom [df]=13,  $p < 0.001$ ), and the I<sup>2</sup> value



**Figure 4:** Forest plot meta-analysis of the prevalence of ageusia in 595 COVID-19 patients. Each study prevalence is displayed as a black square, the horizontal bar represents 95% CI (confidence interval). The diamond represents the summary prevalence for all studies.



**Figure 5:** Forest plot meta-analysis of the prevalence of dysgeusia in 514 COVID-19 patients. Each study prevalence is displayed as a black square, the horizontal bar represents 95% CI (confidence interval). The diamond represents the summary prevalence for all studies.

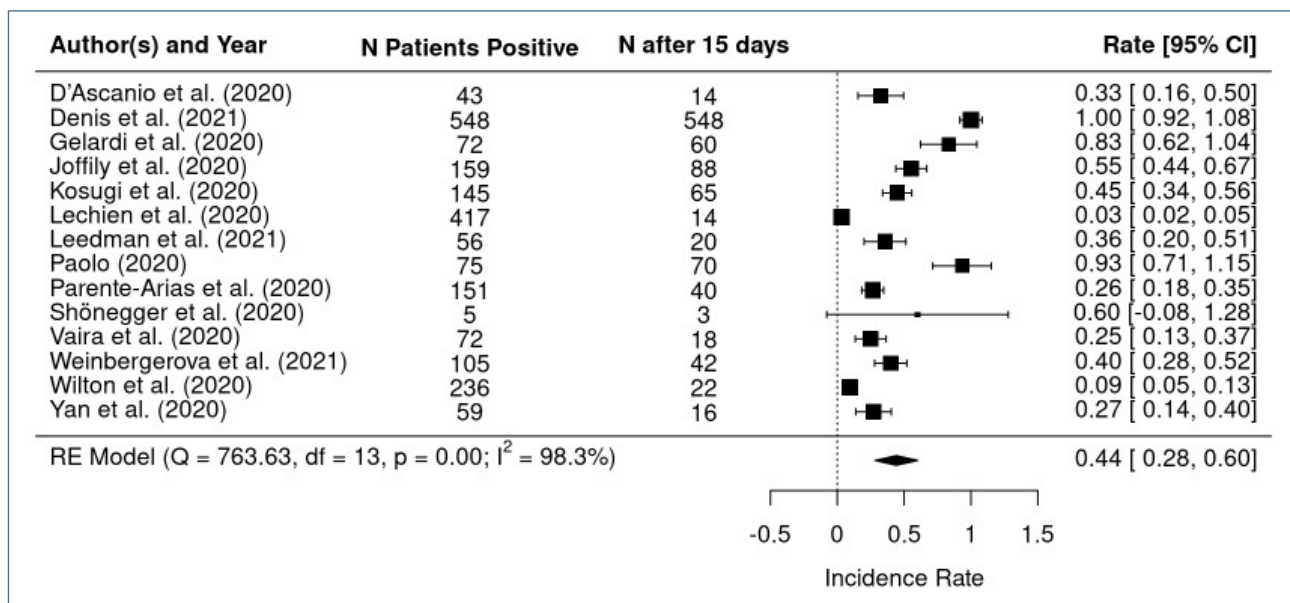
of 98.3%, confirming the heterogeneity of the meta-analysis across the subjective studies. The pooled estimate for the prevalence for the overall cohort was 44% with a 95% CI of 28-60% (Figure 6).

## DISCUSSION

This systematic review and meta-analysis provide a synthesis of early evidence on the persistent loss of smell and taste in COVID-19-positive patients. A meta-analysis using the random-effect

model computed an overall prevalence estimate of 44% of patients with SARS-CoV-2 infection experience persistent and chronic olfactory and gustatory dysfunction, which have been shown to result in a decreased quality of life and leads to nutrition issues<sup>22,29</sup>.

The loss of sense of smell (anosmia) emerged as one of the revealing symptoms of COVID-19, being noted in 73% of patients before diagnosis, and considered as a clinical criterion for COVID-19 prognostic factor, being the first symptom for some patients and, sometimes, the only one<sup>3,27,34</sup>. In a report of the



**Figure 6:** Forest plot meta-analysis of the prevalence of 1,020 patients with COVID-19 sensory symptoms for more than 15 days. Each study prevalence is displayed as a black square, the horizontal bar represents 95% CI (confidence interval). The diamond represents the summary prevalence for all studies.

multicenter prospective European study, an olfactory and gustatory dysfunction occurred in 85.6% and 88.8% of patients, respectively, with a majority of patients (65.4%) experiencing abnormalities in olfaction after the appearance of the general symptoms<sup>29,35</sup>.

A study with 72 COVID-19-positive patients showed that 34% of the patients have a low rate of spontaneous recovery of sensory dysfunctions for 30 days or more<sup>22</sup>. Most patients regain their sense of smell and taste after recovering, usually within weeks, as occurs during the latent period of respiratory symptoms in COVID-19. However, in a minority of patients, the loss of sense of smell and taste persists, causing a significantly impaired quality of life<sup>1,36</sup>.

A study with 319 patients reported a prevalence of safety-related issues, such as the inability to smell smoke/fire that others could perceive, was the most common complaint from 45% of the patients. Due to smell and taste disturbances, 87% of the patients in the survey reported a reduced enjoyment of food, which can increase the risk of nutritional deficit and nutritional risk due to excessive consumption of salt and sugar, which can lead to health issues<sup>37</sup>.

An online self-reported questionnaire survey on the quality of life in COVID-19 patients showed that 76% of the patients reported a general decline in their quality of life. Patients with smell dysfunction felt an interference with daily activities and an all-around deterioration in well-being. The patients with olfactory loss presented less awareness of personal hygiene, decreased pleasure in food or drinks, poor appetite, and various degrees of difficulty with cooking and detecting the right amount of seasoning or spoiled food, which can lead to malnutrition and weakness<sup>38</sup>.

Studies demonstrated the substantial impact of persistent olfactory and gustatory dysfunction, irrespective of cause, on quality of life and personal safety, also leading to the development of psychological disorders, being an important risk factor for mental health deterioration<sup>37,39</sup>. A study utilizing Cox proportional hazards models had findings implicating that patients with sensory symptoms of anosmia and ageusia have a 30% higher increase in the instantaneous risk of suicidal ideation or depression<sup>37</sup>.

Depression had a substantial incidence in patients with COVID-19, alongside post-traumatic stress disorder (PTSD), anxiety, obsessive-compulsive (OC) symptoms, and insomnia<sup>40</sup>. A report outlined that 15.8% of patients affected by smell loss had depression as the main effect on their well-being<sup>38</sup>. However, those studies did not have a baseline level of depression or any other psychiatric disease before the patient had developed COVID-19, thus interpreting this evidence less straightforward<sup>38,40</sup>.

The studies selected for this systematic review presented a big ratio between loss of smell at 53% and loss or dysfunction of taste at 21% and 18%, respectively. Dysgeusia may be related to alteration in the perception of taste due to loss of sense of olfaction since smell is intricately linked to taste<sup>3</sup>. All studies assessed the lack of smell and taste through a survey instrument, which the patients filled out based on their own experiences, therefore it is necessary to consider that patients with anosmia may have deduced that they also have dysgeusia, because one is integral to the other. From this, it is concluded that some of the statistics collected may not be presented as accurately.

## Conclusion

Our meta-analysis has demonstrated that the olfactory and gustatory symptoms persisted for more than 15 days in 44% of the COVID-19-positive patients analyzed. Those sensory symptoms such as sudden dysfunction or absence of sensitivity to sensory stimuli in COVID-19 patients can have a profound impact on the quality

of life if presented for a longer period, which is the case for 1020 (44%) patients analyzed, as smells serve as a primary alarm system warning of dangers in our environment. Thus, monitoring patients who continue with persistent symptoms of loss of sense of smell and taste for an extended period is extremely important to understand and assess the health of those who continue to present the symptoms.

## REFERENCES

- Naeini AS, Karimi-Galougahi M, Raad N, Ghorbani J, Taraghi A, Haseli S, et al. Paranasal sinuses computed tomography findings in anosmia of COVID-19. *Am J Otolaryngol*. 2020;41(6):102636. <https://doi.org/10.1016/j.amjoto.2020.102636>
- World Health Organization (WHO). Coronavirus disease (COVID-19) pandemic. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- Kaye R, Chang CWD, Kazahaya K, Brereton J, Denny JC. COVID-19 Anosmia reporting tool: initial findings. *Otolaryngol Head Neck Surg*. 2020;163(1):132-4. <https://doi.org/10.1177/0194599820922992>
- Spinato G, Fabbris C, Polesel J, Cazzador D, Borsetto D, Hopkins C, et al. Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection. *JAMA*. 2020;323(20):2089-90. <https://doi.org/10.1001/jama.2020.6771>
- Tong JY, Wong A, Zhu D, Fastenberg JH, Tham T. The Prevalence of olfactory and gustatory dysfunction in COVID-19 patients: a systematic review and meta-analysis. *Otolaryngol Head Neck Surg*. 2020;163(1):3-11. <https://doi.org/10.1177/0194599820926473>
- Wiersinga HCPWJ, Rhodes A, Cheng AC, Peacock SJ. Pathophysiology, transmission, diagnosis, and treatment of Coronavirus disease 2019 (COVID-19) a review. *JAMA*. 2020;324:782-93. <https://doi.org/10.1001/jama.2020.12839>
- Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020;581:465-9. <https://doi.org/10.1038/s41586-020-2196-x>
- Hannum ME, Ramirez VA, Lipson SJ, Herriman RD, Toskala AK, Lin C, et al. Objective sensory testing methods reveal a higher prevalence of olfactory loss in COVID-19-positive patients compared to subjective methods: a systematic review and meta-analysis. *Chem Senses*. 2020;45(9):865-74. <https://doi.org/10.1093/chemse/bjaa064>
- Borsetto D, Hopkins C, Philips V, Obholzer R, Tirelli G, Polesel J, et al. Self-reported alteration of sense of smell or taste in patients with COVID-19: a systematic review and meta-analysis on 3563 patients. *Rhinology*. 2020;58(5):430-6. <https://doi.org/10.4193/Rhin20.185>
- Agyeman AA, Chin KL, Landersdorfer CB, Liew D, Ofori-Asenso R. Smell and Taste Dysfunction in Patients With COVID-19: A Systematic Review and Meta-Analysis. *Mayo Clin Proc*. 2020;95(8):1621-31. <https://doi.org/10.1016/j.mayocp.2020.05.030>
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. <https://doi.org/10.1371/journal.pmed.1000097>
- Ottawa Hospital Research Institute (OHRI). Newcastle - Ottawa Quality Assessment Scale. Available from: [https://www.ohri.ca/programs/clinical\\_epidemiology/nosgen.pdf](https://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf)
- Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Statist Software*. 2010;36(3):1-48. <https://doi.org/10.18637/jss.v036.i03>
- R Core Team. A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna: 2018. Available from: <https://www.R-project.org/>
- Wickham H, François R, Henry L, Müller K, Vaughan D. dplyr: a Grammar of Data Manipulation. Available from: <https://cran.r-project.org/web/packages/dplyr/index.html>
- Wickham H, Vaughan D, Girlich M, Ushey K. Tidy Messy Data. Available from: <https://cran.r-project.org/web/packages/tidyr/index.html>
- Wickham H; RStudio. stringr: Simple, Consistent Wrappers for Common String Operations. Available from: <https://rdr.io/cran/stringr/>
- Wickham H. ggplot2: Elegant Graphics for Data Analysis. New York: Springer-Verlag, 2016.
- Viechtbauer W. Conducting meta-analyses in R with the metafor package. Available from: <https://www.metafor-project.org>
- D'Ascanio L, Pandolfini M, Cingolani C, Latini G, Gradoni P, Capalbo M, et al. Olfactory dysfunction in COVID-19 patients: prevalence and prognosis for recovering the sense of smell. *Otolaryngol Head Neck Surg*. 2021;164(1):82-6. <https://doi.org/10.1177/0194599820943530>
- Denis F, Septans AL, Periers L, Maillard JM, Legoff F, Gurden H, et al. Olfactory Training and Visual Stimulation Assisted by a Web Application for Patients with Persistent Olfactory Dysfunction After SARS-CoV-2 Infection: Observational Study. *J Med Internet Res*. 2021;23(5):e29583. <https://doi.org/10.2196/29583>
- Vaira LA, Deiana G, Fois AG, Pirina P, Madeddu G, De Vito A, et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single-center experience on 72 cases. *Head Neck*. 2020;42(6):1252-8. <https://doi.org/10.1002/hed.26204>
- Weinbergerova B, Mayer J, Hrabovsky S, Novakova Z, Pospisil Z, Martykanova L, et al. COVID-19's natural course among ambulatory monitored outpatients. *Sci Rep*. 2021;11:10124. <https://doi.org/10.1038/s41598-021-89545-1>
- Wilton A, Kilich E, Chaudhry Z, Bell LC, Gahir J, Cadman J, et al. Delayed healthcare seeking and prolonged illness in healthcare workers during the COVID-19 pandemic: a single-center observational study. *BMJ Open*. 2020;10:e040216. <https://doi.org/10.1136/bmjopen-2020-040216>



25. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and COVID-19 in patients presenting with influenza-like symptoms. *Int Forum Allergy Rhinol.* 2020;10(7):806-13. <https://doi.org/10.1002/alar.22579>
26. Gelardi M, Trecca E, Cassano M, Ciprandi G. Smell and taste dysfunction during the covid-19 outbreak: a preliminary report. *Acta Biomed.* 2020;91(2):230-1. <https://doi.org/10.23750/abm.v91i2.9524>
27. Joffily L, Ungierowicz A, David AG, Melo B, Brito CLT, Mello L, et al. The close relationship between sudden loss of smell and COVID-19. *Braz J Otorhinolaryngol.* 2020;86(5):632-38. <https://doi.org/10.1016/j.bjorl.2020.05.002>
28. Kosugi EM, Lavinsky J, Romano FR, Fornazieri MA, Luz-Matsumoto GR, Lessa MM, et al. Incomplete and late recovery of sudden olfactory dysfunction in COVID-19. *Braz J Otorhinolaryngol.* 2020;86(4):490-6. <https://doi.org/10.1016/j.bjorl.2020.05.001>
29. Lechien JR, Chiesa-Estomba CM, De Siaty DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Otorhinolaryngol.* 2020;277(8):2251-61. <https://doi.org/10.1007/s00405-020-05965-1>
30. Leedman SR, Sheeraz M, Sanfilippo PG, Edgar DW, D'Aulerio GV, Robb DM, et al. Olfactory dysfunction at six months after coronavirus disease 2019 infection. *J Laryngol Otol.* 2021;135(9):839-43. <https://doi.org/10.1017/S0022215121002085>
31. Paolo G. Does COVID-19 cause permanent damage to olfactory and gustatory function? *Med Hypotheses.* 2020;143:110086. <https://doi.org/10.1016/j.mehy.2020.110086>
32. Parente-Arias P, Barreira-Fernandez P, Quintana-Sanjuas A, Patiño-Castiñeira B. Recovery rate and factors associated with smell and taste disruption in patients with coronavirus disease 2019. *Am J Otolaryngol.* 2021;42(5):102648. <https://doi.org/10.1016/j.amjoto.2020.102648>
33. Schönegger CM, Gietl S, Heinzle B, Freudenschuss K, Walder G. Smell and taste disorders in COVID-19 patients: objective testing and magnetic resonance imaging in five cases. *SN Compr Clin Med.* 2020;2(12):2535-9. <https://doi.org/10.1007/s42399-020-00606-4>
34. Mullol J, Alobid I, Mariño-Sánchez F, Izquierdo-Domínguez A, Marin C, Klimek L, et al. The loss of smell and taste in the COVID-19 outbreak: a tale of many countries. *Curr Allergy Asthma Rep.* 2020;20(10):61. <https://doi.org/10.1007/s11882-020-00961-1>
35. Yachou Y, El Idrissi A, Belapasov V, Benali SA. Neuroinvasion, neurotropic, and neuroinflammatory events of SARS-CoV-2: understanding the neurological manifestations in COVID-19 patients. *Neurol Sci.* 2020;41(10):2657-69. <https://doi.org/10.1007/s10072-020-04575-3>
36. Sayin I, Yazici ZM. Taste and smell impairment in SARS-CoV-2 recovers early and spontaneously: experimental data strongly linked to clinical data. *ACS Chem Neurosci.* 2020;11(14):2031-3. <https://doi.org/10.1021/acscchemneuro.0c00296>
37. Coelho DH, Reiter ER., Budd SG, Shin Y, Kons ZA, Costanzo RM. Quality of life and safety impact of COVID-19 associated smell and taste disturbances. *Am J Otolaryngol.* 2021;42(4):103001. <https://doi.org/10.1016/j.amjoto.2021.103001>
38. Elkholi S, Abdelwahab MK, Abdelhafeez M. Impact of the smell loss on the quality of life and adopted coping strategies in COVID-19 patients. *Eur Arch Otorhinolaryngol.* 2021;278(9):3307-14. <https://doi.org/10.1007/s00405-020-06575-7>
39. Yom-Tov E, Lekkass D, Jacobson NC. Association of COVID-19-induced anosmia and ageusia with depression and suicidal ideation. *J Affect Disord Rep.* 2021;5:100156. <https://doi.org/10.1016/j.jadr.2021.100156>
40. Mazza MG, De Lorenzo R, Conte C, Poletti S, Vai B, Bollettini I, et al. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain Behav Immun.* 2020;89:594-600. <https://doi.org/10.1016/j.bbi.2020.07.037>