



SYSTEMATIC REVIEW

Anosmia and dysgeusia in COVID-19: A systematic review

[version 1; peer review: 2 approved, 1 not approved]

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Abstract

Background: This systematic review had three aims: i) to determine the frequency of anosmia (or other smell disorders) and dysgeusia (or other taste disorders) in COVID-19 patients; ii) to determine whether anosmia or dysgeusia are independently associated with COVID-19 diagnosis; and iii) to determine whether anosmia or dysgeusia are prognostic factors for impaired outcomes among COVID-19 patients.

Methods: On April 20th, 2020, we search MEDLINE, Embase, Global Health, Scopus, Web of Science and MedXriv. We used terms related to COVID-19, smell and taste disorders. We selected case series, cross-sectional, case-control and cohort studies. We included studies with COVID-19 patients describing their symptoms; studies that compared smell and taste disorders between COVID-19 patients and otherwise healthy subjects; and studies comparing smell and taste disorders between COVID-19 severe and mild/moderate cases. Because of methodological heterogeneity and the limited number of results, a qualitative synthesis is presented.


Results: From 31 reports, we selected six (n=2,757). Six studies reported the proportion of smell and taste disorders among COVID-19 patients. Two reports studied whether smell and taste disorders were independently associated with COVID-19 diagnosis. No reports studied the association with impaired outcomes among COVID-19 patients. The frequency of anosmia ranged between 22%-68%. The definition of taste disorders varied greatly, with dysgeusia present in 33% and ageusia in 20%. People who reported loss of smell and taste had six-fold higher odds of being COVID-19 positive; similarly, anosmia and ageusia were associated with 10-fold higher odds of COVID-19 diagnosis.


Conclusions: The frequency of smell and taste disorders is as high as other symptoms, thus, at least anosmia for which the definition was more consistent, could be included in lists of COVID-19 symptoms. Although there is promising evidence, it is premature to conclude that smell and taste disorders are strongly associated with COVID-19 diagnosis.

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Any reports and responses or comments on the article can be found at the end of the article.

Keywords

COVID-19, smell disorders, taste disorders, neurological symptoms

Corresponding author: Rodrigo M. Carrillo-Larco (rcarrill@ic.ac.uk)**Author roles:** **Carrillo-Larco RM:** Conceptualization, Formal Analysis, Investigation, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Altez-Fernandez C:** Conceptualization, Investigation, Methodology, Writing – Review & Editing**Competing interests:** No competing interests were disclosed.**Grant information:** This work was supported by the Wellcome Trust through an International Training Fellowship [214185] to Rodrigo M Carrillo-Larco.*The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.***Copyright:** © 2020 Carrillo-Larco RM and Altez-Fernandez C. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.**How to cite this article:** Carrillo-Larco RM and Altez-Fernandez C. **Anosmia and dysgeusia in COVID-19: A systematic review [version 1; peer review: 2 approved, 1 not approved]** Wellcome Open Research 2020, 5:94 <https://doi.org/10.12688/wellcomeopenres.15917.1>**First published:** 13 May 2020, 5:94 <https://doi.org/10.12688/wellcomeopenres.15917.1>

Introduction

COVID-19 is certainly the greatest global health problem nowadays and for the foreseeable future. Clinicians and scientists from all over the world have been producing evidence to understand the epidemiology, clinical profile and prognostic factors of COVID-19. Ever since the first report was published, the world has moved from knowing a few symptoms and risk factors to a large list of COVID-19 symptoms that can also be used for screening and risk stratification purposes¹. However, as more evidence becomes available, it is relevant to ascertain its quality and build on this evidence to reach strong conclusions to advance clinical medicine and public health.

Smell and taste disorders, such as anosmia (smell loss) and dysgeusia (taste impairment), have garnered recent attention as potential frequent symptoms and relevant variables for COVID-19 screening²⁻⁷. They are particularly relevant because their assessment does not require interventions or procedures, making them a friendly variable to include in questionnaires or screening algorithms. However, the strength of the evidence for an association between smell and taste disorders and COVID-19 is limited to case reports or anecdotal experiences. Consequently, it is largely unknown whether smell and taste disorders are a frequent symptom among COVID-19 patients, whether they are associated with higher odds of COVID-19 diagnosis, and whether they are prognostic factors for COVID-19 impaired endpoints. To answer these questions and to strengthen the evidence about smell and taste disorders in COVID-19 diagnosis and prognosis, we conducted a systematic review.

Methods

Protocol

This systematic review of the scientific literature pursued three aims: i) to determine the frequency of anosmia (or other smell disorders) and dysgeusia (or other taste disorders) in COVID-19 patients; ii) to determine whether anosmia or dysgeusia are independent risk factors for COVID-19 diagnosis; and iii) to determine whether anosmia or dysgeusia are independent prognostic factors for impaired outcomes among COVID-19 patients. We followed the PRISMA reporting guidelines⁸ (see *Reporting guidelines*)⁹ and the protocol was prospectively registered at PROSPERO (CRD42020181308).

Eligibility criteria

Selected reports included COVID-19 patients (as defined by the original report), men and women. For aims two and three the exposures were anosmia or dysgeusia, both as defined by the original report; similarly, for aims two and three, the comparator was individuals without anosmia or dysgeusia. For the second aim the outcome was COVID-19 diagnosis, whereas for the third aim the outcome was unfavourable endpoints (e.g., admission to intensive care) among COVID-19 patients. For all aims, patients could have been recruited from hospitals or from the community.

We selected observational studies, including case-series, cross-sectional, case-control and retrospective/prospective cohorts.

We excluded case reports and trial or intervention studies. We included both published and unpublished materials (pre-prints) and had no language restriction.

Information sources and search

We used five sources for published materials: MEDLINE, Embase, Global Health, Scopus and Web of Science; the first three through OVID with restriction to reports published in 2020. We also searched MedRxiv for unpublished materials. The search was conducted on April 20th, 2020. The search terms we used are available in Supplementary material table 2 (see *Extended data*)⁹.

Study selection

The search results were downloaded to remove duplicate registries. The titles and abstracts were screened to verify whether they met the inclusion criteria described above by two reviewers independently (RMC-L and CA-F). We then studied in detail the reports the two reviewers agreed should be included, as well as those on which the reviewers disagreed. The in-depth evaluation was conducted by two reviewers independently (RMC-L and CA-F); discrepancies at this stage were solved by consensus.

Data collection

The authors designed a data extraction form and piloted it with two of the selected reports. The form was updated, and one reviewer extracted the information (CA-F) and another verified the extraction (RMC-L); discrepancies were solved by consensus. The information collected included: country where the study took place, sample size, proportion of men and mean age, proportion of anosmia and dysgeusia symptoms (or other smell and taste disorders), and association metrics between exposure and outcomes of interest.

Risk of bias of individual studies

We used three tools to assess risk of bias, depending on the study design. Studies that assessed the association between anosmia and dysgeusia with COVID-19 were scrutinized with the QUIPS tool¹⁰. Conversely, cross-sectional studies were assessed with the Appraisal tool for Cross-Sectional Studies (AXIS)¹¹, and case series were analysed with the IHE Quality Appraisal Checklist for Case Series Studies instrument¹². Risk of bias was conducted by one reviewer (CA-F).

Synthesis of results

We summarized the results qualitatively, by reporting characteristics of the selected reports and studied populations; this included the proportion of COVID-19 patients with anosmia and dysgeusia (or other smell and taste disorders). In addition, we described the association estimates between anosmia and dysgeusia and COVID-19 diagnosis. Because of great heterogeneity in the methods studies used to collect information and the methods used to ascertain anosmia and dysgeusia, we did not pool the proportion of COVID-19 patients with these complaints. Similarly, we did not pool the association estimates because of the limited number of reports.

Ethics

This is a systematic review of the scientific literature. No human subject participated in the investigation. We did not request approval by an Institutional Review Board or Ethics Committee.

Results

Study selection

The search yielded 31 results, of which 14 met the inclusion criteria and were studied in detail; finally, six (n=2,757) reports were selected for data extraction (Figure 1). Of the selected reports¹³⁻¹⁸, six provided information for the first aim (frequency of anosmia and dysgeusia in COVID-19 patients)¹³⁻¹⁸, and two informed the second aim (association between anosmia and dysgeusia with COVID-19 diagnosis)^{16,18}. We did not find any reports that studied the association between anosmia and dysgeusia with impaired outcomes (e.g., admission to intensive care) in COVID-19 patients.

Study characteristics

The studies were conducted in China (n=214)¹⁵, Iran (n=120)¹⁷, Israel (n=42)¹⁴, the UK (n=1,702)¹⁶ and US (n=262)¹⁸; Lechien and colleagues (n=417) studied patients in four countries in Europe (Table 1)¹³. All but one study (case-series)¹⁵ followed a cross-sectional design (Table 1). The mean age of the study participants ranged from 34 to 52 years^{14,15}; the proportion of men ranged from 28% to 66% (Table 1)^{16,17}.

There was great heterogeneity regarding how the information was collected. Most researchers used questionnaires, and these were applied through email, apps and mobiles (Table 1). Moein *et al.* used a validated questionnaire (University of Pennsylvania Smell identification Test)¹⁷, while Mao's group used electronic medical records based on information collected by neurologists (Table 1)¹⁵. There was also a lack of detail on how anosmia and dysgeusia were ascertained, and some authors used

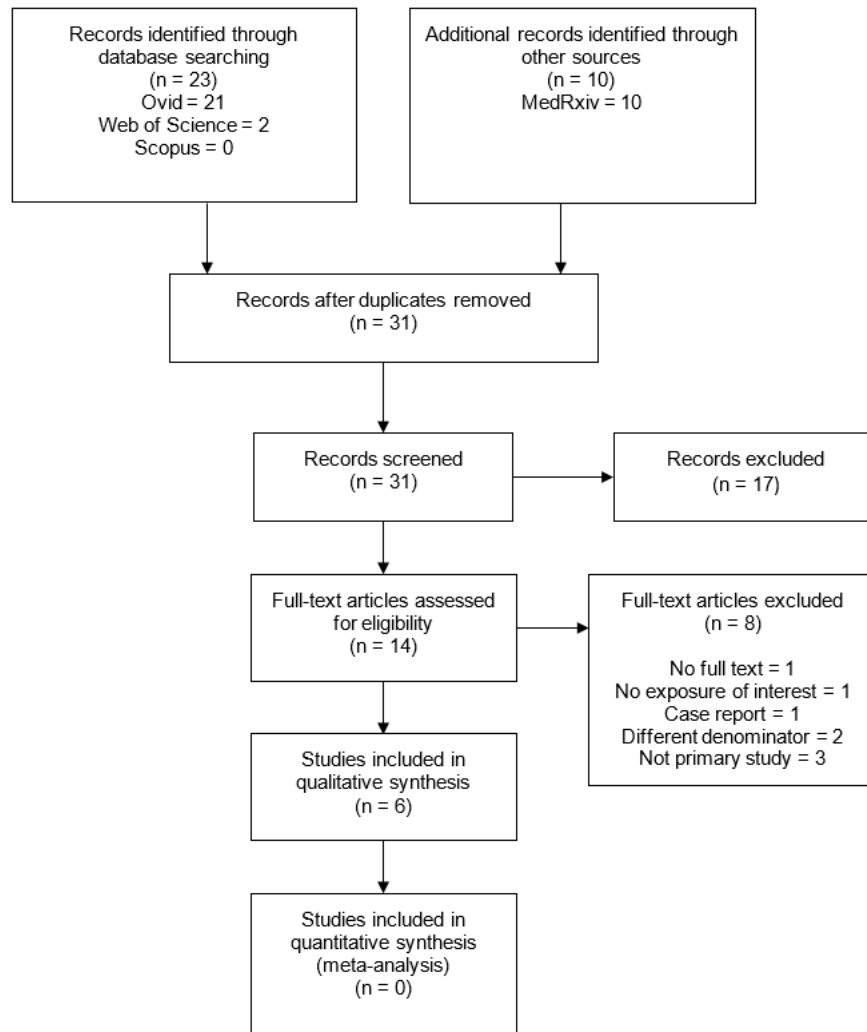


Figure 1. Selection process.

Table 1. Anosmia and dysgeusia in COVID-19 patients.

First author	Country	Study design	Total sample	Mean age	Men proportion	COVID-19 proportion	Method of smell problems evaluation	Proportion of smell problems in COVID-19	Method of taste problems evaluation	Proportion of taste problems in COVID+
<i>Lechein</i>	Belgium; France; Spain; Italy	Cross-sectional	417	36.9	36.9	1.00	Consultation or online questionnaire for house-bound patients	Anosmia = 68.1% (284/417); Hyposmia = 17.5% (73/417)	Consultation or online questionnaire for house-bound patients	Reduced/discontinued taste = 78.9%; Distorted taste = 21.1%
<i>Moein</i>	Iran	Cross-sectional study in which COVID-19 cases were 1:1 matched with people of a previous study	120	46.5 (among COVID-19 patients)	66.6 (among COVID-19 patients)	0.5	University of Pennsylvania Smell identification Test (UPSIT) assisted by a trained examiner	Normosmia = 2% (1/60); Mild microsmia = 13% (8/60); Moderate microsmia = 27% (16/60); Severe microsmia = 33% (20/60); Anosmia = 25% (15/60)	Not reported	Not reported
<i>Yan</i>	USA	Cross-sectional	262	17.6% (60+ years)	37.4	22.5	Questionnaire through email	Anosmia = 22% (13/59)	Questionnaire through email	Ageusia= 20.3% (12/59)
<i>Levinson</i>	Israel	Cross-sectional	42	34.0	54.8	1.00	Questionnaire through mobile phone or email	Anosmia= 35.7% (15/42)	Questionnaire through mobile phone or email	Dysgeusia= 33.3% (14/42)
<i>Mao</i>	China	Case series	214	52.7	40.7	1.00	Electronic medical records based on the evaluation of two neurologists	Smell Impairment= 5.1% (11/214)	Electronic medical records based on the evaluation of two neurologists	Taste impairment= 5.6% (12/214)
<i>Menni</i>	UK	Cross-sectional	1702	41.1	28.0	34.0	Questionnaire through mobile app	Loss of taste and smell = 59.4% (343/579)	Questionnaire through mobile app	Loss of taste and smell = 59.4% (343/579)

broader categories like ‘smell impairment’ or ‘loss of taste and smell’ (Table 1).

Frequency of anosmia and dysgeusia among COVID-19 patients

The frequency of anosmia in COVID-19 patients ranged from 22% to 68%^{13,18}. The definition of taste impairment was more heterogeneous, with dysgeusia present in 33% of COVID-19 patients¹⁴, ageusia in 20%¹⁸, and distorted taste was found in 21% of patients with COVID-19¹³.

Association between anosmia and dysgeusia with COVID-19

Two reports studied the association between anosmia and dysgeusia with COVID-19 diagnosis^{16,18}, and we did not find any reports studying anosmia and dysgeusia with impaired outcomes in COVID-19 patients.

Menni and colleagues found that people with loss of smell and taste had six-fold higher odds of being COVID-19 positive (Table 2)¹⁶. Similarly, Yan *et al.* found that people presenting anosmia had 10-fold higher odds of being diagnosed with COVID-19¹⁸ (Table 2). Yan’s work also studied taste disorders and reported that people with ageusia had 10-fold higher odds of having COVID-19¹⁸ (Table 2). Notably, all the association estimates were adjusted for co-variables including age, sex and other symptoms (Table 2)^{16,18}.

Risk of bias

The reports by Menni *et al.* and Yan *et al.* were assessed with the QUIPS tool. These studies showed low risk of bias in three criteria: study participation, outcome measurement and statistical analysis and reporting; similarly, they both had moderate risk of bias in the criteria: prognostic factor measurement and study confounding. These studies were assessed differently regarding the study attrition criterion: Menni’s work had low risk whereas Yan’s study showed moderate risk of bias (Table 3). Overall, the risk of bias assessment for the other studies did not reveal an alarming high risk of bias (see *Extended data*)⁹.

Discussion

Main findings

This systematic review and critical appraisal of the scientific evidence showed that anosmia may be present in one of every five COVID-19 patients; on the other hand, the frequency of taste disorders varied greatly depending on the definition. This review also found two studies that assessed the association between smell and taste disorders with COVID-19 diagnosis; both studies showed a strong association between anosmia and COVID-19 diagnosis, as well as between ageusia and COVID-19 diagnosis. Notably, these associations were adjusted for socio-demographic variables and other symptoms. There were no reports that studied the association between smell and taste disorders with impaired endpoints among COVID-19 patients.

Table 2. Association between anosmia and dysgeusia with COVID-19 diagnosis.

First author	Exposure	Method of exposure evaluation	Outcome	Outcome definition	Exposure proportion in COVID+	OR for COVID-19 diagnosis (95% CI)	Adjusted for
Menni	Loss of taste and smell	Questionnaire through app	COVID-19 infection	rt-PCR confirmation	59.41%	6.59 (5.25-8.27)	Sex, age, BMI
Yan	Anosmia	Questionnaire through email	COVID-19 infection	rt-PCR confirmation	22.00%	10.92 (5.08-23.53)	Myalgia/Arthralgia; fatigue; fever; nausea; sore throat
Yan	Ageusia	Questionnaire through email	COVID-19 infection	rt-PCR confirmation	20.30%	10.23 (4.74-22.09)	Myalgia/Arthralgia; fatigue; fever; nausea; sore throat

OR, odds ratio; PCR, polymerase chain reaction; BMI, body mass index.

Table 3. Risk of bias of independent studies.

	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
Menni	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	Low risk
Yan	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk	Low risk

Implications for clinical practice

Available evidence may suggest that anosmia is frequently found among COVID-19 patients, as much as or even more frequently than other symptoms^{19–22}. This may be the reason why the American Centres for Diseases Control and Prevention included smell loss in their list of COVID-19 symptoms²³; however, smell loss was not included in the list by the World Health Organization²⁴. Our results may support including anosmia in the lists of COVID-19 symptoms.

The American Centres for Diseases Control and Prevention included taste loss in their list of COVID-19 symptoms²³, yet the World Health Organization did not²⁴. Our review found huge heterogeneity on how dysgeusia was assessed and defined. Therefore, our results do not support including taste impairment as a COVID-19 symptom. As more evidence becomes available, ideally including a large sample of patients and consistent definitions, this recommendation can be revisited.

It has been argued that smell loss could be useful for COVID-19 screening^{25,26}, and it certainly has a huge advantage as its assessment may be inexpensive and harmless²⁷. Our review found two reports signalling that anosmia or smell impairment was independently associated with COVID-19 diagnosis. Nonetheless, and despite the promising evidence^{16,18}, it seems premature to undoubtedly conclude that anosmia is a strong risk factor for COVID-19 diagnosis or that it can be a successful screening test.

Implications for research

The clinical and research community will keep on producing evidence about COVID-19, and the associated risk and prognostic factors. Nevertheless, studies with consistent methodologies and definitions are much needed to make comparisons and reach strong conclusions. We invite neurology and otorhinolaryngology professionals to propose a standard definition for anosmia and dysgeusia, along with recommendations on how to assess these symptoms. This way, and as more evidence is published, we will have a better understanding of the role of anosmia and dysgeusia in COVID-19 diagnosis and prognosis.

Limitations of the review

We conducted a systematic review using six data sources, including one for unpublished materials. We followed standard methods and used relevant tools to appraise the risk of bias. Nonetheless, there are a few limitations we need to acknowledge. The search did not offer any results from Latin America or Africa. Probably, reports from these regions are in local journals not included in the five search engines we used, or it takes a longer time to have their reports uploaded. Future

studies in these regions could include regional search engines or other local sources of grey literature. We did not adhere to a strict definition of anosmia or dysgeusia, trying to retrieve as much evidence as possible; despite this decision, the search did not give many results.

Limitations of the selected reports

The selected reports provided relevant information, though there was great heterogeneity regarding how the exposure of interest was defined and ascertained, and how the information was collected. Also, they studied a limited number of patients. There seems to be a dearth of tools to assess anosmia and dysgeusia, yet Moein and colleagues used the University of Pennsylvania Smell identification Test¹⁷. This review provides a comprehensive framework of available evidence about anosmia and dysgeusia in COVID-19, so that researchers interested in this field can build on and advance the available evidence. This could include using standard definitions for the exposure variables and including more patients, ideally from multiple sites or countries, like the work by Lechein and colleagues¹³.

Conclusions

Although anosmia seems to be a frequent finding among COVID-19 patients, and it was independently associated with COVID-19 diagnosis, the evidence is still insufficient to claim that anosmia is a strong predictor for COVID-19 diagnosis. The evidence for dysgeusia is much more limited. As the clinical and research community struggle to find predictors to early identify COVID-19 cases, several potential variables should be considered yet studied thoroughly before they can be recommended as risk factors or to be included in risk stratification tools.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Figshare: Systematic Review: Anosmia/Dysgeusia & COVID-19. <https://doi.org/10.6084/m9.figshare.12203435.v2>⁹

The Supplementary Material DOCX file contains the following extended data:

- Supplementary material table 2 (search terms)
- Risk of bias for Lechien *et al.*, Levinston *et al.*, Moein *et al.*, and Mao *et al.*

Reporting guidelines

PRISMA checklist for 'Systematic Review: Anosmia/Dysgeusia & COVID-19'. <https://doi.org/10.6084/m9.figshare.12203435.v2>⁹

References

1. Wynants L, Van Calster B, Bonten MMJ, *et al.*: **Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal.** *BMJ.* 2020; **369**: m1328. [PubMed Abstract](#) | [Publisher Full Text](#)
2. Eliezer M, Hautefort C, Hamel AL, *et al.*: **Sudden and Complete Olfactory Loss Function as a Possible Symptom of COVID-19.** *JAMA Otolaryngol Head Neck Surg.* 2020. [PubMed Abstract](#) | [Publisher Full Text](#)

3. Gane SB, Kelly C, Hopkins C: **Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome?** *Rhinology*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#)
4. Hopkins C, Surda P, Kumar N: **Presentation of new onset anosmia during the COVID-19 pandemic.** *Rhinology*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#)
5. Keyhan SO, Fallahi HR, Cheshmi B: **Dysosmia and dysgeusia due to the 2019 Novel Coronavirus; a hypothesis that needs further investigation.** *Maxillofac Plast Reconstr Surg*. 2020; 42(1): 9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. Russell B, Moss C, Rigg A, *et al.*: **Anosmia and ageusia are emerging as symptoms in patients with COVID-19: What does the current evidence say?** *Ecanermedicalscience*. 2020; 14: ed98.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
7. Vaira LA, Salzano G, Deiana G, *et al.*: **Anosmia and Ageusia: Common Findings in COVID-19 Patients.** *Laryngoscope*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Moher D, Liberati A, Tetzlaff J, *et al.*: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.** *PLoS Med*. 2009; 6(7): e1000097.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
9. Carrillo Larco R: **Untitled Item.** *figshare*. 2020.
<http://www.doi.org/10.6084/m9.figshare.12203435.v2>
10. Riley RD, Moons KGM, Snell KIE, *et al.*: **A guide to systematic review and meta-analysis of prognostic factor studies.** *BMJ*. 2019; 364: k4597.
[PubMed Abstract](#) | [Publisher Full Text](#)
11. Downes MJ, Brennan ML, Williams HC, *et al.*: **Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS).** *BMJ Open*. 2016; 6(12): e011458.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
12. Institute of Health Economics: **IHE Quality Appraisal Checklist for Case Series Studies.** (Accessed April 22nd, 2020).
[Reference Source](#)
13. Lechien JR, Chiesa-Estomba CM, De Siatl DR, *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.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
14. Levinson R, Elbaz M, Ben-Ami R, *et al.*: **Anosmia and dysgeusia in patients with mild SARS-CoV-2 infection.** *medRxiv*. 2020.
[Publisher Full Text](#)
15. Mao L, Jin H, Wang M, *et al.*: **Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China.** *JAMA Neurol*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
16. Menni C, Valdes A, Freydin MB, *et al.*: **Loss of smell and taste in combination with other symptoms is a strong predictor of COVID-19 infection.** *medRxiv*. 2020.
[Publisher Full Text](#)
17. Moein ST, Hashemian SMR, Mansourafshar B, *et al.*: **Smell dysfunction: a biomarker for COVID-19.** *Int Forum Allergy Rhinol*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#)
18. Yan CH, Faraji F, Prajapati DP, *et al.*: **Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms.** *Int Forum Allergy Rhinol*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#)
19. Wang D, Hu B, Hu C, *et al.*: **Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China.** *JAMA*. 2020.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
20. Huang C, Wang Y, Li X, *et al.*: **Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.** *Lancet*. 2020; 395(10223): 497–506.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
21. Guan WJ, Ni ZY, Hu Y, *et al.*: **Clinical Characteristics of Coronavirus Disease 2019 in China.** *N Engl J Med*. 2020.
[Publisher Full Text](#)
22. Chen N, Zhou M, Dong X, *et al.*: **Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.** *Lancet*. 2020; 395(10223): 507–13.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Centres for Diseases Control and Prevention: **Symptoms of Coronavirus.** (Accessed April 22nd, 2020).
[Reference Source](#)
24. World Health Organization: **Q&A on coronaviruses (COVID-19).** (accessed April 22nd, 2020).
[Reference Source](#)
25. Medscape: **Sudden Loss of Taste and Smell Should Be Part of COVID-19 Screen.** (Accessed April 22nd, 2020).
[Reference Source](#)
26. Proclama Cauca y Valle: **Prueba de olfato para comprobar síntomas de coronavirus.** (Accessed April 22nd, 2020).
[Reference Source](#)
27. Xydakis MS, Dehgani-Mobaraki P, Holbrook EH, *et al.*: **Smell and taste dysfunction in patients with COVID-19.** *Lancet Infect Dis*. 2020; pii: S1473-3099(20)30293-0.
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In this paper, the authors perform a systematic review on anosmia and dysgeusia in COVID-19 patients and define three aims: to determine 1) the prevalence of anosmia and dysgeusia, 2) whether there are independent associations of anosmia or dysgeusia with the disease and 3) whether those symptoms influence the course of the disease.

1. My major concern with this study is a concern that the authors have expressed as well: that the various studies ascertaining prevalence of olfactory and taste dysfunction in COVID-19, and which have been included, are quite heterogeneous in design/methods (specifically asking patients about olfactory and taste dysfunction vs. chart review) and patient populations (e.g. mild COVID-19, those with flu-like symptoms, non-hospitalized vs. hospitalized). The degree of heterogeneity is too much to synthesize the data and the authors have correctly not performed a meta-analysis. However, I also question whether these data - especially in light of the continually increasing data that are being published on this topic - are sufficient for a systematic review.

2. Title: "Anosmia and dysgeusia in COVID-19..."

- A) The authors also mention hyposmia, mild microsmia, smell impairment. Why would therefore the title not be "Olfactory dysfunction and dysgeusia in COVID-19..."

3. Introduction:

- A) Further, the authors state that smell and taste disorders are particularly relevant because their assessment does not require interventions or procedures, making them a "friendly" variable to include in questionnaires or screening algorithms.
- This might be true, I believe that the symptoms of smell and taste disorders as symptoms of COVID disease are even more important, as many COVID positive patients experience smell and taste disorders as one of their symptoms and sometimes also as their only symptom. Therefore in my opinion it is not the potential "easiness" of assessment/includement in a questionnaire/history of

why smell and taste disorders are so important regarding the disease, but more so as positive patients who “only” suffer from smell and/or taste disorders might be possible spreaders of the disease and therefore it is important to render attention to those patients.

- B) Further in the introduction it is stated that it is largely unknown whether smell and taste disorders are a frequent symptom among COVID-19 patients. I believe many recent articles have shown that smell and taste disorders are frequent symptoms of COVID-19 patients (see for example Lechien *et al.*, 2020¹).
- C) In additions the authors state that it is further unknown whether smell and taste disorders are associated with higher odds of COVID-19 diagnosis, and whether they are prognostic factors for COVID-19 impaired endpoints. Please specify that you mean ****new onset**** smell and taste disorders.

4. Methods:

A) Eligibility criteria: “the comparator was individuals without anosmia or dysgeusia”.

- grammar: “ the comparator were individuals..:”

B) I disagree with using articles from a preprint server. At this point, there are so many articles that have been published on olfactory dysfunction and taste dysfunction in COVID-19, that we should be relying entirely on peer-reviewed studies.

5. Results:

- A) Study characteristics: “Moein *et al.* used a validated questionnaire (UPSIT)”. The UPSIT is an objective smell test, thus the word “questionnaire” sounds a bit confusing.
- B) Frequency of anosmia and dysgeusia among COVID-19 patients: “The definition of taste impairment was more heterogeneous, with dysgeusia present [..], ageusia in [...], and distorted taste in [...]”.
- C) I do not understand why the “definition of taste impairment was more heterogeneous? Dysgeusia is something different than ageusia.
- D) Association between anosmia and dysgeusia with COVID-19: As stated above, please specify that you are referring to ****new onset**** anosmia and dysgeusia.
- E) Table 2: Exposure: to be coherent, I would suggest to either write about loss of taste and smell or about anosmia or ageusia.

6. Discussion:

- A) Main findings: “This systematic review [...] in one of every five COVID-19 patents.” - a grammar/typo: “patents”, please change to “patients”.
- B) Implications for clinical practice: “Our results may support including anosmia in the list of COVID-19 symptoms.” In the paper, the authors also included hyposmia, what about this, would it be included as a symptom and what does “may support including” mean? Did the authors come to

the conclusion that **olfactory dysfunction** should be included as a symptom or not or were they not able to draw a conclusion based on what factors?

- C) The authors further come to the conclusion that they do not support including taste impairment as a COVID-19 symptom due to the huge heterogeneity on how dysgeusia is assessed and defined. However, what the authors of the paper cite as heterogeneity in their paper is partly also different medical terms for different medical issues. Thus, it would be utterly important for the authors to study and use the correct medical term.

7. Implications for research:

- “Nevertheless studies with consistent methodologies and definitions are much needed to make comparisons and reach strong conclusions. We invite neurology and otorhinology professionals to propose a standard definition for anosmia and dysgeusia, along with recommendations on how to assess these symptoms”.
- Anosmia and dysgeusia are medical terms, which have already been defined (see for example, the Position Paper on Olfactory Dysfunction by Hummel *et al.*, 2017²). Recommendations on how to assess these symptoms have also been made in the past.
- It is of importance to also use these medical terms correctly. Anosmia, dysosmia, hyposmia, ageusia, dysgeusia are in fact not terms applied “heterogeneous”, but are terms used for talking about different medical conditions.

References

1. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, 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. [PubMed Abstract](#) | [Publisher Full Text](#)
2. Hummel T, Whitcroft KL, Andrews P, Altundag A, et al.: Position paper on olfactory dysfunction. *Rhinol Suppl*. 54 (26): 1-30 [PubMed Abstract](#) | [Publisher Full Text](#)

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Partly

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Rhinology, chronic rhinosinusitis, allergy, olfactory dysfunction in covid patients

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 16 June 2020

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B. Nirmal Kumar

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John Rocke

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Thanks for the invitation to perform open peer review. This is a very important topic of great public health importance as appropriate measures can reduce the spread of the virus and help contain the pandemic.

- Are the rationale for, and objectives of, the Systematic Review clearly stated?

The three aims for the systematic review are clearly stated in the context of the COVID-19 outbreak. Identifying the frequency of these symptoms and risk factors for diagnosis is possible in the early stages of this pandemic but the 3rd aim of determining prognostic factors for outcomes is a little unrealistic considering the timeline.

There is clearly interest in the utility of anosmia and dysgeusia and this is a current and appropriately framed review.

The review does not state that the World Health Organisation has now recognized loss of smell as a key symptom in COVID-19 as the review was published in April.

- Are sufficient details of the methods and analysis provided to allow replication by others?

Search terms are included in the Appendix for future replication of searches. Prisma diagram demonstrates review process accurately. The review is framed towards anosmia but search terms also include “smell dysfunction” and “smell impairment” which are terms that are not truly anosmia. The authors may want to consider using another term instead of anosmia to better reflect their search strategy. This will help match the dysgeusia search term more closely as one of their aims is to assess if each are independently associated with diagnosis.

They selected only 6/31 reports and several notable studies have not been included in this review including Giacomelli *et al.*, Kaye *et al.* and Bagheri *et al.* Some of these articles may have been excluded due to the timing of this review but perhaps selection criteria for inclusion was limited.

- Is the statistical analysis and its interpretation appropriate?

No statistical analysis was undertaken in this study.

- Are the conclusions drawn adequately supported by the results presented in the review?

Reasonable and sensible conservative conclusions are drawn. Whilst olfactory dysfunction and anosmia may not be a strong predictor it seems, from the studies included, that it may be a better predictor than cough, fever or dyspnoea. As such it is important that this is recognised by the authors in their conclusions so that the symptom is recognised by public health bodies internationally.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Not applicable

Are the conclusions drawn adequately supported by the results presented in the review?

Yes

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 19 May 2020

<https://doi.org/10.21956/wellcomeopenres.17459.r38756>

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Luigi Angelo Vaira 

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Thanks for the opportunity to review this manuscript.

First, I would like to commend the authors for having collected the data currently present in the literature, regarding olfactory dysfunctions in COVID-19 patients.

The review proposed by the authors provides a useful summary of findings reported until 20th April. The review methodology is clearly stated and described and the data analysis and interpretation is correct.

I have only two minor comments:

1. At the beginning of the discussion section, the authors stated "there were no reports that studied the association between smell and taste disorders with impaired endpoints among COVID-19 patients". I believe that Moein *et al.* gives some prognostic indications without detecting significant correlations between the severity of chemosensitive disorders and the severity of COVID-19.

2. The topic is rapidly evolving and, after April 20, some studies have been published based on objective assessments with psychophysical tests. Before April 20, as rightly reported by the authors, the only one present in the literature was that of Moein *et al.* These studies have shown that observational or interviewing studies (such as almost all the studies published before April 20) underestimate the frequency of chemosensitive disorders. The latter studies show a high recall bias as many patients, who at the time of the visit no longer present the dysfunction, cannot remember it, often distracted by the seriousness of the general clinical picture. At the same time, only objective studies can allow to accurately quantify the disorder and differentiate it in the various clinical subcategories (e.g. anosmia, severe, moderate, mild hyposmia). Something in this sense could be added to the limitations of the selected reports in this sense.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Yes

Are the conclusions drawn adequately supported by the results presented in the review?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Maxillofacial surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
