Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Review

Taste alteration in COVID-19: Significant geographical differences exist in the prevalence of the symptom

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ABSTRACT

Early detection of COVID-19 is important for reduction in the spread of the disease and gustatory disturbances (GD) are known to have a strong predictive value. In the present study, we aimed to map the geographical differences in the prevalence of GD in individuals infected with SARS-CoV-2 during the first wave of COVID-19 in order to improve case identification and to facilitate prioritization. We undertook a rapid scoping review of articles published in the repository of the National Library of Medicine (MEDLINE/PubMed) and medRxiv from their inception until 3rd September, 2020. The minimum requirements for completing a restricted systematic review were fulfilled. Of the 431 articles retrieved, 61 studies (28,374 cases confirmed with COVID-19) from 20 countries were included in the analysis. GD were most prevalent in the Americas [66.78%, 95% CI 54.77–78.79%] compared to Europe [57.18%, 95% CI 52.35–62.01%], the Middle East [38.83%, 95% CI 27.47–50.19%] and East Asia [13.1%, 95% CI 0.14–26.06%]. No differences of GD prevalence were evident between February and August 2020. The data demonstrate that there is a marked geographical distribution of GD in COVID-19 patients which, possibly, might be explained by differences in diagnostic criteria for COVID-19 case definition during the early phase of the pandemic.

Contents

Abbreviations: COVID-19, coronavirus Disease 2019; SARS-CoV- 2, severe acute respiratory syndrome coronavirus 2; EDCD, European Centre for Disease Prevention and Control; CDC, Centers for Disease Control and Prevention (CDC); WHO, World Health Organization; GD, gustatory disease; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; ANOVA, analysis of variance.

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Introduction

The early identification and confirmation of suspected cases of Coronavirus Disease 2019 (COVID-19) is fundamental to limiting the spread of the disease but is particularly challenging for asymptomatic or pauci-symptomatic patients. The sudden loss of taste (ageusia), with or without loss of smell (anosmia), have been cited as independent signs of the disease although, more frequently, these symptoms occur in association with the most common manifestations of the disease, namely, fever, cough and fatigue [1]. Unlike early studies [2,3], recent systematic reviews have indicated that gustatory dysfunction (GD), including ageusia, hypogeusia and dysgeusia, is common in COVID-19 patients [4]. Furthermore, loss of taste and smell have been reported to be distinguishing symptoms of COVID-19 which have a high predictive value [5]. The European Centre for Disease Prevention and Control (EDCD) was one of the first public health bodies to include sudden onset anosmia, ageusia or dysgeusia as clinical criteria to identify possible COVID-19 cases [6]. Unfortunately, these symptoms have not been used unanimously for case identification and for testing prioritization. On 5th August 2020, however, the Centers for Disease Control and Prevention in the USA updated their COVID-19 case definition to include GD as an important clinical criterion for diagnosis [7]. Soon afterwards (7th August, 2020), the World Health Organization updated its COVID-19 case definition to include recent onset ageusia, in the absence of any other identifiable cause, as suggestive of COVID-19 infection [8].

In the present study, we hypothesized that differences in the criteria used for COVID-19 identification by national and/or local public health bodies may reflect, at least in part, the changes of known prevalence rates of these symptoms over time and in a geographically specific manner. Specifically, we undertook a rapid systematic review of the prevalence of GD in COVID-19 cases and examined worldwide data from East Asia, the Middle East (including Turkey), Europe (including Britain) and the Americas.

Results

We identified 431 studies; 91 relevant articles met the inclusion criteria. 61 of the 91 studies were included for data analysis (Fig. 1). The studies were from 20 different countries; 5 studies were derived from multi-national collaborations. The majority of cohorts were from Europe (n = 40), followed by the Middle East (n = 8), North and South America (n = 6 and n = 2, respectively), East Asia (n = 6) and Africa (n = 1). Two articles [9,10] pooled multinational data within Europe and 3 studies [11–13] included cases from two main geographical areas. The study populations and prevalence range are depicted graphically in Fig. 2.

Worldwide, 14,486 of 28,374 confirmed COVID-19 cases (51.05%) reported subjective and/or objective GD (Table 1). Strikingly, there were significant differences of prevalence between subgroups (ANOVA, p = 0.000106; Kruskal–Wallis, p = 0.00071). Further, when each geographical region was compared, there were significant differences between all of the subgroups except Europe vs America (Suppl Table 1). Studies from East Asia reported the lowest prevalence of GD (13.1%, 95% CI 0.14–26.06%), followed by the Middle East (38.83%, 95% CI 27.47–50.19%), Europe (57.18%, 95% CI 52.35–62.01%) and the Americas (66.78%, 95% CI 54.77–78.79). We could not highlight trends of increased GD prevalence in COVID-19 patients over time, except in East Asia (Supplementary Fig. 1).

Discussion

An awareness of the association between taste alterations and COVID-19 infection is important for diagnosing the disease, particularly in dental and oral health settings [14]. In the present study, we followed a streamlined approach to synthesizing evidence (the rapid review) which is typically used for informing emergent decisions faced by decision-makers in health care settings. The results of this rapid systematic review show that there are distinct geographical patterns of GD in patients with established SARS-CoV-2 infection.

The first systematic assessments of the evidence available up to March 2020 failed to identify associations between anosmia/ageusia and COVID-19 [2,3]. For example, in an early systematic review involving a total of 1556 patients, olfactory or gustative dysfunctions were not reported [2]. In another early study which examined evidence of anosmia in COVID-19 patients, researchers found the symptom to be of “limited and inconclusive” value [3]. The first study reporting a 5.1 and 5.6% prevalence

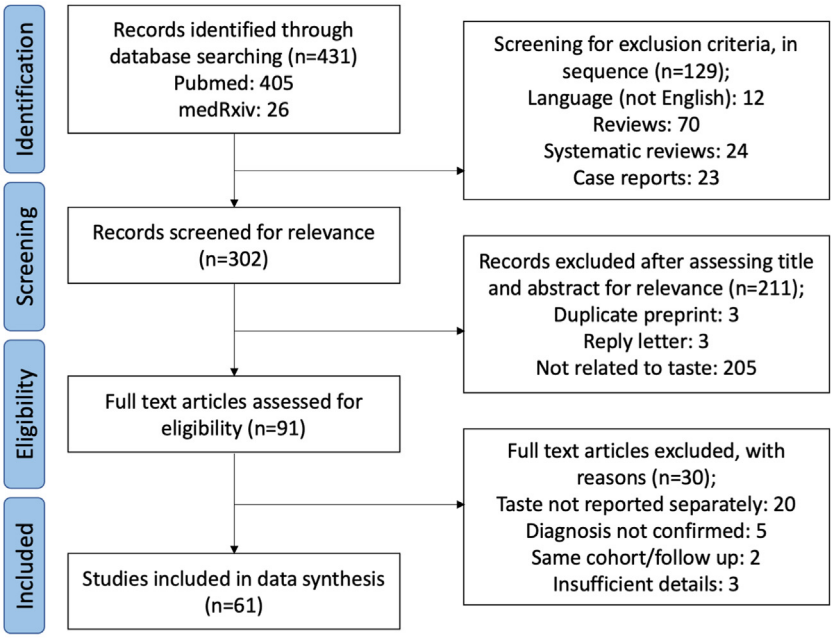

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart of study selection process.

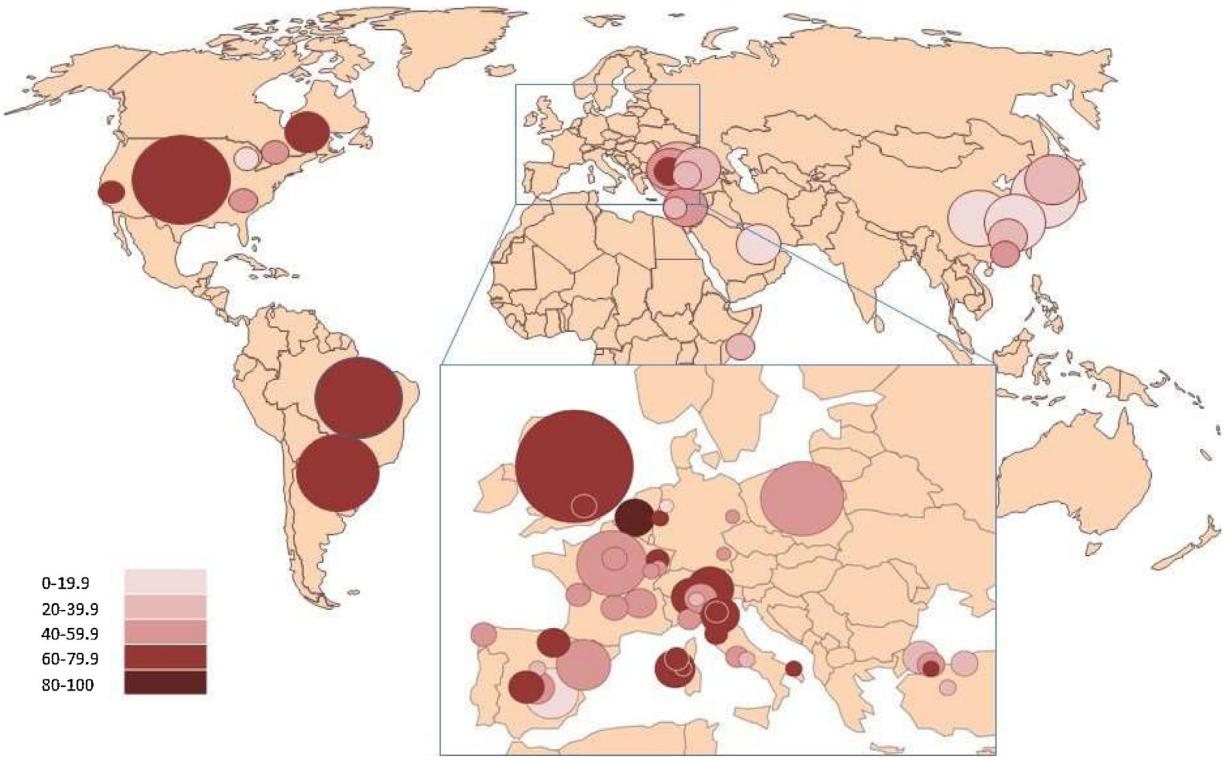

Fig. 2. Worldwide prevalence of gustatory disorders (GD) in COVID-19 positive cases. Circle size is proportional to study population. Color-coded bars indicate percentage range of GD prevalence. The map depicted in the picture was freely downloaded and modified from https://www.freeworldmaps.net/powerpoint/.

of hyposmia and hypogeusia, respectively, was a pre-print (non-peer-reviewed) case series of a Chinese population [15]. In sharp contrast, the most recent meta-analysis analyzing smell and taste alterations not only reported that almost half of COVID-19 patients had these symptoms but also, that 15% of patients had olfactory and gustatory abnormalities as their initial presenting symptoms [16].

Recent systematic reviews have assessed chemosensory alterations in COVID-19 patients [4,16–30]. Only one review, however, has focused specifically on taste changes [31]. In their pooled analysis, Aziz et al. [31] found that almost half of patients (49.8%) with COVID-19 had altered taste sensation. Similarly, when the data was pooled in the reviews assessing chemosensory alterations, the prevalence of olfactory and gustatory alterations occurred in approximately half of COVID-19 patients but when these symptoms were considered individually, there was a marked range of prevalence (3.2–100% olfactory symptoms; 0–92.6% gustatory disturbances), The results of the present study are in agreement with the existing literature on the worldwide prevalence of GD associated with COVID-19 disease; of 28,374 confirmed COVID-19 cases, 14,486 (51.05%) reported GD. Taken together, and in association with other findings [32], there is strong evidence to suggest that gustatory alterations are cardinal symptoms of COVID-19.

A major limitation of the present study is that it includes research with diverse study designs and patients with different disease severity, e.g. severe, mild, or asymptomatic COVID-19 cases. Further, the majority of the studies that were analysed were cross-sectional, retrospective and observational, hence recollection bias may have been present. Most studies were similar to those previously graded as “moderate risk of bias” [29]. Importantly, the presence of taste alterations may not have been reported in the presence of other more severe symptoms such as dyspnea, fever and productive cough which could explain the lack of association between GD and COVID-19 in the first studies published in February and March 2020. For these reasons, the true prevalence of ageusia, hypogeusia and dysgeusia might be significantly higher than reported [31].

Disturbance of taste sensation can occur as a result of local and systemic conditions, including oral, nasal, and sinus disease, metabolic (obesity, diabetes, poor nutrition, hypertension), neurological (epilepsy, Alzheimer’s and Parkinson’s disease, schizophrenia, multiple sclerosis), tumours and radiation associated with cancer treatment, drugs (allopurinol, anti-hypertensives, atatins, lithium), head trauma, and certain habits (smoking, cocaine snorting). Significantly, in the published literature, the measures for assessing GD have not been validated and the definition of dysgeusia has not been unanimously accepted. Further, the more patients and doctors are aware of the possibility of GD with COVID-19, the more cases would have been reported and investigated over time [12] although in the present study, the data failed to show a trend of increased GD prevalence over time except in East Asia. By contrast to other studies [2], our analysis focused on geographical location rather than ethnicity. Whilst this approach may have failed to identify individual genetic/ethnic determinants of infection, we believe that our methodology was better suited to study the clinical manifestations of the disease and to inform the decisions of public health surveillance bodies.

The data that were examined in the present study involved the subjective (self-reported) and objective (testing with the four basic tastes of sweet, sour, salty and bitter modalities sprayed onto the tongue in a supra-threshold doses) interpretation of GD. Previous findings, however, have shown that there are no significant differences between the subjective and objective interpretation of gustatory function [18] and, therefore, we suggest that self-reported taste alterations can be considered a reliable parameter for GD in COVID-19 patients.

In conclusion, we show that GD in COVID-19 exhibits distinct geographical patterns of prevalence. Given the potential usefulness of taste assessment in the diagnosis of mildly and paucisymptomatic patients, we believe that it is imperative to recognize

Table 1
Studies included for the evaluation of gustatory dysfunction (GD).

Reference	GD	COVID+	Prevalence	Area
Romero-Sanchez et al. [33]	52	841	6.2%	Spain
Paderno et al. [34]	320	508	63%	Italy
Zayet et al. [35]	62	95	65%	France
Vaira et al. [36]	39	72	54.2%	Italy
Lapostolle et al. [37]	757	1487	50.9%	France
Martin-Sanz et al. [38]	114	215	53%	Spain
Lechien et al. [39]	770	1420	54.2%	Europe (multiple sites)
Villarreal et al. [40]	161	230	70%	Spain
Petrocelli et al. [41]	184	300	61.3%	Italy
Qiu et al. [13]	50,20	116,39	45.16%	France, Germany (and China)
Abalo-Lojo et al. [42]	74	131	56.5%	Spain
Zayet et al. [43]	34	70	48.6%	France
Tudrej et al. [44]	92	198	46.5%	France
Poncet-Megemont et al. [45]	81	139	58.3%	France
Patel et al. [46]	89	141	63.1%	UK
Chary et al. [47]	64	115	55.65%	France
Sierpinski et al. [48]	923	1942	47.5%	Poland
Izquierdo-Dominguez et al. [49]	442	846	52.2%	Spain
Rojas-Lechuga et al. [50]	128	197	65%	Spain
Giacomelli et al. [51]	17	59	28.8%	Italy
Menni et al., 2020 [12]	4178	6452	64.76%	UK (and USA)
Vaira et al. [52]	76	106	71.7%	Italy
Mercante et al. [53]	113	204	55.4%	Italy
Lechien et al. [10]	1136	2013	56%	Europe (multiple sites)
Klopfenstein et al. [54]	34	70	48%	France
Liguori et al. [55]	48	103	46.6%	Italy
Luers et al. [56]	50	72	69.4%	Germany
Dell'Era et al. [57]	232	355	65.4%	Italy
Magnavita et al. [58]	31	82	37.8%	Italy
Meini et al. [59]	69	100	69%	Italy
Lechien et al. [9]	342	385	88.8%	Belgium
Beltran-Corbe Ilini et al. [60]	28	79	35.44%	Spain
Vaira et al. [61]	234	340	67.8%	Italy
Gelardi et al. [62]	52	72	72.2%	Italy
Vacchiano et al. [63]	66	108	61%	Italy
De Maria et al. [64]	48	95	50.5%	Italy
Fistera et al. [65]	6	43	14%	Germany
Vaira et al. [66]	91	138	65.9%	Italy
Hintschich et al. [67]	18	41	44%	Germany
Chiesa-Estomba et al. [11]	718	1043	68.8%	Europe (multiple sites)
	12,043	**21,062**	57.18%	**TOTAL EUROPE**
Yan et al. [68]	42	59	71%	USA
Menni et al. [12]	490	726	67.49%	USA (and UK)
Carignan et al. [69]	85	134	63.4%	Canada
Pinna et al. [70]	10	so	10%	USA
Chiesa-Estomba et al. [71]	333	542	61.4%	South America (Multiple sites)
Lee et al. [72]	32	56	57.1%	Canada
Kempker et al. [73]	27	51	52.9%	USA
Brandao Neto et al. [74]	499	655	76.2%	Brazil
	1518	**2273**	66.78%	**TOTAL AMERICA**
Sayin et al. [75]	46	64	71.9%	Turkey
Biadsee et al. [76]	67	128	52%	Israel
Altin et al. [77]	22	81	27.2%	Turkey
Salepci et al. [78]	77	223	34.5%	Turkey
AI-Ani and Acharya [79]	28	141	19.86%	Qatar
Sakalii et al. [80]	81	172	47.1%	Turkey
Levinson et al. [81]	14	42	33.3%	Israel
Çalica Utku et al. [82]	51	143	35.7%	Turkey
	386	**994**	38.83%	**TOTAL MIDDLE EAST**
Lee et al. [83]	353	3191	11%	Korea
Mao et al. [84]	12	214	5.6%	China
Kim et al. [85]	58	172	33.7%	Korea
Qiu et al. [13]	30	239	12.55%	China (and France, Germany)
Cho et al. [86]	36	83	43.4%	Hong Kong
Liang et al. [87]	33	86	38.4%	China
	522	**3985**	13.1%	**TOTAL EAST ASIA**
Farah et al. [88]	17	60	28.3%	Somalia
	14,486	**28,374**	**50.05%**	**WORLD**

ageusia/hypogeusia/dysgeusia as a potential clinical manifestation of COVID-19, particularly in Europe and America. Dentists, therefore, may be the first healthcare providers to diagnose taste disturbances and are likely to play an important role in case identification and early diagnosis of COVID-19 cases in the future.

Methods

Study design and literature search

This study was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses

(PRISMA) guidelines and used a rapid review approach due to time constraints [89]. The study complied with the minimum requirements for completing a restricted systematic review [90]. Accordingly, the search was performed by one investigator (N.C.) and verification of a random sample of full texts for accuracy of title/abstract screening and data extraction was undertaken by the same reviewer. Key terms used for the search were (SARS-CoV-2 or COVID or COVID-19) in association with taste or ageusia or hypogeusia or dysgeusia or gustatory. The search was conducted in PubMed/MEDLINE as well as medRxiv using the advanced search (title and abstract) tool.

Study selection and data extraction

The exclusion criteria were as follows: articles not in English, duplicate publications, irrelevant articles, studies where the infection status was not clearly confirmed, studies that did not evaluate gustatory outcomes individually, simple case reports, and review or systematic review articles. Studies using telephone surveys or Apps were only included where the respondents had a confirmed COVID-19 diagnosis. For studies reporting cases from two or more geographical areas (e.g. East Asia and Europe), the data for subgroup analysis were extracted only when information from individual countries was available. Where the date of patient recruitment was not provided, the date of the article submission was used as a surrogate source of information. The primary outcome was to assess the prevalence of gustatory alterations (ageusia, hypogeusia, dysgeusia) in confirmed COVID-19 cases worldwide and in distinct geographical areas; the secondary outcome was to establish a spatio-temporal pattern of GD in published cases. No constraints were placed on the size of the cohorts to ensure a comprehensive search and to identify the maximum number of potential articles.

Statistical analysis

Subgroup analyses were based on the country of origin of the studies by pooling the actual data reported in each individual study. Differences in prevalence (% and category) among subgroups were assessed with chi-square statistics and one-way ANOVA, as appropriate. Tukey's post-hoc test or Student's t tests were used for comparison between group pairs. By making a further assumption that the dependent variable may not be normally distributed, the Kruskal-Wallis test was also used to compare overall differences in prevalence. Where appropriate, Pearson's coefficient was used to assess the correlation between time and prevalence. A level of $p < 0.05$ was chosen to determine statistical significance.

Ethics approval and consent to participate

Not applicable.

Consent for publication

N.C. approved the final version of the manuscript.

Availability of data and material

The datasets used and/or analyzed during the current study can be made available by the corresponding author on a reasonable request.

Competing interests

The author declares no conflict of interest.

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Authors' contributions

N.C. conceived the study, undertook the search and wrote the manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jiph.2021.07.002.

References

[1] Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20.
[2] Lovato A, de Filippis C. Clinical presentation of COVID-19: a systematic review focusing on upper airway symptoms. Ear Nose Throat J 2020;99(9):569–76.
[3] O'Donovan J, Tanveer S, Jones N, et al. Sniffing out the evidence for olfactory symptoms as a clinical feature of COVID-19: a systematic scoping review. Centre for Evidence-Based Medicine; 2020 https://www.cebm.net/wp-content/uploads/2020/03/Rapid-Review-Anosmia-COVID19-.pdf.
[4] Passarelli PC, Lopez MA, Mastandrea Bonaviri GN, Garcia-Godoy F, D'Addona A. Taste and smell as chemosensory dysfunctions in COVID-19 infection. Am J Dent 2020;33(3):135–7.
[5] Dawson P, Rabold EM, Laws RL, et al. Loss of taste and smell as distinguishing symptoms of COVID-19. Clin Infect Dis 2021;72(4):682–5.
[6] European Centre for Disease Prevention and Control (ECDC). Case definition for coronavirus disease 2019 (COVID-19), as of 29 May 2020. https://www.ecdc.europa.eu/en/covid-19/surveillance/case-definition [Accessed 19 August 2020].
[7] Centers for Disease Control and Prevention (CDC). Coronavirus Disease. (COVID-19) 2020 Interim Case Definition, Approved August 5, 2020; 2019 [Accessed 19 August 2020] https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/.
[8] World Health Organization. WHO COVID-19 Case definition, published 7 August 2020 https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.1 [Accessed 19 August 2020].
[9] Lechien JR, Chiesa-Estomba CM, De Siati 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;277(8):2251–61.
[10] Lechien JR, Chiesa-Estomba CM, Hans S, et al. Loss of smell and taste in 2013 European patients with mild to moderate COVID-19. Ann Intern Med 2020;173(8):672–5.
[11] Chiesa-Estomba CM, Lechien JR, Barillari MR, et al. Patterns of gustatory recovery in patients affected by the COVID-19 outbreak. Virol Sin 2020;35(6):833–7.
[12] Menni C, Valdes AM, Freidin MB, et al. Real-time tracking of self-reported symptoms to predict potential COVID-19. Nat Med 2020;26(7):1037–40.
[13] Qiu C, Cui C, Hautefort C, et al. Olfactory and gustatory dysfunction as an early identifier of COVID-19 in adults and children: an international multicenter study. Otolaryngol Head Neck Surg 2020;163(4):714–21.
[14] Cirillo N. COVID-19 outbreak: succinct advice for dentists and oral healthcare professionals. Clin Oral Investig 2020;24:2529–35.
[15] Mao L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. medRxiv 2020, http://dx.doi.org/10.1101/2020.02.22.20026500.
[16] Chi H, Chiu NC, Peng CC, et al. One-seventh of patients with COVID-19 had olfactory and gustatory abnormalities as their initial symptoms: a systematic review and meta-analysis. Life (Basel) 2020;10:E158, http://dx.doi.org/10.3390/life10090158.
[17] Abdullahi A, Candan SA, Abba MA, et al. Neurological and musculoskeletal features of COVID-19: a systematic review and meta-analysis. Front Neurol 2020;11:687, http://dx.doi.org/10.3389/fneur.2020.00687.

[18] Almqvist J, Granberg T, Tzortzakakis A, et al. Neurological manifestations of coronavirus infections – a systematic review. Ann Clin Transl Neurol 2020;7(10):2057–71.
[19] 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;95:1621–31.
[20] Borsetto D, Hopkins C, Philips V, 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.
[21] Carrillo-Larco RM, Altez-Fernandez C. Anosmia and dysgeusia in COVID-19: a systematic review. Wellcome Open Res 2020;5:94, http://dx.doi.org/10.12688/wellcomeopenres.15917.1.
[22] Chen X, Laurent S, Onur OA, et al. A systematic review of neurological symptoms and complications of COVID-19. J Neurol 2021;268(2):392–402.
[23] da Costa KVT, Carnaúba ATL, Rocha KW, Andrade KCL, Ferreira SMS, Menezes PL. Olfactory and taste disorders in COVID-19: a systematic review. Braz J Otorhinolaryngol 2020, http://dx.doi.org/10.1016/j.bjorl.2020.05.008. S1808-8694(20)30066-5.
[24] Hoang MP, Kanjanaumporn J, Aeumjaturapat S, Chusakul S, Seresirikachorn K, Snidvongs K. Olfactory and gustatory dysfunctions in COVID-19 patients: a systematic review and meta-analysis. Asian Pac J Allergy Immunol 2020;38(3):162–9.
[25] Printza A, Constantinidis J. The role of self-reported smell and taste disorders in suspected COVID-19. Eur Arch Otorhinolaryngol 2020;277(9):2625–30.
[26] Romoli M, Jelcic I, Bernard-Valnet R, et al. A systematic review of neurological manifestations of SARS-CoV-2 infection: the devil is hidden in the details. Eur J Neurol 2020;27(9):1712–26.
[27] Samaranayake LP, Fakhruddin KS, Panduwawala C. Sudden onset, acute loss of taste and smell in coronavirus disease 2019 (COVID-19): a systematic review. Acta Odontol Scand 2020;78:467–73.
[28] Struyf T, Deeks Jj, Dinnes J, et al. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. Cochrane Database Syst Rev 2020;7(7):CD013665, http://dx.doi.org/10.1002/14651858.CD013665.
[29] 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.
[30] Wang L, Shen Y, Li M, et al. Clinical manifestations and evidence of neurological involvement in 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis. J Neurol 2020;267(10):2777–89.
[31] Aziz M, Perisetti A, Lee-Smith WM, Gajendran M, Bansal P, Goyal H. Taste changes (Dysgeusia) in COVID-19: a systematic review and meta-analysis. Gastroenterology 2020;159(3):1132–3.
[32] Cirillo N, Colella G. Self-reported smell and taste alteration as the sole clinical manifestation of SARS-CoV-2 infection. Oral Surg Oral Med Oral Pathol Oral Radiol 2021;131(4):e95–9.
[33] Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, et al. Neurologic manifestations in hospitalized patients with COVID-19: the ALBACOVID registry. Neurology 2020;95(8):e1060–70, http://dx.doi.org/10.1212/WNL.0000000000009937.
[34] Paderno A, Schreiber A, Grammatica A, et al. Smell and taste alterations in COVID-19: a cross-sectional analysis of different cohorts. Int Forum Allergy Rhinol 2020;10(8):955–62.
[35] Zayet S, Klopfenstein T, Mercier J, et al. Contribution of anosmia and dysgeusia for diagnostic of COVID-19 in outpatients. Infection 2021;49(2):361–5.
[36] Vaira LA, Deiana G, Fois AG, 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.
[37] Lapostolle F, Schneider E, Vianu I, et al. Clinical features of 1487 COVID-19 patients with outpatient management in the Greater Paris: the COVID-call study. Intern Emerg Med 2020;15(5):813–7.
[38] Martin-Sanz E, Riestra J, Yebra L, et al. Prospective study in 355 patients with suspected COVID-19 infection. Value of cough, subjective hyposmia, and hypogeusia. Laryngoscope 2020;130(11):2674–9.
[39] Lechien JR, Chiesa-Estomba CM, Place S, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med 2020;288(3):335–44.
[40] Villarreal IM, Morato M, Martinez-RuizCoello M, et al. Olfactory and taste disorders in healthcare workers with COVID-19 infection. Eur Arch Otorhinolaryngol 2021;278(6):2123–7.
[41] Petrocelli M, Ruggiero F, Baietti AM, et al. Remote psychophysical evaluation of olfactory and gustatory functions in early-stage coronavirus disease 2019 patients: the Bologna experience of 300 cases. J Laryngol Otol 2020;134(7):571–6.
[42] Abalo-Lojo JM, Pouso-Diz JM, Gonzalez F. Taste and smell dysfunction in COVID-19 patients. Ann Otol Rhinol Laryngol 2020;129(10):1041–2.
[43] Zayet S, Kadiane-Oussou NJ, Lepiller Q, et al. Clinical features of COVID-19 and influenza: a comparative study on Nord Franche-Comte cluster. Microbes Infect 2020, http://dx.doi.org/10.1016/j.micinf.2020.05.016. S1286-4579(20)30094-0.
[44] Tudrej B, Sebo P, Lourdaux J, et al. Self-reported loss of smell and taste in SARS-CoV-2 patients: primary care data to guide future early detection strategies. J Gen Intern Med 2020;35(8):2502–4.
[45] Poncet-Megemont L, Paris P, Tronchere A, et al. High prevalence of headaches during Covid-19 infection: a retrospective cohort study. Headache 2020;60(10):2578–82.
[46] Patel A, Charani E, Ariyanayagam D, et al. New-onset anosmia and ageusia in adult patients diagnosed with SARS-CoV-2 infection. Clin Microbiol Infect 2020;26(9):1236–41.
[47] Chary E, Carsuzaa F, Trijolet JP, et al. Prevalence and recovery from olfactory and gustatory dysfunctions in Covid-19 infection: a prospective multicenter study. Am J Rhinol Allergy 2020;34(5):686–93.
[48] Sierpiński R, Pinkas J, Jankowski M, et al. Sex differences in the frequency of gastrointestinal symptoms and olfactory or taste disorders in 1942 nonhospitalized patients with coronavirus disease 2019 (COVID-19). Pol Arch Intern Med 2020;130(6):501–5.
[49] Izquierdo-Dominguez A, Rojas-Lechuga MJ, Chiesa-Estomba C, et al. Smell and taste dysfunctions in COVID-19 are associated with younger age in ambulatory settings—a multicenter cross-sectional study. J Investig Allergol Clin Immunol 2020;30(5):346–57.
[50] Rojas-Lechuga MJ, Izquierdo-Dominguez A, Chiesa-Estomba C, et al. Chemosensory dysfunction in COVID-19 out-patients. Eur Arch Otorhinolaryngol 2021;278(3):695–702.
[51] Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. Clin Infect Dis 2020;71(15):889–90.
[52] Vaira LA, Hopkins C, Petrocelli M, et al. Do olfactory and gustatory psychophysical scores have prognostic value in COVID-19 patients? A prospective study of 106 patients. J Otolaryngol Head Neck Surg 2020;49(1):56, http://dx.doi.org/10.1186/s40463-020-00449-y.
[53] Mercante G, Ferreli F, De Virgilio A, et al. Prevalence of taste and smell dysfunction in coronavirus disease 2019. JAMA Otolaryngol Head Neck Surg 2020;146(8):1–6, http://dx.doi.org/10.1001/jamaoto.2020.1155.
[54] Klopfenstein T, Zahra H, Kadiane-Oussou NJ, et al. New loss of smell and taste: uncommon symptoms in COVID-19 patients on Nord Franche-Comte cluster, France. Int J Infect Dis 2020, http://dx.doi.org/10.1016/j.ijid.2020.08.012. S1201-9712(20)30637-30638.
[55] Liguori C, Pierantozzi M, Spanetta M, et al. Subjective neurological symptoms frequently occur in patients with SARS-CoV2 infection. Brain Behav Immun 2020;88:11–6.
[56] Luers JC, Rokohl AC, Loreck N, et al. Olfactory and gustatory dysfunction in coronavirus disease 19 (COVID-19). Clin Infect Dis 2020;71(16):2262–4.
[57] Dell'Era V, Farri F, Garzaro G, Gatto M, Aluffi Valletti P, Garzaro M. Smell and taste disorders during COVID-19 outbreak: cross-sectional study on 355 patients. Head Neck 2020;42(7):1591–6.
[58] Magnavita N, Tripepi G, Di Prinzio RR. Symptoms in health care workers during the COVID-19 epidemic. A cross-sectional survey. Int J Environ Res Public Health 2020;17(14):5218, http://dx.doi.org/10.3390/ijerph17145218.
[59] Meini S, Suardi LR, Busoni M, Roberts AT, Fortini A. Olfactory and gustatory dysfunctions in 100 patients hospitalized for COVID-19: sex differences and recovery time in real-life. Eur Arch Otorhinolaryngol 2020;277(12):3519–23.
[60] Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J, et al. Acute-onset smell and taste disorders in the context of COVID-19: a pilot multicentre polymerase chain reaction based case-control study. Eur J Neurol 2020;27(9):1738–41.
[61] Vaira LA, Hopkins C, Salzano G, et al. Olfactory and gustatory function impairment in COVID-19 patients: Italian objective multicenter-study. Head Neck 2020;42(7):1560–9.
[62] 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.
[63] Vacchiano V, Riguzzi P, Volpi L, et al. Early neurological manifestations of hospitalized COVID-19 patients. Neurol Sci 2020;41(8):2029–31.
[64] De Maria A, Varese P, Dentone C, Barisione E, Bassetti M. High prevalence of olfactory and taste disorder during SARS-CoV-2 infection in outpatients. J Med Virol 2020;92(11):2310–1.
[65] Fistera D, Pabst D, Hartl A, et al. Separating the wheat from the chaff-COVID-19 in a German emergency department: a case-control study. Int J Emerg Med 2020;13(1):44, http://dx.doi.org/10.1186/s12245-020-00302-z.
[66] Vaira LA, Hopkins C, Petrocelli M, et al. Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study. J Laryngol Otol 2020;134(8):703–9.
[67] Hintschich CA, Wenzel JJ, Hummel T, et al. Psychophysical tests reveal impaired olfaction but preserved gustation in COVID-19 patients. Int Forum Allergy Rhinol 2020;10(9):1105–7.
[68] 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.
[69] Carignan A, Valiquette L, Grenier C, et al. Anosmia and dysgeusia associated with SARS-CoV-2 infection: an age-matched case-control study. CMAJ 2020;192(26):E702–7, http://dx.doi.org/10.1503/cmaj.200869.
[70] Pinna P, Grewal P, Hall JP, et al. Neurological manifestations and COVID-19: experiences from a tertiary care center at the Frontline. J Neurol Sci 2020;415, http://dx.doi.org/10.1016/j.jns.2020.116969, 116969.
[71] Chiesa-Estomba CM, Lechien JR, Portillo-Mazal P, et al. Olfactory and gustatory dysfunctions in COVID-19. First reports of Latin-American ethnic patients. Am J Otolaryngol 2020;41(5):102605, http://dx.doi.org/10.1016/j.amjoto.2020.102605.
[72] Lee DJ, Lockwood J, Das P, Wang R, Grinspun E, Lee DJM. Self-reported anosmia and dysgeusia as key symptoms of coronavirus disease 2019. CJEM 2020, http://dx.doi.org/10.1017/cem.2020.420.
[73] Kempker RR, Kempker JA, Peters M, et al. Loss of smell and taste among healthcare personnel screened for coronavirus 2019. Clin Infect Dis 2020;72(7):1244–6.

[74] Brandao Neto D, Fornazieri MA, Dib C, et al. Chemosensory dysfunction in COVID-19: prevalences, recovery rates, and clinical associations on a large Brazilian sample. Otolaryngol Head Neck Surg 2020, http://dx.doi.org/10.1177/0194599820954825.
[75] Sayin İ, Yaşar KK, Yazici ZM. Taste and smell impairment in COVID-19: an AAO-HNS anosmia reporting tool-based comparative study. Otolaryngol Head Neck Surg 2020;163(3):473–9.
[76] Biadsee A, Biadsee A, Kassem F, Dagan O, Masarwa S, Ormianer Z. Olfactory and oral manifestations of COVID-19: sex-related symptoms-a potential pathway to early diagnosis. Otolaryngol Head Neck Surg 2020;163(4):722–8.
[77] Altin F, Cingi C, Uzun T, Bal C. Olfactory and gustatory abnormalities in COVID-19 cases. Eur Arch Otorhinolaryngol 2020;277(10):2775–81.
[78] Salepci E, Turk B, Ozcan SN, et al. Symptomatology of COVID-19 from the otorhinolaryngology perspective: a survey of 223 SARS-CoV-2 RNA-positive patients. Eur Arch Otorhinolaryngol 2020, http://dx.doi.org/10.1007/s00405-020-06284-1 (in press).
[79] Al-Ani RM, Acharya D. Prevalence of anosmia and ageusia in patients with COVID-19 at a Primary Health Center, Doha, Qatar. Indian J Otolaryngol Head Neck Surg 2020, http://dx.doi.org/10.1007/s12070-020- 02064-9 (in press).
[80] Sakalli E, Temirbekov D, Bayri E, Alis EE, Erdurak SC, Bayraktaroglu M. Ear nose throat-related symptoms with a focus on loss of smell and/or taste in COVID-19 patients. Am J Otolaryngol 2020;41(6):102622, http://dx.doi.org/10.1016/j.amjoto.2020.102622.
[81] Levinson R, Elbaz M, Ben-Ami R, et al. Time course of anosmia and dysgeusia in patients with mild SARS-CoV-2 infection. Infect Dis (Lond) 2020;52(8):600–2.
[82] Çalıca Utku A, Budak G, Karabay O, Güçlü E, Okan HD, Vatan A. Main symptoms in patients presenting in the COVID-19 period. Scott Med J 2020;65(4):127–32.
[83] Lee Y, Min P, Lee S, Kim SW. Prevalence and duration of acute loss of smell or taste in COVID-19 patients. J Korean Med Sci 2020;35:e174, http://dx.doi.org/10.3346/jkms.2020.35.e174.
[84] Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77(6):1–9, http://dx.doi.org/10.1001/jamaneurol.2020.1127.
[85] Kim GU, Kim MJ, Ra SH, et al. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. Clin Microbiol Infect 2020;26(7):948, http://dx.doi.org/10.1016/j.cmi.2020.04.040.
[86] Cho RH, To ZW, Yeung ZW, et al. COVID-19 viral load in the severity of and recovery from olfactory and gustatory dysfunction. Laryngoscope 2020;130(11):2680–5.
[87] Liang Y, Xu J, Chu M, et al. Neurosensory dysfunction: a diagnostic marker of early COVID-19. Int J Infect Dis 2020;98:347–52.
[88] Farah Yusuf Mohamud M, Garad Mohamed Y, Mohamed Ali A, Ali Adam B. Loss of taste and smell are common clinical characteristics of patients with COVID-19 in Somalia: a retrospective double centre study. Infect Drug Resist 2020;13:2631–5.
[89] Khangura S, Konnyu K, Cushman R, Grimshaw J, Moher D. Evidence summaries: the evolution of a rapid review approach. Syst Rev 2020;1:10, http://dx.doi.org/10.1186/2046-4053-1-10.
[90] Plüddemann A, Aronson JK, Onakpoya I, Heneghan C, Mahtani KR. Redefining rapid reviews: a flexible framework for restricted systematic reviews. BMJ Evid Based Med 2018;23(6):201–3.