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

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has currently infected over 6.5 million people worldwide. In response to the pandemic, numerous studies have tried to identify causes and symptoms of the disease. Emerging evidence supports recently acquired anosmia (complete loss of smell) and hyposmia (partial loss of smell) as symptoms of COVID-19, but studies of olfactory dysfunction show a wide range of prevalence, from 5% to 98%. We undertook a search of Pubmed/Medline and Google Scholar with the keywords "COVID-19," "smell," and/or "olfaction." We included any study that quantified smell loss (anosmia and hyposmia) as a symptom of COVID-19. Studies were grouped and compared based on the type of method used to measure smell loss—subjective measures such as self-reported smell loss versus objective measures using rated stimuli—to determine if prevalence differed by method type. For each study, 95% confidence intervals (CIs) were calculated from point estimates of olfactory disturbances. We identified 34 articles quantifying anosmia as a symptom of COVID-19 (6 objective, 28 subjective), collected from cases identified from January 16 to April 30, 2020. The pooled prevalence estimate of smell loss was 77% when assessed through objective measurements (95% CI of 61.4-89.2%) and 44% with subjective measurements (95% CI of 32.2-57.0%). Objective measures are a more sensitive method to identify smell loss as a result of infection with SARS-CoV-2; the use of subjective measures, while expedient during the early stages of the pandemic, underestimates the true prevalence of smell loss.

Keywords: COVID-19, coronavirus, anosmia, olfactory dysfunction, SARS-CoV-2

Introduction

In December 2019, an outbreak of a novel coronavirus disease, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that originated in Wuhan, China, rapidly spread to almost every country worldwide. As of June 5, 2020, over 6.5 million cases have been identified and over 387,155 deaths have been attributed to the virus (1). The most common symptoms of infection include fever, dry cough, and fatigue (1). Other accepted symptoms include difficulty breathing, sore throat, headache, nasal congestion, diarrhea, skin rash, and body aches and pains (1, 2). However, as knowledge about the virus increased with more confirmed cases, reports of loss of smell and/or taste started to arise. Other the past few months, COVID-19 research has investigated olfactory and taste disturbances as potential symptoms of COVID-19 (3-5). Many of these disturbances include the immediate onset of a complete loss of smell (anosmia) and/or taste (ageusia); other studies report hyposmia, a reduction in perceived odor intensity. Therefore, the Centers for Disease Control and Prevention and the World Health Organization officially included losses of smell and taste as symptoms of COVID-19, though less prevalent than some other symptoms (1).

While olfactory loss is a common symptom of numerous viral respiratory infections (6), recent reports suggest its prevalence might be higher with SARs-CoV-2 infection (7). However, there is a wide reported range of olfactory disturbance prevalence, from 5% (8) to 98% (9). Thus, there is a need to better quantify smell loss during the COVID-19 pandemic (10). Differences in the reported values may be attributed to different recruiting and sampling methodologies, the range of symptom severity across patients, and the amount of information about COVID-19 available at the time of data collection (e.g., symptom recognition).

However, different data collection techniques used by researchers and health care professionals might also account for the different prevalence estimates reported. There are two general types of methods to measure smell loss: objective and subjective. Objective measures of smell encompass

psychophysical testing designed to measure and quantify human responses to physical stimuli. Though sparsely used in COVID-19 research to date, current psychophysical techniques encompass odor threshold tests to determine the lowest concentration of an odor that can be detected, odor discrimination tests to measure the ability to differentiate between odors, and odor identification tests, assessing the ability to correctly name odor qualities. When possible, these tests are performed repeatedly over several days to measure changes in a patient's smell abilities over time. Historically, these objective tests are often executed in a laboratory setting, under surveillance of a researcher or health care professional, to ensure proper completion. Examples of odor threshold tests in a COVID-19 population involve the use of butanol or phenylethyl alcohol at different concentrations (11-13). The Sniffin' Sticks test, an odor discrimination and threshold test, is another method to quantify human olfactory performance (14) used now in COVID-19 patients (15, 16). However, due to the global presence of stay-at-home orders, many researchers have adapted these objective methods to enable testing at home, by patients themselves, with common household odorants (5, 11).

A more common technique employed to quantify smell loss in the COVID-19 population uses subjective methods, self-report through patient questionnaires or interview or the extraction of symptomatic information from a patient's electronic health records (8, 17, 18). However, collecting information from records can be prone to underestimation of smell loss due to an initial lack of awareness that it is a symptom of COVID-19. Other subjective methods directly ask patients about their own perceived sense of smell through an online questionnaire (7, 19), over the phone (18), or in person with a doctor (20, 21). However, retrospective assessments through self-report measures are often prone to recall bias (22). The present review provides a comprehensive assessment of methodologies currently employed to quantify smell loss in COVID-19–positive patients and examines whether method type affects reported prevalence of smell loss in COVID-19 patients. Another recent systematic review examined the prevalence of olfactory loss as a symptom in COVID-19; however, it contained data

collected up until April 19, 2020, encompassed different inclusion criteria, included only 10 papers in its analysis, and additionally examined gustatory dysfunction (23). Building on that prior meta-analysis, we sought to compare differences in prevalence estimates of smell loss collected via objective versus subjective methods. We included any study that quantified smell loss as a symptom of COVID-19, summarizing reports with publication dates up until June 5, 2020.

Methods

Article Selection: This systematic review and meta-analysis followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (24). Figure 1 outlines the steps taken to select articles for inclusion in the meta-analysis. First, Pubmed/Medline and Google Scholar were used to retrieve literature with the keyword "COVID-19" plus "smell" and/or "olfaction" on May 15, 2020, and manual search of relevant articles via Google Scholar was also performed on June 5, 2020, yielding a total of 78 articles.

Titles and abstracts were then screened for their relevance to the topic. Thirty-two articles were initially excluded during the screening test if they were not about smell loss and COVID19, did not report cases or percentage of patients with smell loss, or if they were not written in the English language. If an abstract referenced a measure of prevalence of olfactory dysfunction in COVID-19–positive patients, it was included in the pool of articles (n = 43). Full texts were then screened to confirm positive identification of COVID-19 in patients via a nasopharyngeal swab, throat swab, RT-PCR–confirmed laboratory test, or a clinical assessment by medical professional. Five articles were excluded because patients had not tested positive for COVID-19 by one of these methods (25-29). Three articles were excluded due to population bias, with patients recruited for a specific symptom alone (e.g., olfactory disorders) (30-32). The exact data needed for our analysis were not reported in three articles, which were thus excluded (15, 33, 34). Lastly, one article was excluded (4) because of potential data overlap with another report by the same author (35). The meta-analysis included a total of 34 papers.

Data Extraction: Prevalence of olfactory loss in COVID-19 patients was then extracted as the number of reported cases with olfactory loss divided by the total population of COVID-19 patients surveyed. An exception was made for articles that reported taste and/or smell dysfunction when anosmia or hyposmia were not specifically reported. Articles were labeled as using either objective or subjective methods to measure smell loss based on the method the study employed. Objective methods consisted of studies having patients smell a substance, including both household items being self-administered in their own home and smelling items in a laboratory setting (6 studies in total). Subjective measures included all other methods, for example, self-reports of overall smell loss (28 studies).

Differences in data collection across the studies required further inclusion restrictions regarding how smell loss was reported. When smell loss was reported in tandem with taste loss (e.g., "loss of taste or smell"), this value was extracted. If articles reported smell and taste loss together as well as separately, both values of positive cases with smell loss symptoms were summed to represent all patients presenting smell loss; these values did not include overlapping patients. If articles reported smell and taste loss separately, smell-loss-only values were included.

Three authors (RDH, AKT, and VAR) performed the initial screen and data extraction, and two additional authors (MEH and SJL) validated and resolved disagreements in the data extracted from the articles.

Risk-of-Bias Assessment: Quality of the articles selected was analyzed with a risk-of-bias assessment checklist adapted from Hoy et al (36) that contains 9 questions which are referred to here as "criteria". Two authors (RDH and SJL) completed the risk-of-bias assessment using the assessment tool outlined by Hoy et al. (36), as described and adapted by Tong et al (23). Two additional authors (VAR and AKT) resolved any differences. Supplementary Table S1 details the nine criteria used. Specific questions were scored as 0 (No) or 1 (Yes) for each item, with summary scores of low (0-3), moderate (4-6), and

high (7-9) risk of bias for the entire study. Supplementary Table S1 contains the full risk-of-bias assessment for each article.

Statistical Analysis. All statistical analyses were performed using R 3.6.0 (37) and RStudio 1.2.1564 (38). Meta analysis was conducted using the *meta* package in R (40). Point estimates of the prevalence of olfactory loss were made by dividing the number of cases of olfactory loss by the total number of subjects included in the study. The Freeman-Tukey double arcsine method was used to transform proportions. A 95% CI was calculated using the Wilson score estimate of the confidence interval, as it a robust method that is reliable across small and large sample sizes (39). An inverse variance weighting scheme was employed. These parameters were specified in the metaprop function in the R meta package. Heterogeneity was assessed using Cochran's Q and I^2. Tests for heterogeneity were cut off at Cochran Q-values that were significant ($p < 0.05$) and $I^2 > 50\%$, because an I^2 of 30-50% was suggested as a cutoff for moderate heterogeneity by Higgins and Thompson (41). Tau^2, was reported as a measure of between-study heterogeneity and was estimated by the Dersimmion-Laird method.

Pooled prevalence estimates were computed and reported for both a fixed-effect model and a random-effect model with parameters described. In the fixed-effect model, we assume that there is one true effect size that underlies all the studies in this analysis and that all differences in observed effects are due to sampling error. In the random-effects model, we allow that the true effect size might differ among studies. An overall pooled prevalence estimate was computed for all 34 studies to determine overall prevalence of smell loss in COVID-19 patients.

Subgroup analysis was performed with groupings for objective (N=6 studies) and subjective methods (N=28 studies) for assessing olfactory dysfunction in COVID-19 positive individuals. The R scripts and compiled data used for this analysis are available without restriction on GitHub (https://github.com/vramirez4/COVID19-OlfactoryLoss). Preliminary analysis of age and sex effects yielded no results of interest and were not pursued.

Results

Study characteristics. This meta-analysis included 34 studies, encompassing data collected from January 16, 2020, to April 30, 2020. Table 1 summarizes relevant details from the articles. Figure 2 lists *n*/*N*-values (events/total) for each study. All studies examined COVID-19–positive patients across the globe. Additionally, the levels of symptom severity, settings (hospitalized or home quarantine), and dates of infection differed across the studies and were not controlled in this meta-analysis. All of which could increase heterogeneity across the studies. Six studies used objective methodologies: they measured smell loss in COVID-19 patients by calculating their odor threshold sensitivity, odor discrimination ability and/or odor identification ability with actual odorants, either at home or in hospital settings. Twenty-eight studies used subjective methodologies: they measured smell loss via questionnaires, surveys, and interviews.

Risk-of-Bias Assessment. Among the 34 studies included in this meta-analysis, none had a high risk of bias: 14 categorized as low risk, and 20 as moderate risk. The risk-of-bias scores ranged from 2 to 6 across these studies, with an average risk of 3.79, indicating low to moderate risk of bias in our overall assessment.

Prevalence of olfactory dysfunction in COVID-19 patients. Among the 34 studies, sample sizes ranged from 15 to 7,178 patients with positive verification of COVID-19. The number of cases of smell loss per study ranged from 2 to 4,668, with prevalence estimates ranging from 5% to 98.3%. Collectively, the meta-analysis included a total of 17,109 patients who tested positive for COVID-19. Of these, 8578 evidenced some form of olfactory dysfunction after infection with SARS-CoV-2. Meta-analysis for the pooled prevalence estimate across all studies (N=34) yielded a significant Cochran's Q (Q=5784.14, df=33, p<0.001) and I^2 estimate of 99.4%. The pooled estimate for the prevalence for the overall cohort was 50.2% with a 95% CI of 38.9-61.5% (Figure 2).

Effect of methodology on prevalence estimate. Sub-group analysis was employed for objective and subjective studies and test for heterogeneity between groups was statistically significant (Q=9.94, df=1, p=0.0016).

Six studies used objective methods to assess olfactory loss, comprising 571 COVID-19 patients, with 412 reported cases of smell loss. Per study, the prevalence of olfactory loss ranged from 52% to 98% among COVID-19–positive patients. Pooled estimates of the prevalence were 73.9% and 76.7% under the fixed- and random-effect models, respectively. A significant Cochran's *Q*, approximated from the chi-square distribution (*Q*=53.78, df=5, *p*<0.001), and I^2 of 90.7% were obtained, confirming the heterogeneity of the data collected. When pooled across studies that utilized objective measurement tools, the average prevalence estimate of olfactory loss is 76.7%, with a 95% CI of 61.4-89.2%, under the random-effects model (Figure 2).

A total of 28 studies used subjective methods (questionnaire, interview, etc.), comprising 16538 subjects, with 8,166 cases of smell loss. The reported prevalence of olfactory loss ranged from 5% to 88% per study, a larger range than for studies classified as using objective methods. The pooled estimates of the prevalence were 48.6% and 44.4% under the fixed- and random-effect models, respectively. Similar to the objective subgroup, Cochran's *Q* was significant (*Q*=5585.37, df=27, *p*<0.001), and the I^2 value was 99.5%, confirming the heterogeneity of the meta-analysis across the subjective studies. To account for the observed heterogeneity, our pooled prevalence estimate for olfactory loss among COVID-19 positive patients was 44.4% with a 95% CI of 32.2-57.0% under the random-effects model. (Figure 2).**Discussion**

This systematic review and meta-analysis revealed that olfactory dysfunction is a prominent symptom of COVID-19. Meta-analysis using the random-effects model computed an overall prevalence estimate of 50.2% (95% CI: 38.9-61.5%), which is very similar to, although slightly lower than, the

previously reported value of 53% in a meta-analysis of olfactory dysfunction in 10 studies (23). Both meta-analyses confirmed that olfactory dysfunction, regardless of the measurement methodology, is identified in about half of the patients infected with SARS-CoV-2.

Methodological differences in smell loss measurement tools impact reported prevalence estimate of olfactory loss in COVID-19 patients. We further examined if the type of method used to gather information on olfactory loss caused differences in prevalence estimation. Most studies (28 of 34) included in this meta-analysis used subjective methods (self-report) to quantify the prevalence of smell loss; 6 studies used objective methods (e.g., odor threshold tests). The reliance on self-report was expedient due to the pandemic conditions and global stay-at-home orders. However, our analysis revealed a stark difference in prevalence between the two subgroups; studies using objective methods reported around 77% prevalence overall, whereas those using subjective methods reported around 44%.

There are inherent pros and cons regarding each type of methodology. Objective methods quantify smell loss and can limit any confounds because they are often conducted in a controlled environment with standardized procedures. Objective methods rely on true perception of a stimuli when presented, diminishing response and measurement bias. In contrast, subjective methods naturally encompass more variability due to a lack of standardization in how and what questions were asked. Additionally, subjective methods are often prone to recall bias. However, they are an easy and cost-efficient way to collect information quickly from the intended population, as demonstrated by the numerous studies in our meta-analysis that used this type of method. Objective methods have higher time and cost requirements than do subjective methods.

The higher overall reported prevalence of olfactory loss in the studies using objective methods (77%) compared to those using subjective methods (44%) suggests that subjective methodologies may neglect to capture crucial information and consistently underestimate true smell loss in COVID-19

patients. One major difference between the two types of methods is the number of variables assessed in each study. Often in the studies using subjective methods the researchers were interested in numerous aspects of COVID-19 symptoms, not just smell loss alone, whereas the studies using objective methods focused solely on sensory loss, using numerous stimuli to get a sensitive measurement of the patient's smell loss. Our findings align with a prior meta-analysis by Tong et al. (23) that found that non-standardized methods (though all subjective methods by our criteria) severely underestimated olfactory prevalence (estimated at ~37%) compared to standardized methods (which included both subjective and objective methods), which indicated around 87% prevalence. Standardized methods outlined in the Tong et al. study consisted of both objective and subjective measures—because a method is subjective does not mean that the method is not standardized or validated. Validated subjective methods for collecting information on olfactory dysfunction in our pool of studies include a version of the Questionnaire of Olfactory Dysfunction, and the Sino-Nasal Outcome Test (42, 43).

Overall, however, objective methods have been found to be more sensitive in detecting anosmia and hyposmia than subjective self-reports in a COVID-19 patient population (16). Additionally, among patients who initially self-reported no smell loss, objective analysis showed mild hyposmia in 30%, again pointing to underreporting by subjective methods (13). On the other hand, in a COVID-19 patient population recruited due to suspected olfactory loss, 38% of patients with self-reported olfactory dysfunction had normal olfactory performance using the Sniffin' Sticks test, an objective method (15). This over-reporting could be due to the biased and specific recruitment (patients with suspected olfactory loss) compared to the general COVID-19 patient population recruited for studies in our meta-analysis.

The higher reported prevalence of olfactory loss when using objective as compared to subjective methods to measure olfactory loss calls for further examination of the consequences of the methodologies employed. Researchers might be missing a critical symptom of COVID-19 through the use

of unstandardized, subjective methods to measure smell loss, as demonstrated by the lower prevalence estimate we found in studies classified as using subjective methods. However, objective methods are costly and time-consuming to conduct in standardized laboratory settings. Additionally, more case-control studies are needed to validate the reported prevalence rates and compare the findings to a SARS-Cov-2 negative population to account for pre-existing smell disorders.

Many researchers have adapted objective methods to evaluate smell loss to enable use in a home setting. Varia et al found no significant difference in patient smell loss ratings when conducted with an objective method during hospitalization (standardized setting) versus during home quarantine (13). Irvani et al. used an app to track smell loss in COVID-19 patients over time, which revealed moderate test-retest reliability across sessions among users showing no symptoms, and significant reduction in olfactory function for those who tested positive for COVID-19 compared to those who tested negative (5). The accessibility and adaptability of these objective approaches make them a resource-efficient strategy to obtain an accurate measure of olfactory loss in COVID-19 patients.

Sudden onset of anosmia is frequently reported to be one of the first presenting symptoms of COVID-19 (23, 44, 45). In a cohort specifically of patients complaining of smell loss, researchers found that 83% of people reported anosmia as their first symptom of COVID-19 (32). The actual mechanism by which SARS-CoV-2 may inhibit and disrupt smell perception is currently unknown; however, many potential theories about the cause of smell loss have been proposed. Reports suggest that, different from other coronaviruses, such as those that cause the common cold, SARS-CoV-2 can cause smell loss even in the absence of symptoms such as blockage of the nose, postnasal drip, or a runny nose, which are typical co-occurring manifestations of smell loss from other respiratory viruses (46). The lack of nasal blockage suggests COVID-19 might be a neurotropic and neuroinvasive disease (47). Furthermore, it is now commonly known that SARS-CoV-2 coronavirus binds to ACE2 receptors, allowing the virus to enter and infect cells. ACE2 receptors are expressed in nasal epithelium cells (48), specifically the structures

that support olfactory neurons, leading to a theory that infection of these supporting cells might cause additional damage to the olfactory epithelium, resulting anosmia or hyposmia (49).

Though olfactory dysfunction occurs in high prevalence in patients positive for COVID-19, time to recovery varies across the studies. Several studies report significant improvements quickly after symptom onset, e.g., (7). Other studies reported that many patients still had not returned to normal sense of smell more than 2 weeks after initial onset of smell loss (16). Altogether, our meta-analysis demonstrates a prevalence of identified smell loss in about half of the COVID-19 patients, supporting the need to understand the mechanism of infection, onset of symptoms, and recovery from olfactory loss due to a SARS-CoV-2 infection.

Limitations and Future Research. Due to the nature of data collection amidst an evolving global pandemic, there are inherent limitations to the present meta-analysis, many of which served as driving factors of the observed high heterogeneity across studies. Here, we could not control for the disease severity of the recruited study population (COVID-19–positive patients), which could add to selection bias. Measurement bias may have been introduced by the wide range of methods employed within both objective and subjective categories. Often recall bias occurs in subjective methodologies, as self-recognition may occur only in severe cases and is often forgotten in prolonged, more subtle cases (47). Furthermore, there is lack of awareness regarding chemosensory function in subjects—many researchers combined the "loss of taste or smell" in their symptomatic findings, even though they are two completely different perceptions that may be impacted differently by SARS-CoV-2. In addition, there remains a lack of comprehensive testing of chemesthetic sensations (e.g., burn from capsaicin or cooling from menthol compounds) (50).

With the findings of this meta-analysis and others emerging in the literature, it is important the clinicians incorporate assessment of olfactory function in patients with suspected or confirmed COVID-19 diagnosis as part of their standard of practice. Despite the limitations inherit in subjective measures,

at a minimum, patients need to be interviewed about their sense of smell as a first-line assessment. Given the interrelationship between smell and taste, during clinical assessments patients may report changes in taste rather than changes in smell. For patients who report changes in smell and taste function during screening questionnaires, full testing should be performed using objective standardized chemosensory assessment tools. Considering that psychophysical testing may not be possible for all patients and the current social distancing regulations, regular olfactory and gustatory self-assessment at home may be an initial recommendation. Although regular self-assessment may give information about chemosensory function during the trajectory of the disease, the results should be interpreted with caution. In addition, longitudinal assessments of chemosensory function may help identify those patients with continued impairment who may need further treatment and non-pharmacological interventions (e.g., olfactory training).

More research is needed to better establish procedures to estimate prevalence of sensory loss. Our meta-analysis results reveal underestimates when using subjective techniques, supporting the value of adapting objective methods to estimate smell loss. As information regarding COVID-19 is constantly evolving and is being crowd-sourced, more than ever researchers need to come together on methods to best assess smell loss. To that end, we have created an on-line portal of published studies of COVID-19 and smell loss which is updated frequently (51).

Funding

Dr. Mackenzie Hannum is supported by NIH T32 funding (DC000014). Dr. Paule Joseph is supported by the National Institute of Nursing Research under award number 1ZIANR000035-01. PVJ is also supported by the Office of Workforce Diversity, National Institutes of Health and the Rockefeller University Heilbrunn Nurse Scholar Award.

Acknowledgements

We would like to acknowledge Michael G. Tordoff for his assistance with the review of the literature. Input from the members of the Global Consortium for Chemosensory Research including Valentina Parma, Kathrin Ohla, Thomas Hummel, Steven Munger, John Hayes, Chrissi Kelly, Marga Veldhuizen, and Masha Niv is acknowledged. We thank William Kyle Hamilton and Beverly Cowart for their comments on this manuscript.

Table 1. Summary of studies included in meta-analysis.

Article	*Ref*	*Country*	*Subgroup*	*Specific sensory test*[a]	*Sense(s) measured*
Vaira et al. 1	(11)	Italy	Objective	CCCRC	Taste and smell, smell only
Iravani et al.	(5)	Sweden	Objective	Five-odor smell panel; used test-retest to measure reliability	Smell only
Vaira et al. 2	(12)	Italy	Objective	CCCRC, self-administered olfactory test	Smell only
Vaira et al. 3	(13)	Italy	Objective	CCCRC, home odor discrimination test	Smell
Moein et al.	(9)	Iran	Objective	University of Pennsylvania Smell Identification Test	Smell
Hornuss et al.	(16)	Germany	Objective	Sniffin' Sticks	Smell
Parma et al.	(50)	Global	Subjective	Self-reported	Smell
Merza et al.	(52)	Iraq	Subjective	Unknown, hospital reported	Smell only
Levinson et al.	(45)	Israel	Subjective	Self-reported	Smell only
Haehner et al.	(53)	Germany	Subjective	Self-reported	Smell only
Speth et al.	(54)	Switzerland	Subjective	Self-reported	Smell only
De Maria et al.	(55)	Italy	Subjective	Self-reported	Taste and smell
Menni et al.	(35)	UK and US	Subjective	Self-reported	Taste and smell
Yan et al. 1	(7)	US	Subjective	Self-reported	Smell only
Luers et al.	(56)	Germany	Subjective	Self-reported	Smell only
Roland et al.	(19)	US	Subjective	Self-reported	Taste or smell
Boscolo-Rizzo et al.	(57)	Italy	Subjective	Self-reported	Taste or smell
Liu et al.	(58)	Taiwan	Subjective	Unknown, hospital reported	Taste or smell
Paderno et al.	(21)	Italy	Subjective	Self-reported	Smell only
Lee et al.	(20)	Korea	Subjective	Self-reported	Taste or smell
Lechien et al.	(59)	Belgium, France, Spain, Italy	Subjective	Self-reported, survey based on NHANES and sQOD-NS	Smell only
Gelardi et al.	(60)	Italy	Subjective	Self-reported,	Taste and smell,

					smell only
Giacomelli et al.	(61)	Italy	Subjective	Self-reported	Taste and smell, smell only
Shoer et al.	(62)	Israel	Subjective	Self-reported	Taste or smell
Mao et al.	(8)	China	Subjective	Self-reported, EHR records	Smell only
Spinato et al.	(63)	Italy	Subjective	SNOT-22	Taste or smell
Beltran-Corbellini et al.	(44)	Spain	Subjective	Self-reported	Smell only
Trubiano et al.	(17)	Australia	Subjective	Self-reported	Taste and smell, smell only
Yan et al. 2	(18)	US	Subjective	Self-reported	Smell
Klopfenstein et al.	(64)	France	Subjective	Self-reported	Smell
Gudbjartsson et al.	(65)	Iceland	Subjective	Self-reported	Taste or smell
Wee et al.	(66)	Singapore	Subjective	Self-reported,	Taste or smell
Dawson et al.	(67)	US	Subjective	Self-reported	Smell
Noh et al.	(68)	South Korea	Subjective	Self-reported	Smell only

[a] CCCRC: Connecticut Chemosensory Clinical Research Center orthonasal olfaction test; EHR, electronic health records;

NHANES, National Health and Nutrition Examination Survey; SNOT-22, Sino-nasal Outcome Test; sQOD-NS, short version of the Questionnaire of Olfactory Disorders-Negative Statements.

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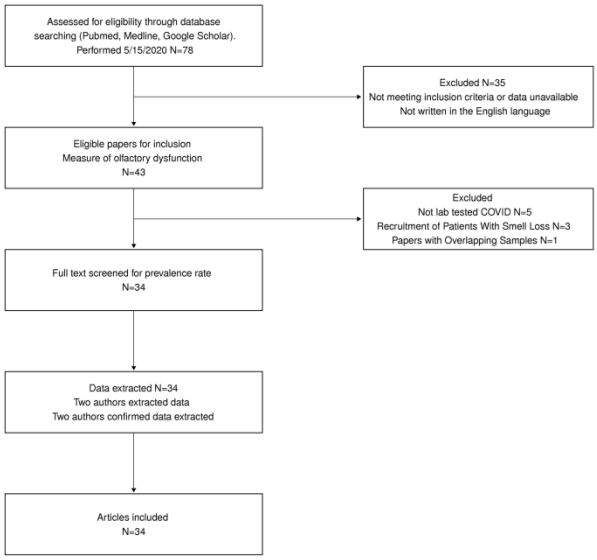

Figure 1. CONSORT flow diagram of the selection process for articles included in this meta-analysis.

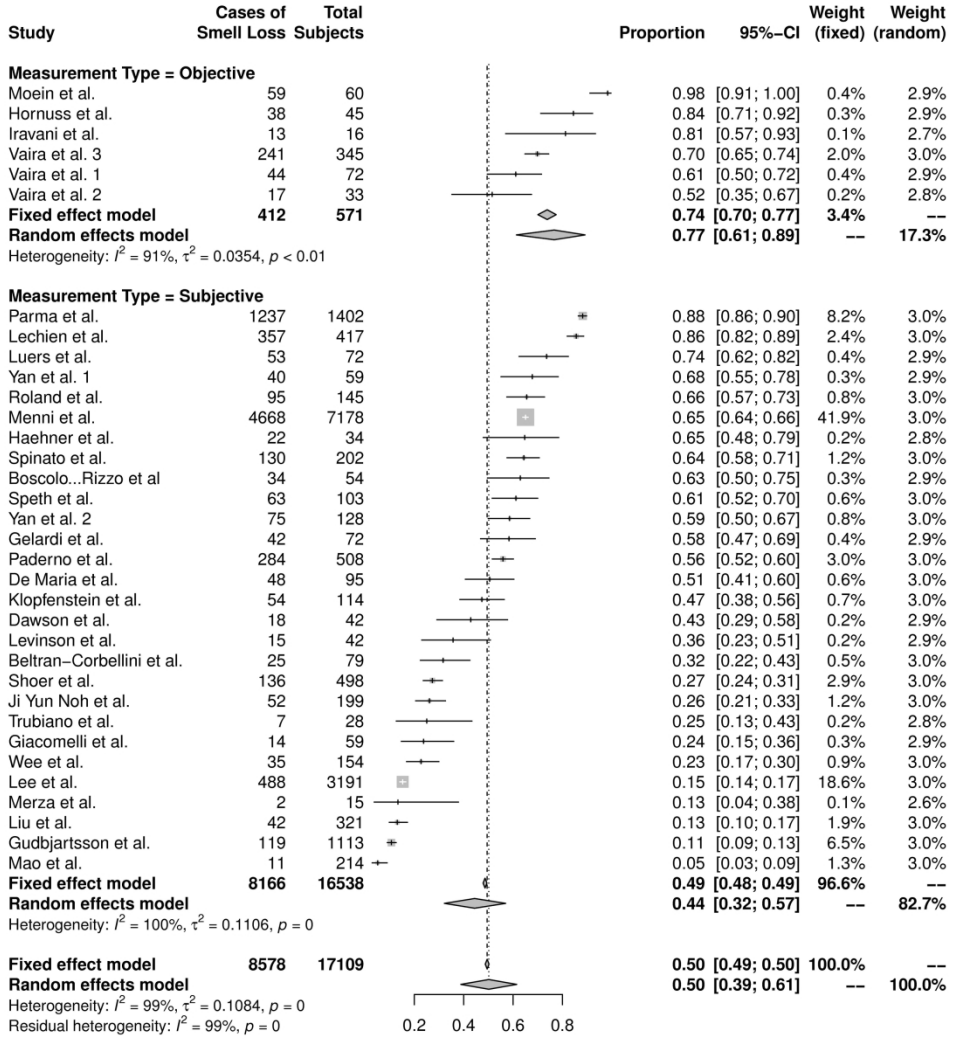

Figure 2. Forest plot meta-analysis of the prevalence of olfactory dysfunction in COVID-19 patients across studies classified as using objective (top) or subjective (bottom) methodologies. “Events” indicates cases of olfactory loss; “Total” indicates total number of COVID-19–positive patients. Both fixed-effects and random-effects models are presented. Individual study estimates are represented as “+” on the continuous horizontal line, which represents the 95% CI.