McMaster University | HEALTH FORUM

RISE Rapid-Improvement Support and Exchange

COVID-19 Rapid Evidence Profile #9 (14 May 2020)

Questions

What is the incremental benefit of using a history of sudden loss of taste (ageusia) and/or smell (anosmia) in symptom screening to identify people who may have COVID-19 and need to take appropriate action?

What we found

Using a list of COVID-19-related symptoms as a screening tool can be used for those at high risk for COVID-19 (such as travellers passing through air, land and sea borders) and for the entire population (e.g., on entering schools, stores and workplaces). It can be used alongside other potential screening tools (e.g., temperature taking, which is the focus of the first rapid evidence profile in this screening series) and operationalized in different ways (e.g., by self-screening prompted by signage, self-screening using a questionnaire, or screening using a questionnaire administered by another person; by randomly selecting individuals for symptom screening or screening everyone; and by varying the frequency of and settings for symptom screening). Appropriate follow-up actions for those with an elevated temperature can include self-isolating and seeking a diagnostic test, among others, however, such follow-up actions are not the focus of this rapid evidence profile.

Symptom screening to date in Ontario initially focused on six symptoms, namely fever, cough, shortness of breath and/or difficulty breathing, headache, runny nose, and sore throat. The Ontario government's self-assessment tool, like the one used by the Government of Canada, now includes a much longer list of symptoms. A recent study published in the journal Nature found that loss of smell (anosmia), skipped meals and fatigue are the three best predictors of COVID-19 and that, while cough is important, it is also common in those who do not have COVID-19. Moreover, among these three top predictors, anosmia was most strongly associated with COVID-19.

We identified 17 evidence documents that provide highly relevant evidence to answer the question:

- three guidelines developed using a robust process (e.g., GRADE);

Box 1: Our approach

We identified research evidence addressing the question by searching the guide to key COVID-19 evidence sources on 13 May 2020 as part of a series of three rapid evidence profiles focused on different aspects of screening for COVID-19.

We searched for guidelines that were developed using a robust process (e.g., GRADE), full systematic reviews (or review-derived products such as overviews of systematic reviews), rapid reviews, protocols for systematic reviews, and titles/questions for systematic reviews or rapid reviews. Single studies were only included if no relevant systematic reviews were identified.

We appraised the methodological quality of full systematic reviews and rapid reviews using AMSTAR. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. It is important to note that: 1) the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to delivery, financial or governance arrangements within health systems; and 2) quality-appraisal scores for rapid reviews are often lower because of the methodological shortcuts that need to be taken to accommodate compressed timeframes.

We identified experiences from other countries and from Canadian provinces and territories by searching jurisdiction-specific websites (e.g., government ministries and web pages dedicated to COVID-19). Our scan of experiences from other countries focused on those that we identified as being further ahead in resuming regular activities within their health and social systems.

This rapid evidence response was prepared in three hours or less to inform next steps in evidence synthesis, guideline development and/or decision-making related to the question that was posed.

- two full systematic reviews;
- two rapid review; and
- 10 primary studies with additional important insights.

We also identified experiences related to the question from five of the six countries examined (Australia, China, New Zealand, Sweden and the United Kingdom, with no information identified for South Korea) and for all Canadian provinces and territories.

We provide below both a narrative summary of lessons learned from highly relevant evidence documents as well as from two jurisdictional scans (one for other countries and the other for Canadian provinces and territories). Additional details for those who want to know more are provided in Table 1 (an overview of the type and number of documents that were identified), Table 2 (the full list of evidence documents found including those deemed of medium and low quality), Table 3 (for experiences from other countries), and Table 4 (for experiences from Canadian provinces and territories). In addition, we provide a detailed summary of our methods in Appendix 1, abstracts for highly relevant documents in Appendix 2, and hyperlinks for documents excluded at the final stage of reviewing in Appendix 3.

Lessons learned from evidence documents about screening for sudden loss of taste and/or smell in symptom screening

None of the evidence documents address directly the incremental benefit of screening for sudden loss of taste and/or smell, but many speak to the value of including it alongside other symptoms. Also, none of the evidence documents address directly how best to operationalize this or other types of symptom screening (e.g., by self-screening prompted by signage or using a questionnaire).

Key findings from the three highly relevant guidelines developed using a robust process (e.g., GRADE) include:

- the most common presenting symptoms of COVID-19 were cough (86%), fever or chills (85%), shortness of breath (80%), diarrhea (27%), and nausea (24%), but other reported symptoms have included anosmia (National Institutes of Health; last updated 12 May 2020);
- the symptoms of COVID-19 vary, but may include ageusia and anosmia (American College of Occupational and Environmental Medicine; last updated 24 April 2020); and
- the typical symptoms for patients with COVID-19 are cough, fever and fatigue, but they may also have breathlessness, muscle aches, sore throat, headache and loss of sense of smell (anosmia) (National Institute for Health and Care Excellence, U.K.; last updated 3 April 2020).

The two highly relevant but low-quality systematic reviews found that:

- presenting symptoms varied widely but, in combination, anosmia, fever, fatigue, persistent cough, diarrhea, abdominal pain and loss of appetite have a reasonable specificity for COVID-19 diagnosis, but the symptoms can have rapid cessation or late onset and some people will also be asymptomatic (AMSTAR rating 1/9; last updated 1 April 2020); and
- anosmia is indicative of COVID-19 infection and should be carefully monitored among healthcare workers (AMSTAR rating 2/9; literature last searched March 2020).

The two highly relevant but low-quality rapid reviews found:

- anosmia has been reported in suspected or confirmed COVID-19 patients around the world, and (despite the limited research evidence) some public-health authorities recommend adding it to the list of COVID-19 symptoms (AMSTAR rating 3/9; last updated 31 March 2020); and

- limited evidence to suggest changes in olfactory sensation is a feature of COVID-19 and clinicians are encouraged to incorporate questions around loss of olfactory sensation into their clinical practice when assessing patients with suspected COVID-19 (AMSTAR rating 3/9; search conducted 23 March 2020).

In addition to the evidence from guidelines, systematic reviews and rapid reviews, the 10 highly relevant primary studies consistently identify loss of taste and/or smell as a strong predictor of COVID-19.

Lessons learned from international and Canadian experiences with including sudden loss of taste and/or smell in symptom screening

Loss of smell and taste is variably included in the self-assessments and other symptom lists across the countries we examined. China, a country that was hit earlier by the effects of COVID-19, has not included ageusia/anosmia as a screening symptom. Countries that continue to develop their responses to the pandemic (Australia, New Zealand and Sweden) have adapted screening tools to include this symptom. The U.K. appears to be the outlier in this regard as it has not included it in the National Health Service self-assessment questions. No information could be found about South Korea's inclusion of loss of taste and smell in their list of screening symptoms.

In Canadian provinces and territories there appears to be significant variation in the inclusion of ageusia/anosmia as a symptom in provincial symptom lists. Many provinces (Alberta, Saskatchewan, Manitoba, Ontario, Quebec, New Brunswick, Newfoundland and Labrador, Yukon, and Northwest Territories) have included ageusia/anosmia as a prioritized symptom as part of their-self assessment or symptom-screening questionnaires, while others like British Columbia, Nova Scotia, Prince Edward Island, and Nunavut have not included it.

Table 1: Overview of type and number of documents that were identified

Type of document	Screening for sudden loss of taste and/or smell
Guidelines developed using a robust process (e.g., GRADE)	3
Full systematic reviews	2
Rapid reviews	2
Guidelines developed using some type of evidence	0
Protocols for reviews that are underway	1
Titles/questions for reviews that are being planned	3
Single studies in areas where no reviews were identified	12

Table 2: Documents that address the question, organized by document type and sorted by relevance to the question and COVID-19

Type of document	Key findings/focus	Recency or status
Guidelines developed using a robust process (e.g., GRADE)	The most common presenting symptoms of COVID-19 were cough (86%), fever or chills (85%), shortness of breath (80%), diarrhea (27%), and nausea (24%), but other reported symptoms have included anosmia (National Institutes of Health)	Last updated 12 May 2020
	The symptoms of COVID-19 vary, but may include ageusia and anosmia (American College of Occupational and Environmental Medicine)	Last updated 24 April 2020
	The typical symptoms for patients with COVID-19 are cough, fever and fatigue, but they may also have breathlessness, muscle aches, sore throat, headache and loss of sense of smell (anosmia) (National Institute for Health and Care Excellence)	Last updated 3 April 2020
Full systematic reviews	Presenting symptoms varied widely but, in combination, anosmia, fever, fatigue, persistent cough, diarrhea, abdominal pain and loss of appetite have a reasonable specificity for COVID-19 diagnosis, but the symptoms can have rapid cessation or late onset and some people will also be asymptomatic (AMSTAR rating 1/9)	Last updated 1 April 2020
	Anosmia is indicative of COVID-19 infection and should be carefully monitored among healthcare workers (AMSTAR rating 2/9)	Literature last searched March 2020
Rapid reviews	Anosmia has been reported in suspected or confirmed COVID-19 patients around the world, and (despite the limited research evidence) some public-health authorities recommend adding it to the list of COVID-19 symptoms (AMSTAR rating 3/9)	Last updated 31 March 2020
	Limited evidence suggests changes in olfactory sensation is a feature of COVID-19 and clinicians are encouraged to incorporate questions around loss of olfactory sensation into their clinical practice when assessing patients with suspected COVID-19 (AMSTAR rating 3/9)	Search conducted in 23 March 2020
Guidance developed using some type of evidence	None identified	

Type of document	Key findings/focus	Recency or status
synthesis and/or expert opinion		
Protocols for reviews that are underway	Signs and symptoms to determine if a patient presenting in general practice or at the emergency department has COVID-19, COVID-19 pneumonia or severe COVID-19 pneumonia/acute respiratory distress syndrome (ARDS) requiring ICU admission	In development
Titles/questions for reviews that are being planned	What is the most effective Covid-19 screening strategy?	Question in development (added 25 March 2020)
	Population screening as an option for the long-term isolation of COVID-19 in the entire population	Question in development (added 25 March 2020)
	Clinical markers or scoring systems that can be used to help in diagnosis or assessment of severity of COVID-19 infection	Question under review
Single studies in areas where no reviews were identified	The three best predictors of COVID-19 infection are loss of smell, skipped meals and fatigue, with cough being common but often present in people who do not have COVID-19	Published 11 May 2020
	Self-reported olfactory or taste disorders were found to have high specificity as a screening criterion for COVID-19 in an Asian cohort where patients with COVID-19 appeared to have higher odds of olfactory or taste disorders compared to those positive for other respiratory viruses and, as a result, routine screening in patients with new-onset olfactory or taste disorders can improve case detection	Published 24 April 2020 (letter to the editor)
	Anosmia, muscle ache, ocular pain, general malaise, headache, extreme tiredness and fever are strongly associated with COVID-19 positive tests, and can contribute to targeted screening strategies for healthcare workers	Published 23 April 2020
	New onset smell/taste disorder disorders were found to occur significantly more frequently among COVID-19 patient than influenza patients, were typically characterized by acute onset and were an initial manifestation, and this symptom is therefore likely helpful to identify COVID-19 and aid in individuals' decision making about self-isolation	22 April 2020
	A relationship between COVID-19 and anosmia should be considered during the pandemic	Published 21 April 2020
	Anosmia was present in half of 114 European COVID-19 patients and was often associated with dysgeusia	Published 17 April 2020
	Quantitative smell testing demonstrates that decreased smell function, but not always anosmia, is a major marker for COVID-19 and suggests the possibility that smell testing may help, in some cases, to identify COVID-19 patients in need of early treatment or quarantine	Published 17 April 2020
	In a non-negligible number of patients, especially if pauci-symptomatic, ageusia and anosmia can represent the first or the only symptomatology manifestation	Published 1 April 2020
	In the absence of other respiratory conditions, anosmia and dysgeusia should be carefully evaluated, and special attention should be given to patients with non-classic COVID-19	Published 3 April 2020

Type of document	Key findings/focus	Recency or status
	symptoms in order to reduce transmission and protect health providers (based on case evaluation of elderly patients)	
	Recently, a probability of association between COVID-19 and altered olfactory function has been reported in South Korea, Iran, Italy, France, U.K. and the United States, but a definitive association between COVID-19 and anosmia has not been established	Published 14 April 2020 (letter to the editor)
	A medical record showing high suspicion for COVID-19 infection based on well-known symptoms also reported total anosmia and ageusia	Published 13 April 2020
	Isolated sudden onset anosmia is identified as a fourth common syndrome of COVID-19 infection based on a single case	Published 2 April 2020

Table 3: International experiences with including sudden loss of taste and/or smell in symptom screening

Country	Key features of implemented strategies
Australia	• The Australian government has established a COVID-19 app to be able to inform individuals when they have been identified as someone who may have been in contact with a confirmed COVID-19 case • The app lists a series of symptoms to look for, namely: headache, muscle pains, runny nose, nausea, vomiting or diarrhea, loss of smell, altered sense of taste, and a loss of appetite
China	• Symptoms related to ageusia/anosmia have not been included in screening questionnaires or in health declaration cards
New Zealand	• The list of symptoms provided by the government for self-screening to contact an established hotline or an individual's doctor, include: a cough, a high temperature of at least 38 degrees Celsius, shortness of breath, sore throat, sneezing and runny nose, and temporary loss of smell
South Korea	• No information could be located about what symptoms are being prioritized in screening
Sweden	• Symptoms listed by the Public Health Agency of Sweden that may be associated with COVID-19, include: cough, fever, difficulty breathing, runny nose, blocked nose, sore throat, headache, nausea, muscle and joint pain, loss of smell, loss of taste, and diarrhea
U.K.	• Ageusia/anosmia is not currently included in the list of symptoms provided for self-assessments created by the National Health Service

Table 4: Canadian provinces' and territories' experiences with including sudden loss of taste and/or smell in symptom screening

Province/ territory	Key features of implemented strategies
Pan-Canadian	• The Government of Canada self-assessment tool does not include symptoms related to ageusia/anosmia
B.C.	• The British Columbia Centre for Disease Control self-assessment tool does not include ageusia/anosmia as a potential symptom
Alberta	• Alberta Health Services' online self assessment includes loss of taste, loss of smell, and unexplained loss of appetite
Saskatchewan	• Saskatchewan Health Authority's online self-assessment tool was adapted from that of Alberta and prioritizes the following symptoms: fever, cough, headache, aches and pains, sore throat, chills, runny nose, loss of sense of taste or smell, and shortness of breath or difficulty breathing
Manitoba	• The Manitoba government's workplace guidance for business owners includes loss of taste or smell in their list of symptoms to use in screening employees, volunteers or clients
Ontario	• The Ontario government's self-assessment tool includes loss of taste or smell
Quebec	• The Quebec government's website lists the main symptoms of COVID-19, which it notes can be mild (similar to a cold) or more severe and include sudden loss of smell without a stuffy nose, with or without loss of taste
New Brunswick	• The government's online self-assessment survey includes loss of sense of smell or taste as a symptom to be used in determining who should be tested in the province
Nova Scotia	• The province's screening questions for symptoms does not currently include ageusia/anosmia as a prioritized symptom
Prince Edward Island	• The province's screening questions for symptoms does not currently include ageusia/anosmia as a prioritized symptom

Newfoundland and Labrador	• The province's online self-assessment survey includes a loss of sense of taste and or smells as a screening symptom
Yukon	• The territorial government's online self-assessment includes loss of taste and/or smell as a screening symptom
Northwest Territories	• The territorial government's online self-assessment includes loss of sense of taste and/or smell as well as loss of appetite
Nunavut	• The territorial government has not included ageusia/anosmia in their self-assessment tools

Waddell K, Wilson MG, Gauvin FP, Mansilla C, Moat KA, Wang Q, Lavis JN. COVID-19 rapid evidence profile #9: What is the incremental benefit of using a history of sudden loss of taste (ageusia) and/or smell (anosmia) in symptom screening to identify people who may have COVID-19 and need to take appropriate action? Hamilton: McMaster Health Forum, 14 May 2020.

The McMaster Health Forum is one of the three co-leads of RISE, which is supported by a grant from the Ontario Ministry of Health to the McMaster Health Forum. To help Ontario Health Team partners and other health- and social-system leaders as they respond to unprecedented challenges related to the COVID-19 pandemic, the Forum is preparing rapid evidence responses like this one. The opinions, results and conclusions are those of the McMaster Health Forum and are independent of the ministry. No endorsement by the ministry is intended or should be inferred.

The authors declare that they have no professional or commercial interests relevant to the rapid evidence profile. The funders played no role in the identification, selection, assessment, synthesis, or presentation of the research evidence or experiences profiled in the rapid evidence profile.

Appendix 1: Methodological details

We use a standard protocol for preparing each rapid evidence profile (REP) to ensure that our approach to identifying research evidence as well as experiences from other countries and from Canadian provinces and territories are as systematic and transparent as possible in the time we were given to prepare the profile.

Identifying research evidence

For each REP, we search our continually updated guide to key COVID-19 evidence sources for:
1) guidelines developed using a robust process (e.g., GRADE);
2) full systematic reviews;
3) rapid reviews;
4) guidelines developed using some type of evidence synthesis and/or expert opinion;
5) protocols for reviews or rapid reviews that are underway;
6) titles/questions for reviews that are being planned; and
7) single studies (when no guidelines, systematic reviews or rapid reviews are identified).

Each source for these documents is assigned to one team member who conducts hand searches (when a source contains a smaller number of documents) or keyword searches to identify potentially relevant documents. A final inclusion assessment is performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment.

During this process we include published, pre-print and grey literature. We do not exclude documents based on the language of a document. However, we are not able to extract key findings from documents that are written in languages other than Chinese, English, French or Spanish. We provide any documents that do not have content available in these languages in an appendix containing documents excluded at the final stages of reviewing.

Identifying experiences from other countries and from Canadian provinces and territories

For each rapid evidence profile we collectively decide on what countries to examine based on the question posed. For international jurisdictions we search relevant sources included in our continually updated guide to key COVID-19 evidence sources. These sources include government-response trackers that document national responses to the pandemic. In addition, we conduct searches of relevant government and ministry websites. In Canada, we search websites from relevant federal and provincial governments, ministries and agencies (e.g., Public Health Agency of Canada).

While we do not exclude countries based on language, where information is not available through the government-response trackers, we are unable to extract information about countries that do not use English, Chinese, French or Spanish as an official language.

Assessing relevance and quality of evidence

We assess the relevance of each included evidence document as being of high, moderate or low relevance to the question and to COVID-19. We then use a colour gradient to reflect high (darkest blue) to low (lightest blue) relevance.

Two reviewers independently appraise the methodological quality of systematic reviews and rapid reviews that are deemed to be highly relevant. Disagreements are resolved by consensus with a third reviewer if needed. AMSTAR rates overall methodological quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. High-quality reviews are those with scores of eight or higher out of a possible 11, medium-quality reviews are those with scores between four and seven, and low-quality reviews are those with scores less than four. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to health-system arrangements or to economic and social responses to COVID-19. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e., the numerator and denominator) in mind. For example, a review that scores 8/8 is generally of comparable quality to a review scoring 11/11; both ratings are considered 'high scores.' A high score signals that readers of the review can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the review should be discarded, merely that less confidence can be placed in its findings and that the review needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. *Health Research Policy and Systems* 2009; 7 (Suppl1):S8.

Preparing the profile

Each included document is hyperlinked to its original source to facilitate easy retrieval. For all included guidelines, systematic reviews, rapid reviews and single studies (when included), we prepare declarative headings that provide a brief summary of the key findings and act as the text in the hyperlink. Protocols and titles/questions have their titles hyperlinked given that findings are not yet available. We then draft a brief summary that highlights the total number of different types of highly relevant documents identified (organized by document), as well as their key findings, date of last search (or date last updated or published), and methodological quality.

Appendix 2: Abstracts for highly relevant documents

Note that the table below only includes the abstracts for the documents that we identified in Table 1 as being highly relevant to the question.

Type of document	Abstract and link to full text
Full systematic reviews	Presenting symptoms varied widely but, in combination, anosmia, fever, fatigue, persistent cough, diarrhea, abdominal pain and loss of appetite have a reasonable specificity for COVID-19 diagnosis, but the symptoms can have rapid cessation or late onset and some people will also be asymptomatic **Key messages** • Cough was observed in less than half of the mild cases in the largest included study and in two-thirds of cases in a systematic review, suggesting it is unreliable as a key diagnostic symptom. • Fever (< 39.1 °C) was the most frequent symptom for mild and moderate cases of COVID-19, though a recent U.K. study suggests anosmia may be a stronger predictor of COVID-19 than self-reported fever amongst people in the community. • Overall, we found scarce and inconclusive evidence on symptoms that easily distinguish mild and moderate cases of COVID-19 from severe cases. • The majority of available evidence was from hospitalized patients. Mild and moderate cases were usually defined as those without pneumonia, acute respiratory distress syndrome (ARDS) or Intensive Care Unit (ICU) admission. Applicability to community cohorts is therefore uncertain. • Other reported symptoms include dyspnea, headache, diarrhea, sore throat, fatigue and rhinorrhea.
	Anosmia is indicative of COVID-19 infection and should be carefully monitored among healthcare workers **Abstract** Background: Healthcare workers are at the forefront of the ongoing COVID-19 pandemic and are at high risk for both the contraction and subsequent spread of virus. Understanding the role of anosmia as an early symptom of infection may improve monitoring and management of SARS-CoV2 infection. Methodology: We conducted a systematic review of the literature of SARS-CoV2 infection/COVID-19 and anosmia to help inform management of anosmia in healthcare works. We report a case series of healthcare workers, who presented with a loss of sense of smell secondary to COVID-19 infection to demonstrate management principles. RT-PCR was used to confirm COVID-19 positivity and psychophysical testing of olfaction was performed using the British version of the University of Pennsylvania Smell Identification Test, UPSIT. Results: The systematic literature search returned 31 articles eligible for inclusion in the study and informed our recommendations for clinical assessment and management. All three healthcare professionals who presented with loss of sense of smell subsequently

Type of document	Abstract and link to full text
	tested positive for SARS-CoV-2. Psychophysical testing of olfaction using the UPSIT confirmed mild and moderate microsmia in two, respectively, and normosmia at day 17 in one. Conclusions: Olfactory (± gustatory) dysfunction is indicative of COVID-19 infection and thus has important implications in the context of healthcare workers, or key workers in general, who work in close contact with others if not recognised as suffering from COVID. This leads to a potentially higher likelihood of spreading the virus. In conjunction with our literature review these findings have helped with creating recommendations on the assessment and management of olfactory dysfunction during the ongoing COVID-19 pandemic, both for healthcare workers and patients.
Rapid reviews	Anosmia has been reported in suspected or confirmed COVID-19 patients around the world, and (despite the limited research evidence) some public-health authorities recommend adding it to the list of COVID-19 symptoms Based on the information available at the time of writing, despite the uncertainty existing in this documentation and in the review process used, it appears that: • several sources of information report a significant number of clinical pictures of anosmia in suspected or confirmed COVID-19 patients around the world; • in the case of an infection with the new coronavirus, the loss of smell would occur suddenly without nasal obstruction, and sometimes accompanied by a disappearance of the taste (ageusia); • the onset of this symptom would generally be seen in young patients with "mild" forms of COVID-19 disease; • loss of smell could occur in isolation without inflammation and without being associated with commonly recognized symptoms of fever and cough; • although this evidence is not yet supported by scientific studies, some French, British and American associations call on the authorities to advise anyone with a loss of smell or taste to isolate themselves and confine themselves as a precaution. Some even recommend adding this symptom to the list of recognized criteria for screening for possible COVID-19 infection; and • contrary to what is done in the case of a classic anosmia, French companies recommend not to administer corticosteroid therapy and to refrain from performing nasal washes. [McMaster Health Forum translation]
	Limited evidence suggests changes in olfactory sensation is a feature of COVID-19 and clinicians are encouraged to incorporate questions around loss of olfactory sensation into their clinical practice when assessing patients with suspected COVID-19 **Key messages** The current evidence base to suggest changes in olfactory sensation is a feature of COVID-19 is limited and inconclusive. More evidence is required to establish whether there is a link between changes in olfaction and COVID-19; we therefore encourage clinicians to incorporate questions around loss of olfactory sensation into their clinical practice when assessing patients with suspected COVID-19.
Primary studies	The three best predictors of COVID-19 infection are loss of smell, skipped meals and fatigue, with cough being common but often present in people who do not have COVID-19

Type of document	Abstract and link to full text
	Abstract A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app. Among the 18,401 who had undergone a SARS-CoV-2 test, the proportion of participants who reported loss of smell and taste was higher in those with a positive test result (4,668 of 7,178 individuals; 65.03%) than in those with a negative test result (2,436 of 11,223 participants; 21.71%) (odds ratio = 6.74; 95% confidence interval = 6.31–7.21). A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19.
	Self-reported olfactory or taste disorders were found to have high specificity as a screening criterion for COVID-19 in an Asian cohort where patients with COVID-19 appeared to have higher odds of olfactory or taste disorders compared to those positive for other respiratory viruses and, as a result, routine screening in patients with new-onset olfactory or taste disorders can improve case detection **No abstract provided**
	Anosmia, muscle ache, ocular pain, general malaise, headache, extreme tiredness and fever are strongly associated with COVID-19 positive tests, and can contribute to targeted screening strategies for healthcare workers **Abstract** Healthcare workers (n = 803) with mild symptoms were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (n = 90 positive) and asked to complete a symptom questionnaire. Anosmia, muscle ache, ocular pain, general malaise, headache, extreme tiredness and fever were associated with positivity. A predictive model based on these symptoms showed moderate discriminative value (sensitivity: 91.2%; specificity: 55.6%). While our models would not justify presumptive SARS-CoV-2 diagnosis without molecular confirmation, it can contribute to targeted screening strategies.
	New onset smell/taste disorders were found to occur significantly more frequently among COVID-19 patients than influenza patients, were typically characterized by acute onset and were an initial manifestation, and this symptom is therefore likely helpful to identify COVID-19 and aid in individuals' decision-making about self-isolation **Abstract** Background: Specific respiratory tract infections, including Covid-19, may cause smell and/or taste disorders (STD) with increased frequency. We aim to determine whether new-onset STD are more frequent among Covid-19 patients than influenza patients. Methods: Case-control study including hospitalized patients of two tertiary care centers. Consecutive patients positive for Covid-19 PCR (cases) and patients positive for influenza PCR (historical control sample) were assessed during specific periods, employing a self-reported STD questionnaire. Results: Seventy-nine cases and 40 controls were included. No significant differences were found in basal features between both groups. New-onset STD were significantly more frequent among cases (31, 39.2%) than in the control group (5, 12.5 %), adjusted

Type of document	Abstract and link to full text
	OR 21.4 (2.77-165.4, p=0.003). Covid-19 patients with new-onset STD were significantly younger than Covid-19 patients without STD (52.6 ± 17.2 vs. 67.4 ±15.1, p<0,001). Among Covid-19 patients who presented STD, 22 (70.9%) recalled an acute onset and was an initial manifestation in 11 (35.5%). Twenty-five (80.6%) presented smell disorders (mostly anosmia, 14, 45.2%), and 28 (90.3%) taste disorders (mostly ageusia, 14, 45.2%). Only four (12.9 %) reported concomitant nasal obstruction. Mean duration of STD was 7.5 ± 3.2 days and 12 patients (40%) manifested complete recovery after 7.4 ± 2.3 days of onset. Conclusion: New-onset STD were significantly more frequent among Covid-19 patients than influenza patients, they usually had an acute onset and were commonly an initial manifestation. We suggest the use of STD assessment in anamnesis as a hint for Covid-19 and to support individuals' self-isolation in the current epidemic context.
	A relationship between COVID-19 and anosmia should be considered during the pandemic **Abstract** Patients with acute olfactory disorders typically present to the otolaryngologist with both acute hyposmia and less often with anosmia. With the onset of COVID-19 we have noticed an increase in the number of patients who have presented with new onset of complete smell loss to the senior author's practice in Tehran, Iran. This anosmia and the frequency with which patients present is highly unusual. Coronaviruses have been known to cause common cold symptoms. COVID-19 infections have been described as causing more severe respiratory infections and the symptoms reported by authors from Wuhan, China have not specifically included anosmia. We describe patients who have presented during a two-week period of the COVID-19 pandemic with complete loss of sense of smell. Most had either no symptoms or mild respiratory symptoms. Many had a normal otolaryngologic exam. A relationship between COVID-19 and anosmia should be considered during the pandemic. We hypothesize that the mechanism of injury is similar to that of other coronavirus infections that cause central and peripheral neurologic deficits.
	Anosmia was present in half of 114 European COVID-19 patients and was often associated with dysgeusia **Highlights** • Fifty-four of 114 patients (47%) with confirmed COVID-19 reported anosmia. • There is no inpatient cohort about COVID-19-related anosmia in the medical literature. In our study, 37% of our patients were hospitalized. To our knowledge, our study is the main monocentric cohort of confirmed COVID-19 patients with anosmia in France and in the medical literature. • Our data is strong due to a standardised follow-up for non-hospitalized and discharged patients. Patients were called seven days (± 7 days) after the first symptoms and every week until recovery (national guidelines recommended a home follow-up for patients with COVID-19). • Our results are similar to the recent multicentric European study conducted by Lechien et al.
	Quantitative smell testing demonstrates that decreased smell function, but not always anosmia, is a major marker for COVID-19 and suggests the possibility that smell testing may help, in some cases, to identify COVID-19 patients in need of early treatment or quarantine

Type of document	Abstract and link to full text
	Abstract Background: SARS-CoV-2, the virus that causes COVID-19 disease, is responsible for the largest pandemic since the 1918 H1N1 influenza outbreak. The symptoms presently recognized by the World Health Organization are cough, fever, tiredness, and difficulty breathing. Patient-reported smell and taste loss has been associated with COVID-19 infection, yet no empirical olfactory testing on a cohort of COVID-19 patients has been performed. Methods: The University of Pennsylvania Smell Identification Test (UPSIT), a well-validated 40-odorant test, was administered to 60 confirmed COVID-19 inpatients and 60 age- and sex-matched controls to assess the magnitude and frequency of their olfactory dysfunction. A mixed effects analysis of variance determined whether meaningful differences in test scores existed between the two groups and if the test scores were differentially influenced by sex. Results: Fifty-nine (98%) of the 60 patients exhibited some smell dysfunction [mean (95% CI) UPSIT score: 20.98 (19.47,22.48); controls: 34.10 (33.31,34.88); p<0.0001]. Thirty-five of the 60 patients (58%) were either anosmic (15/60; 25%) or severely microsmic (20/60; 33%); 16 exhibited moderate microsmia (16/60; 27%), 8 mild microsmia (8/60; 13%), and one normosmia (1/60; 2%). Deficits were evident for all 40 UPSIT odorants. No meaningful relationships between the test scores and sex, disease severity, or comorbidities were found. Conclusions: Quantitative smell testing demonstrates that decreased smell function, but not always anosmia, is a major marker for SARS-CoV-2 infection and suggests the possibility that smell testing may help, in some cases, to identify COVID-19 patients in need of early treatment or quarantine.
	In a non-negligible number of patients, especially if pauci-symptomatic, ageusia and anosmia can represent the first or the only symptomatology manifestation **Abstract** In a not negligible number of patients affected by COVID-19 (coronavirus disease 2019), especially if pauci-symptomatic, anosmia and ageusia can represent as the first or only symptomatology present.
	In the absence of other respiratory conditions, anosmia and dysgeusia should be carefully evaluated, and special attention should be given to patients with non-classic COVID-19 symptoms in order to reduce transmission and protect health providers (based on case evaluation of elderly patients) **Abstract** We describe two elderly patients evaluated at emergency departments for anosmia/dysgeusia in the absence of any other respiratory symptoms prior to or upon admission. In the current epidemiological context, clinical and biological work-up led to a diagnosis of COVID-19 infection. Unfortunately, one of the patients died during hospitalization, but the other recovered and was discharged.

Type of document	Abstract and link to full text
	Recently, a probability of association between COVID-19 and altered olfactory function has been reported in South Korea, Iran, Italy, France, the U.K. and the United States, but a definitive association between COVID-19 and anosmia has not been established **No abstract provided**

Appendix 3: Documents excluded at the final stages of reviewing

Type of document	Focus
Guidelines developed using a robust process (e.g., GRADE)	Not applicable
Full systematic reviews	Not applicable
Rapid reviews	Not applicable
Guidance developed using some type of evidence synthesis and/or expert opinion	Not applicable
Protocols for reviews that are underway	Not applicable
Titles/questions for reviews that are being planned	Not applicable
Single studies in areas where no reviews were identified	Anosmia in a healthcare worker with COVID-19 in Madrid, Spain