Background: Olfactory (OD) and gustatory (GD) dysfunction have been proven to be a typical symptom of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection. However, their prevalence in different patient populations still needs to be clarified.

Methods: A cross-sectional study was performed from March 27 to April 1, 2020, in Northern Italy. Physicians administered a survey-based questionnaire to SARS-CoV-2–positive patients with the aim of assessing symptoms, focusing on OD and GD. Two groups were studied: group A, patients hospitalized at Azienda Socio Sanitaria Territoriale (ASST) Spedali Civili University Hospital of Brescia; and group B, home-quarantined subjects.

Results: A total of 508 patients were enrolled: 295 in group A and 213 in group B. Mean age ± standard deviation (SD) was 55 ± 15 years; 56% were men. Overall, OD and GD were present in 56% (95% confidence interval [CI], 51% to 60%) and 63% (95% CI, 59% to 67%) of cases, respectively. In group A, the prevalence of OD and GD was 44% (95% CI, 38% to 50%) and 52% (95% CI, 46% to 58%), respectively. In group B, the prevalence of OD and GD was 72% (95% CI, 65% to 79%) and 79% (95% CI, 73% to 84%), respectively.

In the entire cohort, total loss of olfaction and taste was reported in 64% and 60% of cases, respectively. OD and GD occurred as the first symptom in 10% and 11% of cases, respectively; in the remaining cases, they occurred after a mean of 4 ± 3 days following the first symptom. At the time of the questionnaire, complete resolution of OD and GD was reported in 52% and 55% of cases, respectively (mean duration, 9 ± 5 days in both).

Conclusion: OD and GD are more prevalent in home-quarantined subjects, and they are independently associated with younger age and female gender. © 2020 ARS-AAOA, LLC.

Key Words: COVID-19; SARS-CoV-2; olfactory dysfunction; gustatory dysfunction; smell; taste

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Since December 2019, the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) pandemic has been placing significant burden on healthcare systems and governments. Countries have applied a wide range of large-scale infection control policies to respond to the crisis, with variable results. Notwithstanding, these policies should be adaptive and evolve according to appropriate evidence.

In this view, 2 peculiarities of SARS-CoV-2 should be underlined. Different from SARS-CoV-1, SARS-CoV-2 is mainly localized in the upper airways and significant viral
load levels are detectable in both asymptomatic and symptomatic patients. These features are expected to cause a higher rate of upper airway complaints, and suggest a potential risk of transmission from asymptomatic and mildly symptomatic subjects. In fact, undocumented but infectious cases are a critical epidemiological issue and play a vital role in the transmission dynamics of SARS-CoV-2, leading to the strong need to better identify this subgroup of subjects.

Recent reports on coronavirus disease 2019 (COVID-19) have highlighted a high prevalence of olfactory (OD) and gustatory dysfunction (GD). OD in SARS-CoV-2-infected subjects has also been demonstrated with olfato-metric tests, and was independently associated with outpatient care in a recent study by Yan et al. In this view, the precise definition of highly specific symptoms may greatly improve the identification of undocumented subjects. However, screening policies should take into account the variability of these symptoms according to the characteristics of different patient populations.

The study aims to estimate the different characteristics of OD and GD in hospitalized patients and home-quarantined subjects with a nasal/pharyngeal swab positive for SARS-CoV-2 in an epidemic area.

Patients and methods

Study population, setting, and data collection

Cases with confirmed infection for SARS-CoV-2 were included in a cross-sectional study. Only laboratory-confirmed cases (positive by real-time polymerase chain reaction [RT-PCR] on a nasal/pharyngeal swab) were included. Serology was not available at the time of the study. Data were collected from March 27 to April 1, 2020, through a survey-based questionnaire on symptoms, focusing on OD and GD (ie, time of onset, duration, severity, characteristics, and relationship with other symptoms). This report followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Inclusion criteria were as follows:

- Signed written informed consent;
- Male or female >18 years of age;
- Willing and able to participate in the study;
- Positive nasal/pharyngeal swab for SARS-CoV-2 (RT-PCR);

Exclusion criteria were as follows:

- Legal incapacity or limited legal capacity;
- Medical or psychological condition or situation which in the opinion of the investigator would not Permit the patient to complete the questionnaire or sign informed consent;
- Invasive ventilation;
- Noninvasive ventilation preventing adequate communication;
- Preexisting chronic anosmia and/or ageusia.

Enrolled cases included:

- Group A: patients hospitalized in COVID-19 Units (Pneumology, Internal Medicine, Infectious Disease, and Emergency) of the ASST Spedali Civili University Hospital (Brescia, Italy);
- Group B: home-quarantined subjects recruited through exponential snowball sampling. Each subject provided the contact information of confirmed positive cases in his/her social circle. After specific consent, positivity to nasal/pharyngeal swab for SARS-CoV-2 was confirmed through access to their clinical data or contact with their general practitioner.

Healthcare system policy for nasal/pharyngeal swab for SARS-CoV-2 were defined as: recent (less than 14 days) close contact (<1 m for >15 minutes and without personal protective equipment) with someone who tested positive for SARS-CoV-2 and symptoms highly suggestive for COVID-19. The test was repeated within 24 to 48 hours in case of negative results and persistent suspicious symptoms.

All subjects with positive nasal/pharyngeal swab for SARS-CoV-2 were home-quarantined or hospitalized. Factors evaluated for hospitalization included:

- Severe or worsening symptoms;
- Partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FIO₂) <350 or PaO₂ <75 mm of mercury (Hg) or blood oxygen saturation (SaO₂) <94%;
- Unfavorable home and social conditions;
- Evidence of moderate/severe interstitial pneumonia at chest X-ray, chest computed tomography (CT), or chest ultrasound;
- Age >65 years;
- Presence of significant comorbidities.

The indication for hospitalization or quarantine was considered as a surrogate marker of full-blown disease (group A) or mildly symptomatic clinical presentation (group B), respectively.

Patients were not informed about the specific study aim to minimize confirmation bias. All subjects signed an informed consent form approved by the institutional review board. The study was performed following the principles of the Declaration of Helsinki and was approved by the Research Review Board, Ethics Committee, of the ASST Spedali Civili of Brescia, Italy (study reference number: NP4037).

Study objectives

The primary objective was the estimate of prevalence and definition of timing of onset, resolution, and characteristics of OD and GD in COVID-19 hospitalized and home-quarantined subjects. The secondary objective was the assessment of the association of OD/GD with patient
characteristics, symptoms, and radiological pulmonary alterations.

Study definitions
Hereinafter, when we refer to our cohort, we intend all individuals included in the study (group A+B) as “cases,” those hospitalized (group A) as “patients,” and those home-quarantined (group B) as “subjects.”

Coexisting conditions were ascertained from physician documentation and questionnaire administration. Symptoms presenting as a consequence of a known pharmacological side effect or oxygen therapy were excluded from evaluation.

Chest X-ray was performed in all hospitalized patients (group A). Since March 4, 2020, in our hospital a chest X-ray scoring system was introduced for semiquantitative assessment of lung disease in COVID-19. It ranked the pulmonary involvement on a 0 to 18-point severity scale (18 being the most severe) according to the extent and characteristics of lung infiltrates.

Specimen collection and testing
Clinical samples for SARS-CoV-2 diagnostic testing were obtained according to World Health Organization (WHO) guidelines. The nasal/pharyngeal swab was performed using UTM® COPAN FLOQSwabs® (COPAN, Murrieta, CA). SARS-CoV-2 nucleic acids were detected by RT-PCR using GeneFinder™ COVID-19 Plus RealAmp Kit by OSANG Healthcare (Anyang, Republic of Korea), or Allplex™ 2019-nCoV Assay by Seegene Inc. (Seoul, Republic of Korea). The 2 kits have comparable diagnostic accuracy.

Survey-based questionnaire
The survey-based questionnaire was precisely defined and administered by a physician. The translated version of the questionnaire and data collection form is described in the Supporting Information. Data were collected in a dedicated database.

Statistical analysis
On the basis of an expected OD prevalence of 30%, we estimated that given a maximum risk of type I error of 5%, a sample size of 500 patients would provide an estimate with a precision plus or minus 4%.

The prevalence of OD, GD, and their corresponding 95% confidence intervals (CIs) were calculated according to binomial distributions. The tetrachoric correlation between OD and GD was also calculated. Comparisons between group A and B were performed using t test, Mann-Whitney, and chi-square tests as appropriate. Multivariable logistic regression models were used to assess factors related to OD and GD, while a multivariable linear regression model was performed to evaluate factors associated with radiologic score. Results were expressed in terms of odds ratios (ORs) and regression coefficients, respectively. The final models included factors associated with outcomes when adjusting for age (bivariable analyses). For more details, see the Supporting Information.

Results

Demographic and clinical characteristics
A total of 575 cases were evaluated; of those, 508 were included in the study. Fifty-six patients were excluded due to critical health conditions (ie, irresponsive, unconscious, and with significant respiratory effort), 6 due to preexisting chronic ageusia or anosmia (5 undocumented and 1 due to total laryngectomy), 3 due to language barrier, and 2 refused to participate in the study.

Group A included 295 (58%) hospitalized patients and group B was composed of 213 (42%) home-quarantined subjects. Mean ± standard deviation (SD) lag time between swab and survey, and between symptoms onset and survey was 11 ± 8 days and 18 ± 7 days, respectively (Table 1). The mean ± SD age was 55 ± 15 years (range, 18–91 years); 56% were men. In all, 40% of cases had no significant comorbidity. Group A had a significantly higher prevalence of older patients, smokers, and comorbidities. Cohort characteristics by group are summarized in Table 1, Supporting Table 1, and Supporting Table 2.

Prevalence
The prevalence of symptoms is detailed in Table 2. In the entire population, OD and GD were present in 56% (95% CI, 51% to 60%) and 63% (95% CI, 59% to 67%) of cases, respectively. In group A the prevalence of OD and GD was 44% (95% CI, 38% to 50%) and 52% (95% CI, 46% to 38%), respectively. Their prevalence was significantly higher in group B: 72% (95% CI, 65% to 78%) and 79% (95% CI, 73% to 84%), respectively. OD and GD were more prevalent in younger patients, females, nonsmokers, and those without comorbidities (Table 3). OD and GD were reported as complete loss (anosmia or ageusia) in 64% and 60% of cases, respectively. GD without OD was present in 10% of cases.

Onset and duration
OD and GD developed at the onset in 10% and 11% of cases, respectively; in 5% they were the only complaint. The remaining developed the symptom after a mean of 4 ± 3 days. At the time of the questionnaire, complete resolution of OD and GD was reported by 56% and 59% of cases, respectively, with a similar mean duration (9 ± 5 days) (Table 4).

Associations at multivariable analysis
At multivariable analyses, older age (10-year age increase; OR 0.76; 95% CI, 0.67 to 0.87; p < 0.001) and male gender (OR 0.62; 95% CI, 0.43 to 0.91; p = 0.015) were associated with a decreased risk of OD; whereas
TABLE 1. Demographic and clinical characteristics

| Variable                              | Hospitalized (Group A) (n = 295) | Home-quarantined (Group B) (n = 213) | p (Group A vs B) |
|---------------------------------------|----------------------------------|-------------------------------------|-----------------|
| Age (years), mean ± SD (range)       | 61.9 ± 12.8 (24–91)             | 44.7 ± 12.1 (18–74)                | <0.001          |
| Gender, n (%)                         |                                  |                                     |                 |
| Male                                  | 204 (69.2)                      | 81 (38.0)                           | <0.001          |
| Female                                | 91 (30.8)                       | 132 (62.0)                          |                 |
| History of smoking, n (%)             |                                  |                                     |                 |
| Nonsmoker                             | 184 (62.4)                      | 158 (74.2)                          | <0.001          |
| Current smoker [average py]           | 12 (4.1) [29.4 py]              | 18 (8.4) [7.3 py]                   |                 |
| Former smoker [average py]            | 99 (33.5) [25.4 py]             | 37 (17.4) [15.7 py]                 |                 |
| Lag time from swab to survey (days), mean ± SD (range) | 6.9 ± 6.1 (1–39) | 16.2 ± 7.9 (0–35) | <0.001 |
| Lag time from onset of symptoms to survey, mean ± SD (range) | 15.9 ± 6.7 (1–45) | 20.9 ± 7.4 (6–45) | <0.001 |
| Major comorbidities, n (%)            |                                  |                                     |                 |
| Obesity                               | 60 (20.3)                       | 7 (3.3)                             | <0.001          |
| Hypertension                          | 140 (47.5)                      | 26 (12.2)                           | <0.001          |
| Cardiac disease                       | 48 (16.3)                       | 4 (1.9)                             | <0.001          |
| Diabetes mellitus                     | 59 (20)                         | 6 (2.8)                             | <0.001          |
| Renal disease                         | 11 (3.7)                        | 1 (0.5)                             | 0.017           |
| Chronic or allergic rhinosinusitis/asthma | 27 (9.2)                   | 26 (12.2)                           | 0.267           |
| Pulmonary disease                     | 21 (7.1)                        | 2 (0.9)                             | 0.001           |
| Immunodeficiencya                     | 26 (8.8)                        | 5 (2.3)                             | 0.005           |
| Othersb                               | 59 (11.6)                       | 29 (5.7)                            | 0.011           |
| Comorbidities, n (%)                  |                                  |                                     |                 |
| None                                  | 63 (21.3)                       | 142 (66.7)                          | <0.001          |
| 1–2                                   | 176 (59.7)                      | 62 (29.1)                           |                 |
| >2                                    | 56 (19.0)                       | 9 (4.2)                             |                 |

*Statistical tests were used as appropriate (t test, Mann-Whitney test, chi-squared test).

a Immunodeficiency includes immunosuppressive therapy, recent or current hematological malignancy.

b Other comorbidities include history of cancer, hypothyroidism, chronic neurological conditions, liver and vascular diseases.

py = pack-year; SD = standard deviation.

arthromyalgia (OR 1.76; 95% CI, 1.21 to 2.57; p = 0.003) and nasal congestion (OR 1.62; 95% CI, 1.01 to 2.6; p = 0.047) with an increased risk. Similar results were found considering GD, demonstrating a negative association with age (OR 0.78; 95% CI, 0.68 to 0.89; p < 0.001) and male gender (OR 0.89; 95% CI, 0.33 to 0.72; p < 0.001), and a positive association with arthromyalgia (OR 1.85; 95% CI, 1.25 to 2.73; p = 0.002) (Supporting Table 3). No evidence of association between OD/GD and the radiologic score was observed (analysis limited to group A) (Supporting Information).

By network analysis, a strong positive connection was detected between OD and GD. Other solid connections were found between diarrhea and nausea, fever and arthromyalgia, and nasal congestion and pharyngodynia (Fig. 1, Supporting Fig. 1).

Discussion

The study describes a sample of more than 500 cases with confirmed SARS-CoV-2 infection, distinguishing between hospitalized patients and home-quarantined subjects. Overall, the prevalence of OD and GD was over 50%. In accordance with recent evidence,8 in our series both symptoms had a significantly higher prevalence in home-quarantined subjects (72% and 79%, respectively). These prevalence rates are in line with 2 recent cross-sectional studies, in which the prevalence of OD and GD was 68%
TABLE 2. Prevalence of symptoms in the series

| Symptom, n (%) | Hospitalized (Group A) (n = 295) | Home-quarantined (Group B) (n = 213) | p (Group A vs B) (chi-squared test) |
|---------------|----------------------------------|--------------------------------------|------------------------------------|
|               | Total (n, %)                     | First symptom (n, %)                 | Total (n, %)                       | First symptom (n, %) |
| Olfactory dysfunction | 130 (44.1) | 34 (11.5) | 153 (71.8) | 18 (8.5) | <0.001 |
| Gustatory dysfunction  | 153 (51.9) | 35 (11.9) | 168 (78.9) | 22 (10.2) | <0.001 |
| Fever | 274 (92.9) | 167 (56.6) | 181 (85.0) | 106 (49.8) | 0.006 |
| Dry cough | 190 (64.4) | 30 (10.2) | 138 (64.8) | 28 (13.1) | 0.995 |
| Dyspnea | 181 (61.4) | 19 (6.4) | 73 (34.3) | 5 (2.3) | <0.001 |
| Headache | 79 (26.8) | 10 (3.4) | 119 (55.9) | 19 (8.9) | <0.001 |
| Asthenia | 200 (67.8) | 36 (12.2) | 152 (71.4) | 28 (13.1) | 0.446 |
| Arthromyalgia | 114 (38.6) | 16 (5.4) | 142 (66.7) | 32 (15.0) | <0.001 |
| Diarrhea | 104 (35.3) | 9 (3.1) | 67 (31.5) | 3 (1.4) | 0.424 |
| Nausea | 75 (25.4) | 2 (0.7) | 39 (18.3) | 1 (0.5) | 0.074 |
| Nasal congestion | 45 (15.3) | 8 (2.7) | 69 (32.4) | 11 (5.2) | <0.001 |
| Pharyngodynia | 41 (13.9) | 13 (4.4) | 67 (31.5) | 16 (7.5) | <0.001 |
| Ocular discomfort | 38 (12.9) | 4 (1.4) | 47 (22.1) | 2 (0.9) | 0.009 |
| Syncope | 25 (8.5) | 3 (1.0) | 17 (8.0) | 1 (0.5) | 0.971 |

TABLE 3. Demographic and clinical characteristics according to olfactory and gustatory dysfunction*

| Variable | No dysfunction (n = 175) | Olfactory dysfunction (n = 283) | p* | Gustatory dysfunction (n = 321) | p* |
|----------|--------------------------|---------------------------------|-----|---------------------------------|-----|
| Age (years), mean ± SD (range) | 59.4 ± 15.2 (24–85) | 52 ± 14.4 (18–91) | <0.001 | 51.9 ± 14.5 (18-91) | <0.001 |
| Gender, n (%) | | | | | |
| Male | 121 (23.8) | 138 (27.2) | <0.001 | 155 (30.5) | <0.001 |
| Female | 54 (10.6) | 145 (28.5) | 166 (32.7) | | |
| History of smoking, n (%) | | | | | |
| No smoker | 112 (22.0) | 195 (38.4) | 0.019 | 223 (43.9) | 0.033 |
| Current smoker [average py] | 6 (1.2) [16.8 py] | 23 (4.5) [11.4 py] | 23 (4.5) [12.1 py] | | |
| Former smoker [average py] | 57 (11.2) [26.2 py] | 65 (12.8) [18.8 py] | 75 (14.8) [18.4 py] | | |
| Comorbidities, n (%) | | | | | |
| None | 52 (10.2) | 134 (26.4) | <0.001 | 148 (29.1) | 0.001 |
| 1–2 | 99 (19.5) | 113 (22.2) | 136 (26.8) | | |
| >2 | 24 (4.7) | 36 (7.1) | 37 (7.3) | | |
| Clinical management | | | | | |
| Hospitalized | 135 (26.6) | 130 (25.6) | <0.001 | 153(30.1) | <0.001 |
| Home-quarantined | 40 (7.9) | 153 (30.1) | 168 (33.1) | | |

*Statistical tests were used as appropriate (t test, chi-square test).

*aOlfactory dysfunction vs no dysfunction, and gustatory dysfunction vs no dysfunction, respectively.

py = pack-year; SD = standard deviation.
TABLE 4. Clinical characteristics of olfactory and gustatory dysfunction

| Variable                                      | Olfactory dysfunction (n = 283) | Gustatory dysfunction (n = 321) |
|-----------------------------------------------|---------------------------------|---------------------------------|
| **Degree of dysfunction**                     |                                 |                                 |
| Partial                                       | 90 (31.8)                       | 118 (36.8)                      |
| Total                                         | 182 (64.3)                      | 193 (60.1)                      |
| Unable to assess the degree of dysfunction    | 11 (3.9)                        | 10 (3.1)                        |
| **Onset (days), mean ± SD (range)**           |                                 |                                 |
| When 1st symptom: time to the 2nd symptom**  | 4.9 ± 4.3 (1–15)                | 4.9 ± 4.3 (1–15)                |
| When not 1st symptom: time after the 1st symptom** | 4.3 ± 2.6 (1–19) | 4.3 ± 2.7 (1–19) |
| Cases with complete resolution of the dysfunction | 3.3 ± 2.7 (0–10) | 3.3 ± 2.8 (0–15) |
| Cases with ongoing dysfunction                | 3.9 ± 3.2 (0–19)                | 3.8 ± 3.3 (0–19)                |
| **Duration of symptoms (days), mean ± SD (range)** |                                 |                                 |
| Cases with complete resolution of the dysfunction | 9.4 ± 5.1 (2–40) | 9.2 ± 5.4 (2–30) |
| Cases with ongoing dysfunction                | 12.7 ± 7.0 (1–40)               | 12.4 ± 6.8 (1–36)               |
| Recovery of symptoms, n (%)**                |                                 |                                 |
| Within 14 days                                | 118 (80.3)                      | 143 (80.3)                      |
| After 14 days                                 | 29 (19.7)                       | 35 (19.7)                       |

*a* Patients affected by olfactory and gustatory dysfunction reported these complaints as single first symptom of the infection with SARS-CoV-2 in 26 cases (5.1%), with a median anticipation of 3 days compared to other symptoms. Isolated dysosmia or isolated dysgeusia have not been observed as first symptoms of presentation.

**b** Patients affected by olfactory and gustatory dysfunction reported these complaints as delayed symptom of presentation of the infection with SARS-CoV-2 in 231 (81.6%) and 264 (82.2%) cases, respectively.

**c** Only patients who reported complete resolution of olfactory (147) and gustatory (178) dysfunction were considered.

SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2; SD = standard deviation.

FIGURE 1. Network analysis. Blue and red lines indicate positive and negative interconnections, respectively. Thicker lines indicate stronger interconnections.
reliability of OD and GD as biomarker of COVID-19 was higher in younger and mildly symptomatic subjects, which represents the fraction of population at a higher risk to be underdiagnosed and become active carriers of disease. In particular, this improvement in diagnosis could be particularly useful during the loosening of lockdown policy, when early detection of positive cases in workers is essential to prevent new outbreaks.

All cases with OD and GD reported an acute onset and a significant degree of dysfunction, without solid connection with other symptoms suggestive of upper airway infection (ie, pharyngodynia and nasal congestion). OD and GD were strongly correlated and clustered separately from other symptoms. These characteristics are indicative of acute sensorineurral OD and GD, which is particularly uncommon in the general population.

A growing body of evidence shows that neurotropism is a common feature of coronaviruses. Notably, SARS-CoV-1 has been found to enter the brain via the olfactory bulb and showed diffuse neuronal death in mice transgenic for human angiotensin-converting enzyme 2 (ACE2). This is an important clue suggesting a similar mechanism in SARS-CoV-2, although direct proof of neuroinvasion is still not available. Analogous damage to the olfactory epithelium and extension to the olfactory bulb has also been described in coronavirus-related sensorineural postviral olfactory dysfunction (PVOD).

However, differently from PVOD, in the present cohort patients were younger and experienced OD early in the course of the disease, often reporting a sudden onset and gradual, quick recovery. The identification of selective OD without GD in 10% of cases is a rarely reported occurrence in other diseases of the upper respiratory tract. This phenomenon may be explained by SARS-CoV-2 infection at the level of epithelial cells of the tongue, in which the expression of ACE2 is highly enriched, similarly to what happens in the olfactory epithelium.

Although various degrees of chronic OD and GD have a non-negligible prevalence in the general population, impairment often occurs gradually and the patient frequently does not report significant changes in perceptual acuity until the dysfunction becomes severe. Conversely, acute OD, often associated with hypogeusia or ageusia, is immediately recognized and can be associated with a variety of pathologic conditions, in particular acute upper respiratory infection, head trauma, toxins, and drugs. In these cases, acute damage to the olfactory epithelium, olfactory fila, and gustatory epithelium can usually be identified by adequate anamnesis (ie, recent head trauma, exposure to toxic inhalants, and new medications). Furthermore, upper respiratory infection leading to olfactory and gustatory alterations is invariably associated with rhinorrhea and nasal congestion. Conversely, OD and/or GD in SARS-CoV-2 infection are weakly connected with nasal congestion and therefore suggestive of predominant sensorineurral chemosensory dysfunction. Further evidence of its neurogenic nature is the high prevalence of GD without other complaints at the level of the oral cavity and, in some cases, in the absence of olfactory alterations. In this view, OD and GD of sudden onset should be safely considered as highly suggestive of COVID-19 in endemic areas and call for particular attention. Moreover, subjects with nonspecific symptoms should be carefully interrogated to identify relatives or close contacts presenting OD and/or GD to further upgrade their risk-profile according to this information. This is of paramount importance in a context of widespread domiciliary confinement imposed by government policies.

The following strengths and limitations should be highlighted. This report clearly shows the different distribution of OD and GD according to distinct populations. All patients were recruited from a specific geographic area and directly interviewed by the authors to minimize the risk of selection and reporting biases. On the other side, current policy on the execution of nasal/pharyngeal swab in our region may have introduced a selection bias, because positive asymptomatic or mildly symptomatic subjects could be largely underrepresented. The impossibility to interview patients in critical conditions prevented us from defining the prevalence of OD and GD in this group with unfavorable outcome. Recall bias should be also considered, although it is likely marginal in view of the short time span between the interview and symptoms onset, and the precision of patient responses. Possible misclassification due to information bias should also be taken into account even if minimized by the structure of the interviews and the characteristics of the onset of the symptoms. Finally, objective tests or comprehensive questionnaires focusing on evaluation of smell and taste were not employed in view of the critical healthcare situation.

**Conclusion**

A radical increase in the identification and isolation of currently undocumented infections is crucial to fully control SARS-CoV-2 diffusion. However, maintaining surveillance during a pandemic is particularly challenging due to shortages in testing materials and facilities. Highly suggestive symptoms such as acute olfactory and gustatory dysfunctions may facilitate the identification of infected individuals. However, the prevalence of these symptoms should be contextualized in view of their different prevalence in different patient populations.

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