INTRODUCTION

In the context of the current coronavirus disease 2019 (COVID-19) pandemic, which is caused by the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Wu et al., 2020), the early detection of new infections is immensely important to identify chains of infection. The rapid spread of this novel coronavirus can only be contained through early isolation of those who have been infected.

BACKGROUND

In the most severe cases, COVID-19 can lead to pneumonia with respiratory failure and the need for ventilation (Zhou et al., 2020). In the majority of cases however, the disease is mild and clinically oligo-to asymptomatic. In mild cases in particular, in addition to unspecific flu-like symptoms, a noticeable reduction in the sense of smell and taste has been reported, even in the early phase of infection. In contrast to the well-known postviral olfactory dysfunction (Hura et al., 2020), these impaired senses can be observed at the onset of the flu-like symptoms, not only after the past infection.

Furthermore, in contrast to allergic rhinitis or other non-specific viral infections of the upper respiratory tract, these sensory dysfunctions are not typically associated with other nasal symptoms such as subjective nasal obstruction and anterior or posterior rhinorrhoea (Lechien et al., 2020; Liang et al., 2020). Therefore, it can be concluded that the pathomechanism of SARS-CoV-2 of neuronal affection is different from that of other viruses.
It seems plausible that an acute restriction of the sense of smell or taste may not be perceived by all potential COVID-19 patients as a specific symptom of illness since the stimuli for this vary in everyday life (e.g. differently seasoned food), and we are used to a certain level of adaptation (e.g. to certain smells that are initially perceived in a specific location, but fade after a while). Certainly, hyposmia and ageusia are not externally perceptible stimuli. In contrast to a cough or fever with chills, people in a patient’s personal environment will not respond to their loss of smell or recommend a medical consultation. A medical assessment is therefore generally not initiated if this symptom is present.

Employees of retirement and nursing homes play a special role in the current pandemic (Ouslander & Grabowski, 2020); they take care of a special risk group among which COVID-19 infection carries a high risk of a complicated course with increased mortality. Nevertheless, the course of the disease can be mild, asymptomatic, and thus undetected in these employees. There is therefore an increased risk of asymptomatically infected employees endangering residents and patients.

In this study, employees of retirement and nursing homes were asked about sensory (olfactory and gustatory) deficits and nasal symptoms before being tested for SARS-CoV-2 to evaluate the value of these symptoms in determining the clinical pre-test probability.

2.1 | Design

As part of a secondary prophylaxis to contain the local spread of COVID-19 at the start of the pandemic, 1,734 employees of retirement and nursing homes in Germany which are affiliated to the University Medical Centre of Mannheim were tested for SARS-CoV-2 on a voluntary basis and without clinical suspicion.

Testing was performed independently of this study for early detection of asymptomatic infections. In addition, they were specifically asked in a structured interview about their symptoms, including the subjective impairment of their sense of taste and smell, in the sense of a prospective cross-sectional survey. If the sense of taste or smell was diminished, they were asked to describe the localization (left or right) and duration of the complaint, as well as any co-symptoms such as nasal breathing obstruction or rhinorrhea. Surveys took place during the first wave of COVID-19 infections, in March and April 2020. Swabbing and interviews took place in the morning, midday and early afternoon.

3 | METHOD

Testing, which comprised a pooled oropharyngeal and nasopharyngeal smear using a sterile cotton swab, was carried out by medical staff of the Clinic for Otorhinolaryngology, Head and Neck Surgery, University Medical Centre in Mannheim, Germany, and a laboratory test was subsequently performed using reverse transcription-polymerase chain reaction (RT-PCR; Altona Diagnostics, Hamburg, Germany; Cepheid Inc., Sunnyvale; Roche, Basel, Swiss; TIB Molbiol) to detect the presence of SARS-CoV-2.

3.1 | Analysis

A descriptive statistical analysis was then conducted. The study followed the STROBE guidelines of the EQUATOR network. To value the sample size, we used the following formula: \( n = \frac{X^2}{\alpha/2 \cdot p \cdot (1 - p) / \text{MOE}^2} \).

\( n: \) approximate sample size = 1724; \( N: \) population size = 80,000,000; \( Z_{\alpha/2}: \) critical value of the Normal distribution at \( \alpha/2 \) (with \( \alpha = 0.01 \)) = 2.575; \( p: \) sample proportion = 0.5 (unknown); MOE: margin of error = 0.031.

3.2 | Ethics

Research Ethics Committee approval was not required, as the testing for SARS-CoV-2 was voluntary and the questioning was carried out as part of secondary prophylaxis.

4 | RESULTS

Related to the German population (80,000,000), the sample size resulted in a margin of error of 3.1% and a confidence level of 99% and could thus be considered appropriate and of high quality (a sample size of 385 would have been necessary for a 95% confidence interval and margin of error of 5%).

Subjectively, all the employees were healthy with no general symptoms such as cough, fever or diarrhoea. In total, 1,433 female and 301 male employees were tested and interviewed. The median age, which ranged from 11 (for a school intern)–77 years, was 48 years.

SARS-CoV-2 could not be detected in any of the employees tested. Accordingly, it was not possible to divide the prevalence of odour or taste disorders into COVID-19-positive and COVID-19-negative subjects (Table 1).

Fifteen employees reported subjective hyposmia. Three employees (two females and one male) reported unilateral hyposmia.
(two on the left side, one on the right side) lasting 2–14 days (median four days). All three employees indicated an accompanying nasal breathing obstruction. Twelve employees reported bilateral hyposmia (eight females and four males), five of them for a period exceeding three months although this could not be more precisely quantified. None of these employees reported accompanying nasal symptoms such as rhinorrhea or nasal difficulty breathing; however, one employee identified flu some months earlier as a triggering factor. Seven employees reported bilateral hyposmia, which had continued for 2–14 days (median 14 days). These seven employees also reported a subjective nasal obstruction during the same period. Complete subjective anosmia was denied by all the employees.

Five employees (three females and two males) reported subjective hypogeusia, one of them for a period exceeding three months, although this could not be quantified more precisely. This employee also reported subjective bilateral hyposmia, which had coexisted with the hypogeusia. The remaining four employees had hypogeusia for a period of 1–60 days, with a median duration of nine days. Among them, two also reported bilateral hyposmia with nasal breathing difficulties during the same period, one noted unilateral hyposmia with nasal breathing difficulties during the same period, and one had negative nasal symptoms concomitantly.

Complete subjective ageusia with duration of 14 days and an accompanying bilateral hyposmia and nasal obstruction was reported by one employee.

## 5 DISCUSSION

A pooled oropharyngeal and nasopharyngeal smear with subsequent RT-PCR is the current gold standard for the detection of SARS-CoV-2 in subjectively healthy populations. In the event of clinical suspicion of COVID-19 with pulmonary symptoms, it is preferred that sputum samples be examined (Pan et al., 2020). If respiratory restriction begins, low-dose-computed tomography of the thorax can be added to the screening process to detect typical radiological characteristics. However, this has no significance in the screening or diagnosis of the asymptomatic population. Another current examination option is the use of a gargle lavage (Mittal et al., 2020); this has not yet become widespread in Europe.

The RT-PCR has a high specificity, but its sensitivity depends on the correct and representative performance of the smear. The predictive prognostic values depend on the prevalence of the disease to be examined and are higher in the acute phase of the pandemic. It therefore cannot be ruled out with certainty that false-negative test results may have occurred in our study. However, none of the employees tested had classic symptoms in the subsequent period; these would have led to a new test being administered to detect any different results. During the smears, particular care was taken to wipe the nasopharynx and not just the main nasal cavity. Due to anatomical conditions (e.g. deviated septum or nasal turbinate hyperplasia) or due to discomfort or retching of the subjects, the swab may not be taken correctly from the depth of the nasopharynx. Therefore, the professionals were trained to perform the swab along the floor of the nose and up to the contact on the dorsal surface of the nasopharynx. After encountering the posterior surface, the cotton swab was rotated three times under contact. It has been proven that the highest viral load outside the sputum is found in the nasopharynx. RT-PCR is the current gold standard for the detection of SARS-CoV-2 in subjectively healthy populations. In the event of clinical suspicion of COVID-19 with pulmonary symptoms, it is preferred that sputum samples be examined (Pan et al., 2020). If respiratory restriction begins, low-dose-computed tomography of the thorax can be added to the screening process to detect typical radiological characteristics. However, this has no significance in the screening or diagnosis of the asymptomatic population. Another current examination option is the use of a gargle lavage (Mittal et al., 2020); this has not yet become widespread in Europe.

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To increase their positive predictive value, all the aforementioned tests are dependent on the preselection of patients, which needs to take place in accordance with the pre-test probability. In addition to epidemiological selection (i.e. after contact with a confirmed infected patient or after returning from a risk area), a clinical/symptomatic selection is also useful for assessing which patients are genuinely suspected of having a SARS-CoV-2 infection and which patients are more likely to have a non-specific viral infection of the upper respiratory tract. This is beneficial for two reasons: first, it minimizes the (rare) possibility of false-positive results, and second, the high burden of disease that the COVID-19 pandemic currently represents in the global health system creates an ethical and moral obligation to use the existing limited diagnostic resources as efficiently as possible.

### TABLE 1 Subjective impairment of smell and/or taste and nasal co-symptoms

|                          | n     | % in cohort | % in subgroup |
|--------------------------|-------|------------|--------------|
| Number of employees      | 1734  | 100        | -            |
| Male                     | 301   | 17.36      | -            |
| Female                   | 1,433 | 82.64      | -            |
| Impairment of smell and/or taste | 20    | 1.15       | -            |
| Single-sided hyposmia    | 3     | 0.17       | 100          |
| Combined with nasal obstruction | 3     | 0.17       | 100          |
| Left-sided hyposmia      | 2     | 0.12       | 66.67        |
| Right-sided hyposmia     | 1     | 0.06       | 33.33        |
| Both-sided hyposmia      | 12    | 0.69       | 100          |
| More than 14 days        | 5     | 0.29       | 41.67        |
| Combined with nasal obstruction | 0     | 0          | 0            |
| Less than 14 days        | 7     | 0.40       | 58.33        |
| Combined with nasal obstruction | 7     | 0.40       | 58.33        |
| Anosmia                  | 0     | 0          | -            |
| Hypogeusia               | 5     | 0.29       | 100          |
| More than 14 days        | 1     | 0.06       | 20           |
| Combined with nasal obstruction | 1     | 0.06       | 20           |
| Less than 14 days        | 4     | 0.23       | 80           |
| Combined with nasal obstruction | 1     | 0.06       | 20           |
| Ageusia                  | 1     | 0.06       | 100          |
| Combined with nasal obstruction | 1     | 0.06       | 100          |
In other studies, a different prevalence of hyposmia, anosmia and hypogeusia has been described (Dong et al., 2017; Fukunaga et al., 2005; Landis et al., 2004). This can most likely be attributed to the fact that targeted clinical tests were carried out in these studies while an interview was conducted in our study. The subjective perception of a sensory deficit in everyday life that cannot be objectively verified in clinical testing appears plausible with changing everyday stimuli, as does the presence of a slight sensory deficit that can be detected in clinical tests without a subjective restriction being experienced in everyday life. At the same time, the subjective restriction of olfactory and gustatory perception may also be based on causes that are seasonal, such as allergic rhinitis (hay fever). The simultaneous consideration of the time of the questioning is therefore just as important as the question about nasal co-symptoms, since many patients already know if and when they have hay fever symptoms.

If hyposmia and hypogeusia are mentioned in the context of the current COVID-19 pandemic, this is mostly with reference to the subjective impressions of those affected since experimental tests of these sensory functions only take place in the context of studies, not in the routine clinical care of COVID-19 patients. Instead, the importance of inquiring about these symptoms lies in the preselection of patients for targeted screening who do not have any serious symptoms requiring an inpatient hospital stay; however, they must be identified early on to be able to interrupt chains of infection, according to the test-trace-isolate strategy (Contreras et al., 2021).

As previously mentioned, an acute restriction in the sense of smell or taste usually does not present a serious handicap in everyday life. It is not typically perceived by those affected or potentially infected or bystanders as a disease symptom such as a fever or cough. Inquiry about these sensory deficits must therefore be specific and explicit as it cannot be expected that patients will describe these symptoms on their own. The use of a standardized questionnaire is recommended here, especially if a large number of subjects need to be examined.

Our data indicate that a subjectively acutely diminished perception of smell and taste rarely occurs in a (COVID-19 negative) population with a subjective feeling of health. In the few affirmed cases, these symptoms could be assigned to a different genesis, particularly if there were accompanying symptoms. These patients were encouraged to seek a further diagnosis by an ear-nose-throat specialist and to initiate a specific therapy if necessary (Scangas & Bleier, 2017).

Acute hyposmia/anosmia without further nasal co-symptoms is therefore suitable as a question parameter to increase the pre-test probability of SARS-CoV-2 detection and to identify possible infection through the identification of typical hyposmia/anosmia as a COVID-19 symptom. However, under no circumstances should SARS-CoV-2 screening not be carried out simply because odour and/or taste impairments are untypical. Rather, further examination must be made based on other parameters (such as contact persons, stay in a risk area or the current incidence values) in such cases (Jehi et al., 2020).

Nursing homes are critical places in the context of the COVID-19 pandemic as elderly people, often with various internal comorbidities, live in these homes, and they rely on close contact with

**FIGURE 1** Flowchart for the evaluation of smell and taste restrictions in the context of the COVID-19 pandemic
care staff. The virus can therefore spread rapidly in these facilities despite the best possible precautions being taken (American Geriatrics, 2020).

The professional services of nurses are urgently needed, especially in the present pandemic situation. Hence, it is logical that employees with pronounced and typical COVID-19 symptoms (e.g., an overt feeling of illness with fever and cough) should go into self-isolation to avoid further infection and to be able to recover. However, if mild cold-like symptoms occur, these employees are faced with a difficult decision: to stay home and thus cause additional stress for their colleagues or to go to work and risk contributing to the spread of the disease as a potential COVID-19 carrier. The identification of typical symptoms of mild COVID-19 and their differentiation from banal, unspecified pathogens is therefore critical in fighting the pandemic.

Ideally, all employees in retirement and nursing homes should be tested regularly for SARS-CoV-2 to detect asymptomatic or mild infections at an early stage, to isolate those affected and to avoid further transmission. However, in addition to the personnel and financial outlays, the additional workload on laboratories is a critical factor as they can reach their capacity limits when there are high numbers of infection. Routine symptom-independent area testing therefore represents an enormous challenge in industrialized countries; in developing countries such as those in Africa with significantly greater limitations on infrastructural and diagnostic resources, it would be even less realistic (Dzinamarira et al., 2020; El-Sadr & Justman, 2020).

It is much more practicable to sensitize employees to the typical presentation of symptoms related to the sense of smell and taste in the context of COVID-19. Increased awareness by employees of their own sensory perceptions could lead to the earlier recognition of symptoms, which in turn would result in prompt and more specific testing (Figure 1). This would enable the timely identification of only mildly symptomatic employees and allow for the consistent application of quarantining and maximum diagnostic resource efficiency.

### 5.1 | Limitations

Since none of the employees tested positive, no distinction and comparison could be made between SARS-CoV-2-positive and SARS-CoV-2-negative individuals in our study. Accordingly, the restriction of smell and taste perception cannot be assigned any sensitivity or specificity. Due to the high number of people examined and questioned, however, a good estimate of the prevalence of subjective smell and taste restrictions in the COVID-19-negative population can be made.

### 6 | CONCLUSION

Querying subjective hyposmia/anosmia or hypogeusia/ageusia thus appears to be a useful anamnestic instrument for the clinical assessment of the probability of SARS-CoV-2 infection. We therefore advocate that medical professionals query the existence of further nasal symptoms such as nasal obstruction or rhinorrhea to differentiate these from hyposmia or ageusia of other origins.

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### CONFLICT OF INTEREST

There is no conflict of interest to be declared.

### AUTHOR CONTRIBUTION

FJ: Organizing the data collection, performing the data analysis as well as the literature review and writing the manuscript. LH, AL, SL and LZ: Reviewing and revision of the manuscript and made significant contributions to its content and design. NR and AS: Formulating the initial idea and designing of the study. AS: Supervision of the study.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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