# Validity and reliability of the Empty Nose Syndrome Index (ENSI)

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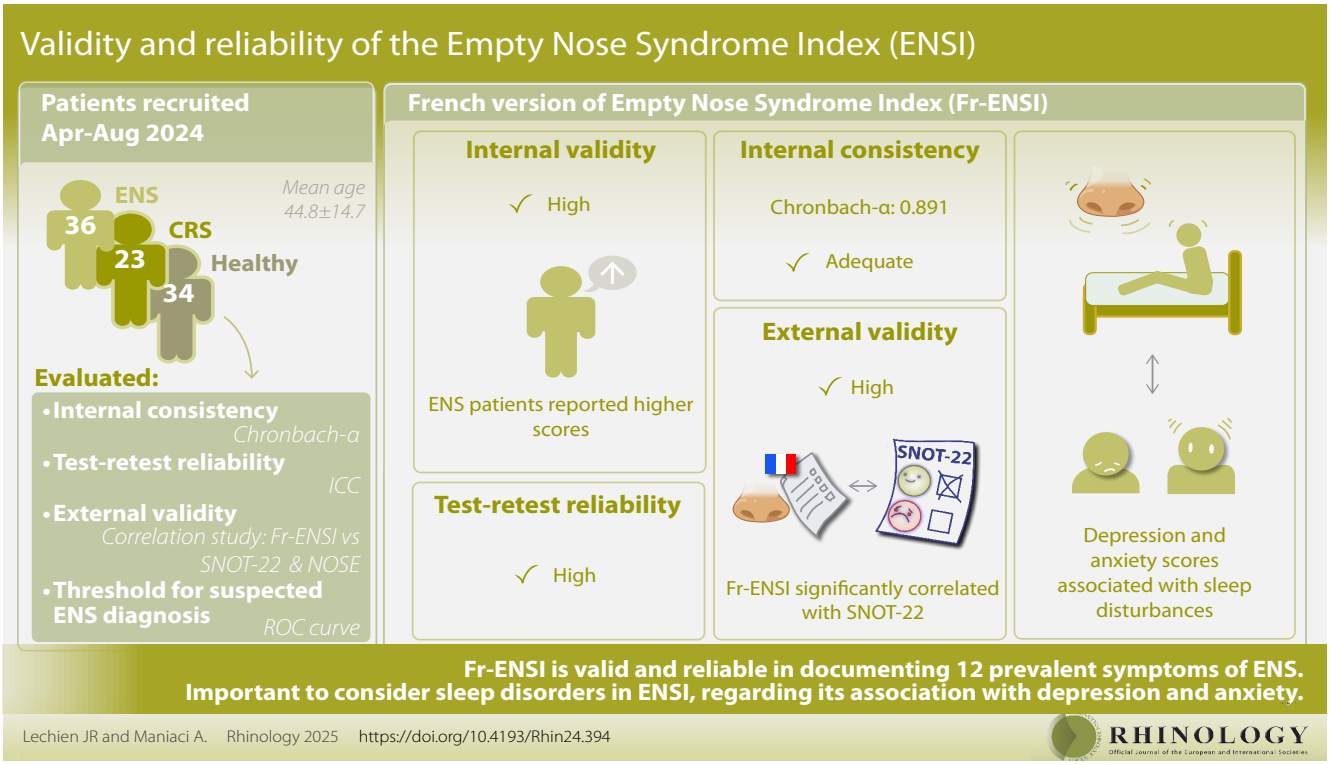


## Abstract

**Objective**: To validate the French version of the Empty Nose Syndrome Index (Fr-ENSI).

**Methods**: Patients with ENS, chronic rhinitis/rhinosinusitis, and asymptomatic individuals were recruited from April to August 2024. The internal consistency was evaluated with Cronbach-α. The test-retest reliability was assessed with the intraclass correlation coefficient (ICC). The external validity was assessed with a correlation study between the Fr-ENSI and the Sinonasal Outcome Tool-22 (Fr-SNOT-22), and Nasal Obstruction Symptom Evaluation (Fr-NOSE). The Fr-ENSI threshold for suspecting the ENS diagnosis was determined with the receiver operating characteristic (ROC) curve.

**Results**: Ninety-three subjects completed the evaluations. There were 36 ENS patients, 23 patients with chronic rhinosinusitis/rhinitis, and 34 healthy individuals. The mean age was 44.8±14.7 years. Patients with ENS reported significantly higher Fr-ENSI scores compared to others, indicating high internal validity. The Cronbach-α of Fr-ENSI was 0.891, which indicates an adequate internal consistency. The test-retest reliability was high. Depression and anxiety scores were associated with sleep disturbances. The Fr-ENSI was significantly correlated with Fr-SNOT-22, which supports a high external validity. The threshold of Fr-ENSI associated with the highest sensitivity and specificity was >23/60.

**Conclusions**: The Fr-ENSI is a valid and reliable questionnaire for documenting 12 prevalent symptoms of ENS. The consideration of sleep disorders in ENSI is important regarding its association with depression and anxiety.

**Key words**: empty nose syndrome, rhinology, otolaryngology, otorhinolaryngology, tool

## Introduction

Empty nose syndrome (ENS) is a disabling condition associated with a paradoxical perception of nasal obstruction despite the widened nasal airway [1]. The prevalence and incidence of ENS remain unknown despite an increasing number of publications in the past decade [2]. The origin of ENS is iatrogenic in most cases with symptoms developing within the months following the nasal surgery [3]. Patients with ENS commonly report paradoxical nasal obstruction, dyspnea or suffocation, burning, crusting, and dryness, which ultimately lead to significant impairments in quality of life (QoL) [2]. Currently, the symptoms' severity can be evaluated with the empty nose syndrome 6-item questionnaire (ENS6Q), which is a validated and standardized patient-reported outcome questionnaire including 6 primary ENS symptoms (dryness, nasal obstruction, suffocation, nose feels too open, crusting, and burning) [4]. However, in our clinical practice, we observed that some ENS patients suffer from symptoms that are not included in the ENS6Q, e.g., facial, ear, or dental pain, blocked nose, breathing difficulties for sleep or sport activity, cold/fresh nasal feeling, or hyperventilation, which was similarly observed in some studies of the literature [5,6]. Moreover, to date, there is no validated ENS-patient-reported outcome question-

Figure 1. The French and the English versions of the Empty Nose Syndrome Index. The item scores of Fr-ENSI were considered the most prevalent symptoms by screened ENS patients. The items range from 0 to 5. The total ENSI ranges from 0 to 60.

| | Symptom severity | | | | | |
|---|---|---|---|---|---|---|
| **Could you complete the following questionnaire:** | **None** | **Very mild** | **Mild** | **Moderate** | **Severe** | **Very severe** |
| 1. I feel nasal dryness | 0 | 1 | 2 | 3 | 4 | 5 |
| 2. I have nasal crusting with or without bleeding | 0 | 1 | 2 | 3 | 4 | 5 |
| 3. I feel nasal burning all the time or during the air flow | 0 | 1 | 2 | 3 | 4 | 5 |
| 4. I feel nasal cold/fresh all the time or during the air flow | 0 | 1 | 2 | 3 | 4 | 5 |
| 5. I feel nasal blockage, congestion or stuffiness | 0 | 1 | 2 | 3 | 4 | 5 |
| 6. The nasal air flow appears reduced | 0 | 1 | 2 | 3 | 4 | 5 |
| 7. My nose appears too open | 0 | 1 | 2 | 3 | 4 | 5 |
| 8. I have difficulty to practice my sport(s) given my nose disorders | 0 | 1 | 2 | 3 | 4 | 5 |
| 9. I have suffocation and/or hyperventilation | 0 | 1 | 2 | 3 | 4 | 5 |
| 10. I have face, eye, ear, or dental pain | 0 | 1 | 2 | 3 | 4 | 5 |
| 11. My ears are blocked | 0 | 1 | 2 | 3 | 4 | 5 |
| 12. I have difficulties for sleeping given my nose disorders | 0 | 1 | 2 | 3 | 4 | 5 |
| Total score | ..... | | | | | |
| | **Severite des symptomes** | | | | | |
| **Pouvez vous evaluer la severite des symptomes suivants:** | **Aucun probleme** | **Tres leger** | **Leger** | **Modere** | **Severe** | **Tres severe** |
| 1. J'ai une sécheresse nasale | 0 | 1 | 2 | 3 | 4 | 5 |
| 2. J'ai des croutes dans le nez avec ou sans saignements | 0 | 1 | 2 | 3 | 4 | 5 |
| 3. J'ai une sensation de brûlure nasale en permanence ou lorsque l'air passe | 0 | 1 | 2 | 3 | 4 | 5 |
| 4. J'ai une sensation de froid/fraicheur dans le nez en permanence ou lorsque l'air passe | 0 | 1 | 2 | 3 | 4 | 5 |
| 5. Mon nez est bouché, plein, ou encombré | 0 | 1 | 2 | 3 | 4 | 5 |
| 6. J'ai une sensation de diminution du flux d'air dans le nez | 0 | 1 | 2 | 3 | 4 | 5 |
| 7. J'ai une sensation de nez "trop ouvert" | 0 | 1 | 2 | 3 | 4 | 5 |
| 8. Mon nez ne me permet pas de respirer suffisamment pendant l'exercice physique | 0 | 1 | 2 | 3 | 4 | 5 |
| 9. J'ai des episodes de suffocation ou d'hyperventilation | 0 | 1 | 2 | 3 | 4 | 5 |
| 10. J'ai des douleurs dans la face, les yeux, les oreilles ou les dents | 0 | 1 | 2 | 3 | 4 | 5 |
| 11. J'ai une sensation d'oreille(s) bouchée(s) | 0 | 1 | 2 | 3 | 4 | 5 |
| 12. J'ai des difficultes à dormir suite à ces problèmes de respiration | 0 | 1 | 2 | 3 | 4 | 5 |
| Score total | ..... | | | | | |

naire for French-speaking countries, which includes more than 400 million inhabitants.

The objective of the present study was to propose and validate the French version of the Empty Nose Syndrome Index (Fr-ENSI), a patient-reported outcomes questionnaire considering the 12 most prevalent symptoms in ENS patients.

## Materials and methods

### Ethical statement

The study protocol was approved by the Institutional Ethics Committee (n°22-02-17). Informed consent was obtained for patients and healthy individuals. This study adhered to the STROBE guidelines for observational studies to ensure transparency and replicability of our findings [7].

### Empty Nose Syndrome Index development

The Fr-ENSI was developed by two board-certified otolaryngologists (J.R.L., A.M.), and a linguist with the collaboration of ENS patients from a French ENS patient organization (Victimes du SNV). The first step consisted of a survey to investigate the prevalence of symptoms in ENS patients (Appendix 1). The symptoms were extracted from the French versions of the ENS6Q, the sinonasal outcome tool-22 (Fr-SNOT-22) [8], and the nasal obstruction symptom evaluation (Fr-NOSE) [9]. The prevalence of symptoms reported by patients in their list of symptoms was analyzed by practitioners to develop the Fr-ENSI. Thus, the second step was the development of Fr-ENSI, which includes the most prevalent symptoms associated with ENS. The following symptoms were then considered: dryness, nasal obstruction, facial pain, blocked nose, blocked ears, reduced nasal airflow, nose too open, crusting/bleeding, burning, cold/fresh nasal feeling, suffocation/hyperventilation, and breathing difficulties for sleep or sport activity (Figure 1). The Fr-ENSI symptoms were evaluated with a 6-point Likert scale ranging from "no problem (0)" to "very severe problem (5)". The third step was the administration of the Fr-ENSI to 5 patients to collect their inputs about the readability and understanding of outcomes. The total Fr-ENSI score ranges from 0 to 60.

### Patients and setting

The study included 3 populations of subjects: patients with a diagnosis of ENS, patients with chronic rhinitis or chronic rhinosinusitis, and healthy individuals. Subjects were recruited from April 2024 to August 2024. The recruitment of ENS patients was facilitated by access to the database of patients involved in the French patient organization (Victimes du SNV). To be included, the ENS diagnosis was carried out by a practitioner, and it was based on a history of nasal surgery, bilateral inferior or middle turbinate reduction, and, potentially, a cotton test [3]. The cotton test consists of the placement of dry cotton in the nasal region without inferior turbinate tissue to simulate the bulk and tubular contour of a native turbinate in the lateral nasal wall. The cotton test was considered as positive in patients with a diminution of nasal symptoms a few seconds/minutes after the cotton placement [3]. The patients with rhinitis or chronic rhinosinusitis with or without nasal polyps were recruited from the consultation of the Dour Medical Center (Dour) and CHU Saint-Pierre (Brussels, Belgium). The diagnoses of chronic rhinitis and rhinosinusitis were based on clinical guidelines (Rhinitis-2020 and EPOS/EUFOREA) [10,11]. The control group consisted of individuals without ear, nose, and throat symptoms and findings at the examination, including rhinitis and rhinosinusitis. Individuals with chronic alcohol or tobacco consumption, nasal malignancies, history of nasal/nasopharyngeal chemo/radiation, or an inability to understand the aim of the study were excluded. Healthy individuals were recruited from the University of Mons population.

### Questionnaires and evaluations

Subjects completed the Fr-ENSI, Fr-SNOT-22 [8], and Fr-NOSE [9]. Regarding the psychological burden of ENS, the authors investigated the psychological health of patients. The anxiety of patients was evaluated with the General Anxiety Disorder-7 (GAD-7) [12], which is a validated and standardized patient-reported outcome questionnaire assessing the severity of anxiety of patients from 0 to 21. Based on a large population database, minimal, mild, moderate, and severe anxiety consisted of 0-4, 5-9, 10-14, and 15-21 scores, respectively [10]. The depression symptoms were documented with the Patient Health Questionnaire-9 (PHQ-9) [13]. PHQ-9 is adapted from the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) and consists of a brief validated and standardized tool used to diagnose and measure the severity of depression. Minimal, mild, moderate, moderately severe, and severe depression can be defined for 1-4, 5-9, 10-14, 15-19, and 20-27 scores, respectively [13].

### Statistical analyses

The statistical analyses were performed with Statistical Package for the Social Sciences for Windows (SPSS version 30.0; IBM Corp, Armonk, NY, USA). The Fr-ENSI was completed twice over 14 days to evaluate the test-retest reliability (intraclass correlation coefficient (ICC)). The internal consistency was evaluated with Cronbach-$\alpha$. External validity was evaluated by correlation analysis between Fr-ENSI, Fr-SNOT-22, and Fr-NOSE (Spearman correlation coefficient). The internal validity was evaluated with a comparison of the Fr-ENSI scores between ENS, chronic rhinitis/rhinosinusitis patients, and healthy subjects (Kruskal-Wallis and Mann-Whitney U test). A study of correlation was conducted between Fr-ENSI, Fr-SNOT-22, Fr-NOSE, and the psychological questionnaires (GAD-7 and PHQ-9). The recruitment of two control groups (asymptomatic individuals and rhinitis/rhinosinusitis subjects) was supported to assess the threshold of ENSI with the receiver operating characteristic (ROC) curve and the

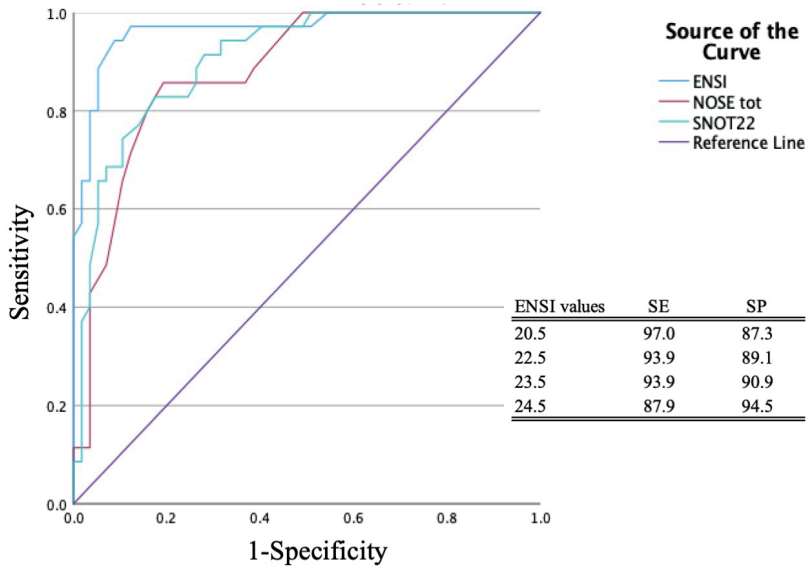


Figure 2. Receiver operating characteristic curve. The Fr-ENSI curve was significantly higher than the Fr-SNOT-22 and Fr-NOSE curves. The threshold of Fr-ENSI associated with the highest sensitivity (93.9%) and specificity (90.9%) was >23/60.

area-under-the-curve (AUC). The area-under-the-curve (AUC) statistic and corresponding confidence intervals were reported to compare ROC curves of Fr-ENSI, Fr-ENS6Q, and Fr-SNOT-22. The best cut-off score was reported that maximized the sensitivity and minimized the false-positive rate. Note that because the prevalence of ENS remains unknown, authors could not carry out a formal power analysis to calculate the sample size. The outcome association was considered as low, moderate, and strong for k<0.40, 0.40-0.60, and k>0.60, respectively. A level of significance of p<0.05 was used.

## Results

Ninety-three adult subjects completed the evaluations. There were 36 ENS patients, 23 patients with chronic rhinosinusitis/rhinitis, and 34 healthy individuals (Table 1). The mean age was 44.8 ± 14.7 years. The proportion of males was significantly higher in the ENS group compared to the two control groups (p=0.04; Table 1). The diagnosis approaches and the etiologies of ENS are reported in Table 2. The development of ENS has been observed in the following conditions: septoplasty and bilateral inferior turbinoplasty (n=16, 44.4%); septoplasty, bilateral turbinoplasty, and functional endoscopic sinus surgery (n=8, 22.2%), bilateral inferior turbinoplasty (n=8, 22.2%), septorhinoplasty and bilateral inferior turbinoplasty (n=3, 8.3%), and frontal osteoma and bilateral middle turbinoplasty (n=1, 2.8%). In most cases, the diagnosis was based on nasofibroscopy and CT-scan (50.0%), and nasofibroscopy and cotton test (44.4%). Among patients, 8/36 (22.2%) patients had made the diagnosis themselves before consulting an otolaryngologist who confirmed objectively the diagnosis.

The primary comorbidities of subjects included allergy (N=9; 25%), irritable bowel syndrome (N=9; 25%), asthma (N=9; 25%), and suspected laryngopharyngeal reflux disease (N=8; 22%) (Appendix 2). Ten (43%) patients with chronic rhinosinusitis/rhinitis had a history of allergy, while asthma was found in 5 (22%) patients.

The primary symptom scores of patients and controls are reported in Table 1. Patients with ENS reported significantly higher Fr-ENSI, Fr-SNOT-22, and Fr-NOSE compared to patients with chronic rhinosinusitis/rhinitis, and healthy controls (Table 1), indicating a high internal validity.

The Cronbach-$\alpha$ of Fr-ENSI was 0.891 (95%CI: 0.855, 0.922), which indicates an adequate internal consistency. The test-retest reliability was high (ICC=0.895; 95%CI: 0.763-0.971).

The depression and anxiety outcomes are reported in Table 3. Depression and anxiety were found in 97.2% and 88.9% of ENS patients, respectively. Thirty-one (86.1%) and twenty-seven (75.0%) ENS patients met the criteria for requiring assessment for significant depression and anxiety according to the standard of care (Table 3) [12,13]. The following Fr-ENSI symptoms were particularly associated with depression: sleep disorders, suffocation/hyperventilation, and difficulties in practicing sports (Table 4). The study of association reported that the Fr-ENSI was significantly correlated with Fr-SNOT-22 (rs=0.697; 95%CI: 0.466-0.839), and Fr-NOSE (rs=0.509; 95%CI: 0.202-0.725; Table 4), which supports a high external validity. The area under the curve (AUC) for Fr-ENSI (0.966) was higher than the AUC of Fr-SNOT-22 (0.911), and Fr-NOSE (0.883; Table 5). The threshold of Fr-ENSI associated with the highest sensitivity (93.9%) and specificity (90.9%) was >23/60 (Figure 2).

Table 1. Features and clinical scores of patients and controls.

| Features | ENS N=36 | CRS/CR N=23 | Controls N=34 | KW (p-value) |
|---|---|---|---|---|
| **Age (mean, SD)** | 42.3 ± 13.1 | 46.1 ± 12.4 | 46.6 ± 17.5 | NS |
| **Gender (N, %)** | | | | |
| Females | 18 (50) | 17 (74) | 26 (76) | 0.04* |
| Males | 18 (50) | 6 (26) | 8 (24) | |
| **Total SNOT-22** | 72.3 ± 17.9 | 47.7 ± 20.6 | 25.3 ± 16.7 | 0.001 |
| **Total NOSE** | 14.0 ± 4.6 | 9.0 ± 5.2 | 2.8 ± 3.6 | 0.001 |
| **ENSI** | | | | |
| (1) Dryness | 4.4 ± 0.7 | 1.5 ± 1.5 | 0.9 ± 1.1 | 0.001 |
| (2) Nasal crusting/bleeding | 3.3 ± 1.5 | 1.3 ± 1.4 | 1.1 ± 1.3 | 0.001 |
| (3) Nasal burning | 3.0 ± 1.8 | 0.3 ± 0.8 | 0.3 ± 0.9 | 0.001 |
| (4) Nasal cold/fresh | 2.8 ± 2.0 | 0.2 ± 0.5 | 0.1 ± 0.4 | 0.001 |
| (5) Nasal blockage/congestion/stuffiness | 2.8 ± 1.7 | 2.6 ± 1.2 | 0.8 ± 1.1 | 0.001 |
| (6) Reduced nasal air flow | 3.8 ± 1.3 | 2.0 ± 1.4 | 0.9 ± 1.4 | 0.001 |
| (7) Too open nose | 3.4 ± 1.8 | 0.5 ± 1.1 | 0.1 ± 0.5 | 0.001 |
| (8) Difficulty to practice sport(s) | 3.6 ± 1.5 | 1.0 ± 1.3 | 0.5 ± 1.1 | 0.001 |
| (9) Suffocation/hyperventilation | 3.1 ± 1.7 | 0.7 ± 1.1 | 0.2 ± 0.8 | 0.001 |
| (10) Face, eye, ear, or dental pain | 3.1 ± 1.7 | 1.7 ± 1.5 | 0.5 ± 1.1 | 0.001 |
| (11) Blocked ears | 2.4 ± 1.6 | 1.9 ± 1.6 | 0.6 ± 0.8 | 0.001 |
| (12) Sleep Disorders | 4.0 ± 1.2 | 1.6 ± 1.6 | 0.4 ± 1.0 | 0.001 |
| **Total ENSI** | 39.4 ± 11.2 | 15.1 ± 9.6 | 6.5 ± 7.0 | 0.001 |

*Chi-Square test; Abbreviations: CRS/CR=chronic rhinosinusitis/chronic rhinitis; ENS=empty nose syndrome; ENS6Q=empty nose syndrome 6-item questionnaire; ENSI=empty nose syndrome index; KW=Kruskal-Wallis test; N=number; NOSE=nasal obstruction symptom evaluation; SD=standard deviation; SNOT-22=sinonasal outcome tool-22.

## Discussion

The present investigation supports that the Fr-ENSI is a valid and reliable patient-reported outcome questionnaire documenting the ENS symptoms and measuring their severity.

The internal consistency of Fr-ENSI, which can be defined as the extent to which items within each domain are interrelated (14,15), was high ($\alpha$=0.89). The internal consistency of Fr-ENSI corroborates those of other clinical instruments, including the Fr-SNOT-22 (0.93) [8], Fr-NOSE (0.86) [9], ENS6Q (0.93) [4], and the rhinosinusitis quality of life survey (0.57-0.83) [9]. The external validity of a patient-reported outcome questionnaire evaluates the degree to which the sign score correlates with other instruments measuring the same construct or with related clinical indicators. (14,15) Accordingly, Fr-ENSI reported a high correlation with Fr-SNOT-22 (rs=0.697), and a moderate correlation with Fr-NOSE (rs=0.509), respectively. The external validity of the ENS6Q was not assessed by Velasquez et al. [4], which limits our comparison with the ENS literature. However, considering other nasal clinical instruments, the external validities of Fr-NOSE (rs=0.40) [9] and Fr-SNOT-22 (rs=0.64) [8] were lower than the value found for the Fr-ENSI.

The test-retest reliability evaluates the stability of scores over time when no change is expected [14,15]. The data of test-retest reliability of Fr-ENSI (ICC=0.895) are consistent with the cutoffs considering a patient-reported outcome as reliable [16], and the test-retest reliability of ENS6Q (ICC=0.96), and Fr-SNOT-22 (r=0.78). The test-retest reliability of Fr-NOSE was adequate but the comparison with our data remains difficult given substantial differences in the statistical approaches of test-retest reliability (ICC versus Wilcoxon test) [9].

Considering the overlap of some ENS symptoms with those of chronic rhinitis or rhinosinusitis, it was important to evaluate the internal validity, which can be defined as the extent to which the instrument can discriminate between groups that are known to differ on the variables being measured. The findings of the present study support that Fr-ENSI is adequate for discriminating ENS patients from those with chronic rhinitis or rhinosinusitis. Precisely, ENS patients reported significantly higher item and total Fr-ENSI scores compared to both control populations. In the ENS6Q validation study, Velazquez et al. [4] similarly reported

Table 2. Diagnosis and etiologies of Empty Nose Syndrome.

| Outcomes | ENS patients (N=36) |
|---|---|
| **Diagnosis (N, %)** | |
| Nasofibroscopy | 2 (5.6) |
| Nasofibroscopy & CT scan | 18 (50.0) |
| Nasofibroscopy & Cotton test | 16 (44.4) |
| **Etiologies (N, %)** | |
| Septoplasty & inferior turbinoplasty | 16 (44.4) |
| Septoplasty, inferior turbinoplasty, & FESS | 8 (22.2) |
| Turbinoplasty without septoplasty | 8 (22.2) |
| Septorhinoplasty & inferior turbinoplasty | 3 (8.3) |
| Frontal osteoma & middle turbinectomy | 1 (2.8) |

Abbreviations: ENS=empty nose syndrome; FESS=functional endoscopic sinus surgery; N=number.

Table 3. Depression and anxiety in Empty Nose Syndrome patients.

| Depression and anxiety outcomes (N, %) | ENS (N=36) |
|---|---|
| **Depression (PHQ-9) scores** | |
| Minimal or none (0-4) | 1 (2.8) |
| Mild (5-9) | 3 (8.3) |
| Moderate (10-14) | 1 (2.8) |
| Moderately severe (15-19) | 16 (44.4) |
| Severe (20-27) | 15 (41.7) |
| Patients requiring assessment (>14) | 31 (86.1) |
| **Anxiety (GAD-7) scores** | |
| Minimal or none (0-4) | 4 (11.1) |
| Mild (5-9) | 5 (13.9) |
| Moderate (10-14) | 9 (25.0) |
| Severe (15-21) | 18 (50.0) |
| **Patients requiring assessment (>9)** | 27 (75.0) |

Abbreviations: GAD-7=general anxiety disorder-7; PHQ-9= Patient Health Questionnaire-9.

that ENS6Q item and total score were significantly higher in 15 ENS patients compared to 30 patients with chronic rhinosinusitis with nasal polyps, and 30 healthy individuals. Interestingly, Velazquez et al. [4] observed that SNOT-22 was higher in ENS patients compared to their two control groups, which corroborates our observation [4].

The consideration of additional symptoms, including facial, ear, or dental pain, blocked nose, breathing difficulties for sleep or sport activity, cold/fresh nasal feeling, or hyperventilation is the primary difference between ENS6Q and Fr-ENSI. The evaluation of the symptom's prevalence in the disease is an important step for constructing a reliable patient-reported outcome questionnaire, which can considerably improve the management of disease through more accurate documentation of symptoms at baseline and throughout treatment [17]. The inclusion of some missing ENS6Q symptoms has led to the observation of a significant positive association between the score of the ENS-induced sleep disturbance and the PHQ-9 score, which can suggest a significant role of sleep disorder in the development of depression and vice versa. The importance of considering sleep disturbance in ENS was supported by Huang et al. [5] who report a substantial link between the ENS-induced sleep disturbance and the psychological burden of patients. Interestingly, the dryness and sleep items reported the highest AUC, sensitivities, and specificities, which is an additional argument for including some of the symptoms in Fr-ENSI that were previously ignored, such as sleep disturbance. In the same vein, the ENS-related difficulty in practicing sport(s) (AUC=0.89), suffocation or hyperventilation (AUC=0.892), and face, eye, ear, or dental pain (AUC=0.831) report high AUC values. The analysis of the importance of some missing symptoms in previous clinical instrument(s) is however limited by the lack of evaluation of the Fr-ENSI responsiveness to change. The responsiveness to change is the extent to which an instrument detects meaningful changes over time that have occurred at baseline [14,15]. In that way, the responsiveness to change can evaluate the importance of some symptoms of the instrument, which can significantly improve throughout treatment, contributing to improve the patient's QoL [14]. Future studies are needed to evaluate the evolution of Fr-ENSI symptoms after treatment and to determine their importance in the disease's relief.

In this study, ENS patients reported higher SNOT-22 scores compared to CRS/rhinitis patients. This observation is related to the inclusion in SNOT22 of many items highlighting the mental health of patients, e.g. discomfort item, annoyance, loss of productivity, sleep disorders. Because ENS is associated with a significant decrease in mental health, the SNOT22 score can be impacted, and consequently higher in this population compared to others.

Another important issue highlighted in the present paper and literature is the association between mental health and the development of ENS. The Fr-ENSI score could be compared between patients with depression and healthy individuals in future studies. Moreover, future psychological investigations could be conducted to explore the personality profile of ENS patients to better understand if the patients are initially more susceptible to develop depression than others.

The lack of evaluation of responsiveness to change of Fr-ENSI is therefore the primary limitation of the present study. The lack of an effective and validated treatment for ENS can make difficult the evaluation of responsiveness to change of a clinical instrument regarding the unpredictable effectiveness of treatment(s). Some therapeutic approaches have been proposed but their

Table 4. Correlation analysis.

| | Spearman correlation coefficient | | | |
|---|---|---|---|---|
| **Outcome measures** | **NOSE** | **SNOT-22** | **GAD-7** | **PHQ-9** |
| Dryness | 0.032 | 0.104 | 0.241 | 0.136 |
| Nasal crusting/bleeding | 0.154 | 0.355 | 0.177 | 0.028 |
| Nasal burning | 0.288 | 0.295 | 0.180 | 0.138 |
| Nasal cold/fresh | 0.175 | 0.176 | 0.178 | 0.092 |
| Nasal blockage/congestion/stuffiness | 0.648 | 0.507 | 0.273 | 0.247 |
| Reduced nasal air flow | 0.550 | 0.420 | 0.400 | 0.375 |
| Too open nose | 0.201 | 0.365 | 0.379 | 0.322 |
| Difficulty to practice sport(s) | 0.473 | 0.579 | 0.238 | 0.485 |
| Suffocation/hyperventilation | 0.281 | 0.575 | 0.569 | 0.538 |
| Face, eye, ear, or dental pain | 0.117 | 0.339 | 0.069 | 0.021 |
| Blocked ears | 0.261 | 0.553 | 0.352 | 0.154 |
| Sleep Disorders | 0.407 | 0.491 | 0.376 | 0.525 |
| **Total ENSI** | 0.509 | 0.697 | 0.445 | 0.433 |

The outcome association was considered as low, moderate, and strong for k<0.40, 0.40-0.60, and k>0.60, respectively. Abbreviations: ENSI=empty nose syndrome index; GAD-7=general anxiety disorder-7; NOSE=nasal obstruction symptom evaluation; PHQ-9=Patient Health Questionnaire-9; SNOT-22=sinonasal outcome tool-22.

Table 5. Receiver operating characteristic curve features.

| | AUC | 95% CI | Threshold | SE | SP |
|---|---|---|---|---|---|
| **Total SNOT-22** | 0.911 | 0.852-0.971 | 51.5 | 84.8 | 83.6 |
| **Total NOSE** | 0.883 | 0.813-953 | 10.0 | 84.8 | 81.8 |
| Dryness | 0.973 | 0.941-1.000 | 3.5 | 87.9 | 96.4 |
| Nasal crusting/bleeding | 0.847 | 0.761-0.933 | 1.5 | 87.9 | 70.9 |
| Nasal burning | 0.872 | 0.785-0.960 | 0.5 | 81.8 | 85.5 |
| Nasal cold/fresh | 0.871 | 0.781-0.960 | 0.5 | 78.8 | 89.1 |
| Nasal blockage/congestion/stuffiness | 0.707 | 0.590-0.823 | 2.5 | 63.6 | 70.9 |
| Reduced nasal air flow | 0.875 | 0.796-0.954 | 2.5 | 87.9 | 72.7 |
| Too open nose | 0.919 | 0.845-0.987 | 0.5 | 87.9 | 89.1 |
| Difficulty to practice sport(s) | 0.894 | 0.816-0.971 | 2.5 | 81.8 | 89.1 |
| Suffocation/hyperventilation | 0.892 | 0.815-0.969 | 0.5 | 87.9 | 81.8 |
| Face, eye, ear, or dental pain | 0.831 | 0.739-0.924 | 1.5 | 78.8 | 70.9 |
| Blocked ears | 0.745 | 0.636-0.853 | 1.5 | 66.7 | 65.5 |
| Sleep Disorders | 0.929 | 0.872-0.986 | 2.5 | 90.9 | 81.8 |
| **Total ENSI** | 0.966 | 0.929-1.000 | 23.5 | 93.9 | 90.9 |

The outcome association was considered as low, moderate, and strong for k<0.40, 0.40-0.60, and k>0.60, respectively. Abbreviations: ENSI=empty nose syndrome index; GAD-7=general anxiety disorder-7; NOSE=nasal obstruction symptom evaluation; PHQ-9=Patient Health Questionnaire-9; SNOT-22=sinonasal outcome tool-22.

post-operative outcomes need to be compared in randomized controlled study [18,19].

The low number of patients and the heterogeneity between patient and control groups for gender are additional limitations. The rarity of ENS makes difficult to have a large cohort study, while, to date, there is no study supporting a gender difference in the clinical presentation of ENS. The limited sample size can bias the generalizability of the findings found in the study be-

cause the French community includes many different cultures in which the expression of symptoms can widely vary. In that way, the severity of Fr-ENSI could vary from one to another population, and only a large sample cohort study can address this potential bias. Moreover, the prevalence, incidence, and phenotype of mental health disorders can be influenced by gender (20). This impact was not investigated in this small cohort study, and should be addressed in future studies.

The development of the first French patient-reported outcome questionnaire evaluating ENS symptoms is the primary strength of the study. The use of validated French-speaking questionnaires (Fr-SNOT-22 [8] and Fr-NOSE [9]) in the investigation of the validity and reliability of Fr-ENSI is an additional strength.

## Conclusion

The Fr-ENSI is a valid and reliable questionnaire for documenting the most prevalent symptoms of ENS. The consideration of sleep disorders in ENSI was important regarding its sensitivity, specificity, and association with depression and anxiety. Future studies are needed to evaluate the validity and reliability of Fr-ENSI, especially its responsiveness to change.

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## Authors' contributions

JRL: writing, patient recruitment, analysis, draft. AM: proofread and review of the draft, statistical analysis.

## Conflicts of interest

Authors have no conflict of interest.

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Patients consented to participate to the study.

## References

1. Manji J, Nayak JV, Thamboo A. The functional and psychological burden of empty nose syndrome. Int Forum Allergy Rhinol. 2018; 8(6):707-712.
2. Amanian A, Hari K, Habib AR, Dholakia SS, Nayak J, Thamboo A. The empty nose syndrome 6-item questionnaire (ENS6Q): a diagnostic tool to distinguish empty nose syndrome from primary nasal obstruction. Int Forum Allergy Rhinol. 2021; 11(7):1113-1115.
3. Malik J, Thamboo A, Dholakia S, et al. The cotton test redistributes nasal airflow in patients with empty nosesyndrome. Int Forum Allergy Rhinol. 2020 Apr;10(4):539-545.
4. Velasquez N, Thamboo A, Habib AR, Huang Z, Nayak JV. The Empty Nose Syndrome 6-Item Questionnaire (ENS6Q): a validated 6-item questionnaire as a diagnostic aid for empty nose syndrome patients. Int Forum Allergy Rhinol. 2017; 7(1):64-71.
5. Huang CC, Wu PW, Lee YS, et al. Impact of sleep dysfunction on psychological burden in patients with emptynose syndrome. Int Forum Allergy Rhinol. 2022; 12(11):1447-1450.
6. Hong HR, Jang YJ. Correlation between remnant inferior turbinate volume and symptom severity of empty nose syndrome. Laryngoscope. 2016; 126(6):1290-1295.
7. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008; 61(4):344-349.
8. de Dorlodot C, Horoi M, Lefebvre P, et al. French adaptation and validation of the sino-nasal outcome test-22: a prospective cohort study on quality of life among 422 subjects. Clin Otolaryngol. 2015; 40(1):29-35.
9. Marro M, Mondina M, Stoll D, de Gabory L. French validation of the NOSE and RhinoQOL questionnaires in the management of nasal obstruction. Otolaryngol Head Neck Surg. 2011; 144(6):988-93.
10. Dykewicz MS, Wallace DV, Amrol DJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol. 2020; 146(4):721-767.
11. Fokkens WJ, Viskens AS, Backer V, et al. EPOS/EUFOREA update on indication and evaluation of biologics in Chronic Rhinosinusitis with Nasal Polyps 2023. Rhinology. 2023; 61(3):194-202.
12. Micoulaud-Franchi J-A, Lagarde S, Barkate G, Dufournet B, Besancon C, Trébuchon-Da Fonseca A, Gavaret M, Bartolomei F, Bonini F, McGonigal A. Rapid detection of generalized anxiety disorder and major depression in epilepsy: validation of the GAD-7 as a complementary tool to the NDDI-E in a French sample. Epilepsy Behav. 2016;57:211–216.
13. Pfizer Patient health questionnaire (PHQ) screeners. Availabe: http://www.phqscreeners.com. Accessed 2024 June 1.
14. Lechien JR, Schindler A, De Marrez LG, et al. Instruments evaluating the clinical findings of laryngopharyngeal reflux: A systematic review. Laryngoscope. 2019; 129(3):720-736.
15. Francis DO, McPheeters ML, Noud M, Penson DF, Feurer ID. Checklist to operationalize measurement characteristics of patient-reported outcome measures. Syst Rev 2016;5:129.
16. Matheson GJ. We need to talk about reliability: making better use of test-retest studies for study design and interpretation. Peer J. 2019; 7:e6918.
17. Desomer A, Van den heede K, Triemstra M, et al. Use of patient-reported outcome and experience measures in patient care and policy. KCE Report 303, Belgian Healthcare Knowledge Center, 2018. Consulted July 23, 2024.
18. Huang CC, Wu PW, Huang CC, Chang PH, Fu CH, Lee TJ. A 3-year follow-up study after nasal reconstruction surgery in patients with empty nose syndrome. Int Forum Allergy Rhinol. 2024;14(4):841-844.
19. Malik J, Dholakia S, Spector BM, et al.. Inferior meatus augmentation procedure (IMAP) normalizes nasal airflow patterns in empty nose syndrome patients via computational fluid dynamics (CFD) modeling. Int Forum Allergy Rhinol. 2021;11(5):902-909.
20. Wierenga LM, Ruibrok A, Aksnes E, et al. Recommendations for a better understanding of sex and gender in the neuroscience of mental health. Biol Psy Global Op Sci. 2024.

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## SUPPLEMENTARY MATERIAL

Appendix 1. List of symptoms.

| | Present | Absent |
|---|---|---|
| Nasal dryness | | |
| Diminished nasal airflow | | |
| Suffocation | | |
| Nose feels too open | | |
| Nasal crusting | | |
| Nasal burning | | |
| Nasal congestion or stuffiness | | |
| Nasal blockage or obstruction | | |
| Trouble breathing through my nose | | |
| Trouble sleeping related to the nose | | |
| Unable to get enough air through my nose | | |
| Blow nose | | |
| Sneezing | | |
| Runny nose | | |
| Cough | | |
| Postnasal discharge | | |
| Thick nasal discharge | | |
| Ear fulness | | |
| Dizziness | | |
| Ear pain | | |
| Facial pain | | |
| Difficulty failling asleep | | |
| Waking up at night | | |
| Lack of good night sleep | | |
| Walking up tred | | |
| Day fatigue | | |
| Reduced productivity | | |
| Reduced concentration | | |
| Irritability | | |
| Sad | | |
| Embarrassed | | |
| Sense of taste/smell | | |

Patients evaluated the presence/absence of symptoms.

Appendix 2. Comorbidities of patients and controls.

| Comorbidities | ENS N=36 | CRS/CR N=23 | Controls N=34 |
|---|---|---|---|
| Severe sleep disorders | 23 (64) | 3 (13) | 3 (9) |
| Allergy | 9 (25) | 10 (43) | 1 (3) |
| Irritable bowel syndrome | 9 (25) | 3 (13) | 3 (9) |
| Asthma | 9 (25) | 5 (22) | 2 (6) |
| Laryngopharyngeal reflux disease | 8 (22) | 1 (4) | 1 (3) |
| Migraine | 8 (22) | 6 (26) | 3 (9) |
| Gastroesophageal reflux disease | 7 (19) | 4 (17) | 7 (21) |
| Autoimmune disorders | 3 (8) | 1 (4) | 2 (6) |
| Chronic obstructive pulmonary disease | 3 (8) | 1 (4) | 0 (0) |
| Heart disease | 3 (8) | 0 (0) | 1 (3) |
| Hypertension | 3 (8) | 4 (17) | 4 (12) |
| Arthrosis | 3 (8) | 3 (13) | 5 (15) |
| Osteoporosis | 2 (6) | 0 (0) | 3 (9) |
| Thyroid disorder | 1 (3) | 3 (13) | 3 (9) |
| Hypercholesterolemia | 1 (3) | 1 (4) | 5 (15) |
| Anemia | 1 (3) | 0 (0) | 1 (3) |
| Diabetes | 0 (0) | 1 (4) | 3 (9) |
| Liver disorder | 0 (0) | 1 (4) | 0 (0) |

Abbreviations: CRS/CR=chronic rhinosinusitis/chronic rhinitis; ENS=empty nose syndrome; N=number.