SNOT-22 in general population, a Spanish cohort study with an

updated meta-analysis

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Rhinology 62: 6, 700 - 709, 2024 https://doi.org/10.4193/Rhin24.033



Piñeros-García LM, González-Sánchez NI, Calvo-Henriquez C, et al. Rhinology 2024. https://doi.org/10.4193/Rhin24.033

Abstract

Background: The SNOT-22 is a questionnaire that evaluates the impact of chronic rhinosinusitis (CRS) on the patient's quality of life. This calculation allows measures to define therapeutic strategies and to estimate the response to treatment. Therefore, having this measure in the general population allows to establish normal values to guide decision-making in clinical practice. The objective was to determine the SNOT-22 score in a general Spanish population without CRS, according to gender, age, and comorbidities and to perform a systematic review of the literature and a meta-analysis.

Methods: The SNOT-22 questionnaire was used to evaluate whether demographic factors, smoking habits, or comorbidities can influence the score in the general population. A systematic literature review was performed to identify studies where the SNOT-22 questionnaire was applied in a population without CRS.

Results: 289 patients were included in the study (170 women), mean age 46.6 (17.8) years, range 18-89. No statistically significant difference between age subgroups (18-30, 31-50. 51-70, >70 years). The mean SNOT-22 was 11.9 (14.6), with no difference between genders. There was a positive association between obstructive sleep apnea (OSA) and anxiety-depression, with a higher SNOT-22 score. The metanalysis included 23 studies (3500 participants), with a mean value 10.52 under fixed effects model. Conclusion: This study has defined the normal value of the SNOT-22 questionnaire in the general Spanish population without gender-based differences. The included studies had demonstrated homogeneity, despite being performed in different populations. Conditions such as anxiety/depression and sleep apnea increase baseline SNOT-22 scores.

Key words: sinonasal outcome test 22, healthy population, control population, general population, guality of life

Introduction

Chronic rhinosinusitis (CRS) affects 5-12% of the general population, making it a condition with significant individual and socioeconomic impact ⁽¹⁾. The main relevance of CRS lies in its negative impact on patients' quality of life (QoL) ⁽²⁾. Research indicates that CRS may even have a greater impact on QoL than conditions like Parkinson's disease, chronic bronchitis, or heart failure ⁽³⁾. Patient experience and symptoms are evaluated through Patient-Reported Outcome Measures (PROMs). PROMs are increasingly gaining relevance among the scientific community since the primary goal of any CRS treatment is to alleviate symptoms and improve the patient's QoL.

The most widely accepted and validated PROM in CRS is the sinonasal outcome test 22 (SNOT-22) ⁽⁴⁾. The SNOT-22 consists of 22 items divided into five subdomains: nasal, facial, sleep, functional, and mood. Each of the 22 items may be rated from 0 (no problem) to 5 (severe problem). The total score may, therefore, range from 0 to 110.

Despite the primary utility of the SNOT-22 in facilitating patient and treatment comparisons and assessing disease progression over time, another important usage is to classify patients ⁽⁵⁾. This raises one main question: what is considered normal or healthy in the SNOT-22? According to the authors, the total score stratifies symptom intensity into four categories: no symptoms (score 0-10), mild (score >10-20), moderate (>20-50), and severe (>50) ⁽⁴⁾.

However, these reference values may vary among different populations, and patients with other conditions different from CRS, such as depression or sleep apnea, may distort the final score.

Different authors have published data assessing the SNOT-22 in patients without sinonasal illnesses. However, up to date, there is no Spanish data and no meta-analysis encompassing all these individual studies.

This study has been designed with two objectives. First, to determine SNOT-22 values in a general population without a history of sinonasal disease and investigate potential variations based on age, gender, smoking habits, and the presence of comorbidities. Additionally, to conduct a systematic review and meta-analysis of published evidence, to determine the mean SNOT-22 score in the population without CRS.

Materials and methods

This is a descriptive cross-sectional study associated with a systematic review and meta-analysis.

Cross-sectional study

The sample was collected at a tertiary referral Hospital (Hospital

Clínic de Barcelona) between June and September 2021. The subjects recruited were adults (over 18 years of age) who accompanied patients attending the otolaryngology consultation, and health personnel working at the Hospital without any diagnosed nasal condition or previous nasal surgery. The following sinonasal symptoms: nasal obstruction, anterior rhinorrhea, posterior rhinorrhea, facial pressure, sneezing, hyposmia, and epiphora, were measured using a Visual Analog Scale (VAS). The VAS was measured from 0 to 100mm, with 0mm being the minimum and 100mm being the maximum of symptoms.

Exclusion criteria involved the presence of known sinonasal disease, previous nasal or nasosinusal surgery, or hospital admission for any cause in the last 12 months. Patients scored sinonasal VAS greater than 3mm were also excluded. The 3mm cutoff value was chosen according to EPOS2020 definition of mild to moderate symptoms⁽³⁾.

Participants signed a consent form and were instructed to fill in the Spanish validated version of the SNOT-22 questionnaire ⁽⁶⁾, along with additional questions. These questions included their medical history, presence of known sinonasal disease, hospital admission in the last year, history of sinonasal surgery, age, weight, height, smoking habits, and presence of comorbidities such as diabetes, asthma, systemic arterial hypertension (SAH), anxiety/depression, and obstructive sleep apnea (OSA). Participants were then asked to rate their nasal symptoms on a VAS (0-100mm) for nasal obstruction, anterior rhinorrhea, posterior rhinorrhea, facial pressure, sneezing, loss of smell, and epiphora. All data were transferred to an Excel database for statistical analysis by a single researcher. The Research and Ethics Committee of the Barcelona Clinic Hospital approved the study protocol (HCB/2021/0965).

Systematic review

This review was conducted according to PRISMA guideline, and a formal PROSPERO protocol was published according to the NHS International Prospective Register of Systematic Reviews prior to the initiation of the study. The recommendations of the AMSTAR-2 guidelines were also followed.

Studies were included if they: 1) used SNOT-22 in the general population without CRS; 2) report the total mean score; 3) report demographic characteristics as age, sex; and 4) sample size >20 (as it is the minimum sample size to estimate a 95% confidence interval for a population mean assuming a minimum width of the interval of 5). No publication dates or publication status restrictions were imposed.

Exclusion criteria included: SNOT-20 score, pediatric population, no access to the full text, other languages different from English or Spanish, review articles, meta-analysis, editorial, commentaries, letters or studies not related to the objective of this review.

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Age (years)	N (%)	SNOT-22 total mean (SD), Median (range)	SNOT-22 nasal mean (SD), Median (range)	SNOT-22 facial mean (SD), Median (range)	SNOT-22 sleep mean (SD), Median (range)	SNOT-22 functional mean (SD), Median (range)	SNOT-22 emotional mean (SD), Median (range)
Total	289 (100)	11.9 (14.6); 7 (0-89)	3.5 (4.8); 2 (0-29)	1.2 (2.7); 0 (0-19)	3.7 (4.7); 2 (0-20)	1.7 (2.9); 0 (0-15)	1.7 (3.0); 0 (0-14)
18-30	58 (20.1)	10.8 (14.9); 7 (0-89)	3.7 (4.8); 2 (0-25)	1.2 (2.9); 0 (0-19)	2.8 (4.7); 1 (0-20)	1.5 (2.9); 0 (0-15)	1.6 (2.8); 0 (0-12)
31-50	105 (36.3)	11.1 (15.4); 6 (0-85)	3.1 (5.2); 1 (0-29)	1.1 (3.1); 0 (0-19)	3.4 (4.3); 2 (0-16)	1.6 (2.7); 0 (0-12)	1.7 (2.9); 0 (0-12)
51-70	86 (29.8)	12.2 (12.3); 8 (0-54)	3.2 (4.2); 2 (0-20)	1.1 (2.2); 0 (0-10)	4.2 (4.7); 3 (0-20)	1.8 (2.9); 0 (0-14)	1.8 (2.9); 0 (0-14)
>70	40 (13.8)	14.9 (16.8); 1 2 (0-65)	4.9 (5.1); 3 (0-18)	1.6 (2.6); 0 (0-12)	4.3 (5.8); 3 (0-20)	2.2 (3.6); 0 (0-13)	2.1 (3.8); 0 (0-14)
$\chi^{\rm 2}$ p-value		3.02 0.388	6.2 0.102	6.03 0.110	5.20 0.158	0.45 0.930	0.25 0.969

SD (standard deviation).

Search strategy and data extraction

Studies were identified by searching the following electronic databases by two authors (NGZ and LPG): Pubmed, Cochrane and Embase. All databases queried on May 31, 2023. The following search strategy was formulated: ("SNOT-22" OR "Sino-Nasal Outcome Test 22" OR "SNOT 22" OR "sinonasal outcome test 22") AND ("validation").

Abstracts of retrieved articles were thoroughly reviewed by two authors (NGZ and LPG), and those potentially meeting the inclusion criteria were selected for full-text review. In case of discrepancies between reviewers regarding the selection of abstracts, the corresponding papers were included in the full-text review phase for final assessment. The references of all selected articles were also manually reviewed to identify any potentially missing publications.

Data extraction

Two authors (NGZ, LPG) independently analyzed the articles meeting the inclusion criteria and extracted the relevant data. Discrepancies were resolved by discussion with the senior author (IA) and method assistant (CCH). Variables extracted encompassed: mean SNOT-22 score, its standard deviation, demographic characteristics (age and sex), and comorbidities if reported were extracted, including the current study.

Statistical analysis

The sample size was calculated to estimate a population mean from the sample using the formula $n=((z\alpha/2\sigma)/E)^2$, where Za was set to 0.05. The variance was taken as 16, the largest published variance in healthy subjects ⁽⁷⁾, and the margin of error was set to 5. Under these conditions, the minimum required sample size

(n) was 48.

Categorical variables are reported as frequency and percentage (%), while continuous variables are presented as mean and standard deviation (SD) or median with interquartile range (IQR).

Univariate analysis was performed for quantitative variables using linear regression (SNOT-22 score with age, BMI), for dichotomous qualitative variables using rank sum (SNOT-22 score with sex, diabetes mellitus, asthma, apnea, anxiety/depression), and for qualitative variables with more than 2 groups, Kruskal-Wallis test was used (SNOT-22 score with tobacco).

Multivariate adjustment included the variables that were found to be relevant in the univariate analysis. The level of significance or alpha value was set at 0.05.

All data were coded and analyzed using Stata (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX, USA). For the meta-analysis. All individual calculations to complete data were performed with STATA 2023. Meta-analysis was performed with SPSS 29.0.1 (IBM Corp, New York, NY, USA)

Results

Cross-sectional study

The quantitative variables were assessed for normal distribution. Only the height followed a normal distribution according to Kolmogorov-Smirnov test.

A total of 289 subjects were recruited. Table 1 describes the value of the whole SNOT-22 for the total population and segmented by age subgroups. The Kruskall-Wallis contrast could not demonstrate any statistically significant difference between age subgroups, despite the scores are slightly higher for older patients (>70 years old).

Table 2. SNOT-22 total score by subgroup.

Variables		N (%)	SNOT-22 Mean (SD); Median (range)	p-value
Gender	Male	119 (41.2)	10.9 (12.3); 8 (0-66)	0.921
	Female	170 (58.8)	12.6 (16.1); 7 (0-89)	0.821
Smoker	No	211 (73.5)	12.9 (16.9); 6 (0-89)	
	Yes	68 (23.6)	12.2 (13.0); 10 (0-66)	0.108
	Quitted smoking	8 (2.8)	4.3 (5.1); 14.5 (0-37)	
SAH	No	136 (85.0)	12.1 (14.1); 7 (0-89)	0.212
	Yes	24 (15.0)	17.6 (19.4); 12.5 (0-65)	0.312
Diabetes	No	153 (95.6)	12.5 (15.1); 7 (0-89)	0.007*
	Yes	7 (4.4)	20.9 (11.2); 22 (6-37)	0.027*
Asthma	No	154 (95.3)	12.8 (15.1); 7 (0-89)	0 511
	Yes	6 (3.7)	15.2 (15.1); 12 (1-42)	0.511
OSA	No	153 (95.6)	11.9 (14.0); 7 (0-89)	0.000
	Yes	7 (4.4)	34.1 (22.5); 37 (3-65)	0.006*
Depression/anxiety	No	145 (90.6)	11.6 (14.2) 7 (0-89)	0.001*
	Yes	15 (9.4)	25.7 (17.6); 23 (0-65)	0.001^
COPD	No	160 (100.0)	12.9 (15.0); 7 (0-89)	
	Yes	0 (0)	NA, NA	NA

SD (standard deviation). SAH (Systemic Arterial Hypertension). OSA (obstructive sleep apnea). COPD (chronic obstructive pulmonary disease) NA (not applicable). Asterisk if the association is statistically significant (p<0.05). Note: SAH, diabetes, asthma, OSA, depression/anxiety and COPD are calculated only over 160 responses.



Figure 1. SNOT-22 mean and standard deviation (between brackets) according to diagnosis of depression/anxiety (dep/anx) and obstructive sleep apnea (OSA).

Table 2 describes the values of the different variables studied and their statistical association with the score on the SNOT-22 questionnaire. This univariate analysis reveals a statistically significant association between the SNOT-22 score and the presence of diabetes, depression/anxiety, obstructive sleep apnea (OSA), and body mass index (BMI).

All these variables (diabetes, depression/anxiety, OSA, and BMI) were studied in a multivariate analysis through multiple regression (Table 3). This analysis demonstrated a statistically significant association with OSA and depression/anxiety (p<0.001) but

showed no association with BMI or diabetes.

The SNOT-22 scores according to OSA and depression/anxiety diagnosis are graphically summarized in Figure 1. The mean value of the SNOT-22 in the general population was 11.9 (95% CI -16.72; 40.52).

Visual analogue scale (VAS)

A correlation study was conducted between the score on the SNOT-22 questionnaire and the symptoms measured by the VAS.

Table 3. Multiple regression.

Variable	Regression Coefficient (SD)	p-value
ВМІ	0.37 (0.29)	0.204
Depression/ anxiety	13.67 (3.78)	<0.001*
Diabetes	5.23 (5.42)	0.337
OSA	19.37 (5.67)	0.001*

SD (standard deviation). BMI (body mass index). OSA (obstructive sleep apnea). Asterisk if the association is statistically significant (p<0.05).

A statistically significant association (p<0.001) was observed with nasal obstruction, anterior rhinorrhea, posterior rhinorrhea, sneezing, and epiphora. Results are documented in Table 3 and Figure 2.

Systematic review

The search process is summarized in the PRISMA flowchart (Figure 3). A total of 547 articles were identified. Out of these, 45 were selected based on their titles or abstracts. After conducting a full-text review, 26 articles (including ours) encompassing 3049 participants were chosen for inclusion in the systematic review ⁽⁶⁻³¹⁾, and 23 articles (including our study) were used in the meta-analysis.

The summary of all the selected articles can be found in Table 4. For the calculation and adaptation of the table we transformed the data from Gillett et al. ⁽¹⁶⁾ and Lange et al. ⁽²¹⁾, who provide the 95% confidence interval, but not the standard deviation. The standard deviation was calculated from the confidence interval, which is the data shown in the table.

All the included studies were cross-sectional or prospective studies (level of evidence: 3). The mean sample size was 153; being the minimum 25 (Plaas et al. ⁽²⁵⁾) and the maximum 1000 (Plath et al. ⁽³²⁾) The weighted mean age was 40.1 years old, being the minimum 19.5 (Asiri et al. ⁽¹⁰⁾) and the maximum 53.4 (Farhood et al. ⁽¹⁴⁾). The mean SNOT-22 ranged from 4.5 ⁽⁶⁾ to 20.2 ⁽³²⁾. These studies were outliers as the interquartile range was 8.2; 14.5.

Meta-analysis

From the 26 selected studies, 23 provided enough data to be included in a meta-analysis. Adding our own data, it encompassed 3520 participants. The meta-analysis, under a fixed effects model (I² coefficient 0%), reveals a mean SNOT-22 in healthy volunteers of 10.52 (95% CI 9.22; 11.82).

This meta-analysis data could be compared against our individual study, the Student's t test could not demonstrate any statistically significant difference between both samples (t=1.61; p=0.108).



Figure 2. Linear regression (blue line) between SNOT-22 total score (Y axis) and symptoms assessed with visual analogue scale (VAS) (X axis). In gray the 95% confidence interval.

Discussion

This is the first study assessing the SNOT-22 questionnaire in a Spanish cohort of healthy volunteers.

This is not the first meta-analysis assessing the SNOT-22 questionnaire in a healthy population, as Farhood et al. ⁽¹⁴⁾ have already performed one in 2016. However, it was worth the effort to update it, as they only included 10 studies, while we were able to include 22. Interestingly, our updated results barely differ from theirs (11.3 vs 10.5). However, the margin of error (standard deviation) does vary, as we included a larger cohort (9.8 vs 0.66).

Our meta-analysis encompassed a substantial number of studies conducted across 21 different countries, involving diverse age groups. Despite this apparent heterogeneity of samples, the results exhibited a striking similarity, as indicated by a heterogeneity index of 0%. This homogeneity assumes paramount importance in clinical practice as it establishes a normative reference value for the "normal" or "healthy" range on the SNOT-22 questionnaire. It means that these data can be confidently generalized to any population, considering its wide-ranging global data collection. Consequently, when diagnosing the clinical impact of sinonasal diseases or evaluating treatment efficacy, we should consider an optimal value of 10.5 rather than 0.



Study	TE	seTE	95%-CI	(fixed)	(random)
Kosuai (2011)	11.40	9.5000	11.40 [-7.22: 30.02]	0.5%	0.5%
Jalessi (2013)	7.60	9.1000	7.60 [-10.24; 25.44]	0.5%	0.5%
Marambaia (2013)	8.00	10.0000	8.00 [-11.60; 27.60]	0.4%	0.4%
Vaitkus (2013)	16.78	16.1000	16.78 [-14.78; 48.34]	0.2%	0.2%
Lachanas (2014)	13.00	11.7000	13.00 [-9.93; 35.93]	0.3%	0.3%
de los Santos (2015)	4.50	7.3000	4.50 [-9.81; 18.81]	0.8%	0.8%
de Dorlodot (2015)	8.30	8.7000	8.30 [-8.75; 25.35]	0.6%	0.6%
Gregório (2015)	9.83	8.2000	9.83 [-6.24; 25.90]	0.6%	0.6%
Lange (2016)	10.50	0.7000	10.50 [9.13; 11.87]	89.1%	89.1%
Shapira Galitz (2016)	13.15	14.2000	13.15 [-14.68; 40.98]	0.2%	0.2%
Adnane (2016)	14.50	5.1000	14.50 [4.50; 24.50]	1.7%	1.7%
Farhood (2016)	14.60	15.2000	14.60 [-15.19; 44.39]	0.2%	0.2%
Lumyongsatien (2017)	7.70	7.4000	7.70 [-6.80; 22.20]	0.8%	0.8%
Erskine (2017)	12.00	13.6000	12.00 [-14.66; 38.66]	0.2%	0.2%
Maningding (2018)	11.90	10.6000	11.90 [-8.88; 32.68]	0.4%	0.4%
Plaas (2019)	13.10	9.2000	13.10 [-4.93; 31.13]	0.5%	0.5%
Asiri (2019)	19.50	13.1000	19.50 [-6.18; 45.18]	0.3%	0.3%
Thakur (2021)	7.58	6.8000	7.58 [-5.75; 20.91]	0.9%	0.9%
Riedl (2021)	15.10	10.9000	15.10 [-6.26; 36.46]	0.4%	0.4%
Albrecht (2022)	10.10	8.9000	10.10 [-7.34; 27.54]	0.6%	0.6%
Piñeros et al (our study)	11.90	14.6000	11.90 [-16.72; 40.52]	0.2%	0.2%
Palth (2023)	20.20	19.4400	20.20 [-17.90; 58.30]	0.1%	0.1%
Chen (2023)	7.20	9.7000	7.20 [-11.81; 26.21]	0.5%	0.5%
Fixed effect model			10.52 [9.22; 11.82] 1	00.0%	-
Random effects model			the second seco	-	100.0%

Figure 4. Forest plot for a one-group mean. Left column: studies according to its first-author.

noting that CRSwNP occurs predominantly in older patients (average age of 43 years). Although the small difference between the two age averages might not significantly affect the results, considering the findings of Gregório et al. ⁽¹⁵⁾, wherein older patients had higher SNOT-22 values, it is possible that the real mean adjusted by age could be higher.

Figure 3. PRISMA flow diagram.

However, this meta-analysis may have certain limitations. Firstly, each study employed the SNOT-22 questionnaire in a translated version, potentially introducing biases stemming from the translation process or item interpretation. However, the homogeneity found in this metanalysis does not suggest the presence of this specific bias.

Secondly, there was significant variation in mean age across the studies, spanning from 19.5 to 53 years. This variation may have introduced bias if the normal SNOT-22 scores were age-dependent. Though debated, our study, like others, did not identify a significant relationship between the SNOT-22 score and age, although certain studies, e.g., Gregório et al. ⁽¹⁵⁾, suggest that older participants (above 60 years of age) exhibit lower scores. However, the inclusion of numerous studies may have diluted the potential age-related deviations.

Thirdly, our study revealed that other non-sinonasal diseases can influence the SNOT-22 scores, an aspect not considered in the selection of a "healthy cohort," which pertains solely to sinonasal health. Consequently, if the prevalence of such diseases, like OSA or anxiety/depression, varies among the studies, the SNOT-22 scores may also vary accordingly. Nonetheless, the large number of included studies helped mitigate the impact of this potential confounding factor.

Fourthly, the mean age in the selected studies was relatively low, with a weighted mean age of 40.1. However, it is worth

Regarding our individual study on the Spanish cohort, it was the third-largest study, surpassed only by Gregório et al. ⁽¹⁵⁾ (539 participants) and Plath et al. ⁽³²⁾ (1000 participants). Our mean value was slightly higher (11.9) compared to the meta-analysis (10.5) (Figure 4), and our standard deviation was also considerable (14.6). This indicates a considerable dispersion in our results, potentially limiting their generalizability. However, this issue was rectified by the meta-analysis, which generated a narrow confidence interval.

Our results align with previously published data, as demonstrated by the absence of statistically significant differences between our cohort and the meta-analysis cohort. Interestingly, in contrast to Gregório et al. ⁽¹⁵⁾, we did not identify any significant gender-based differences. While Gregório et al. ⁽¹⁵⁾ reported higher SNOT-22 scores in females (10.94 vs. 8.58; p=0.005), our observations showed slightly higher values in females (12.6) compared to males (10.9), but the differences were not statistically significant. This lack of significance may be attributed either to genuine absence of gender differences or to the high standard deviation in our study. Other authors ⁽¹²⁾, like us, also reported higher values for females but did not find statistically significant differences. Even if such differences exist, they are of minimal magnitude and are unlikely to substantially impact research or clinical practice outcomes.

The primary finding of our study lies in the differential SNOT-22 scores observed when considering other illnesses apart from

Table 4. Summary of systematic review articles.

Author	Population	Sample size (n)	Age (years) (mean ± SD)	SD	Men	Women	SNOT-22 Mean (SD)
de los Santos (2015) ⁽⁶⁾	Patients and their relatives, physicians and their relatives, neighbors	59	41		25	34	4,5 (7,3)
Vaitkus (2013) (7)	Members of the medical staff, hospital staff and residents, and among students of the university	115	45,58	14,96	37	78	16,78 (16,1)
Adnane (2016) (8)	Healthy volunteers	51	35,1	11,9	23	28	14,49 (5,143)
Albrecht (2022) (9)	Family members accompanying patients	31	48,4	15,2	12	19	10,1 (8,93)
Asiri (2019) (10)	Members of the hospital employees and accom- panying persons or relatives	50	19,5	13,1	43	7	19,5 (13,1)
de Dorlodot (2015)	Medical staff and sports clubs	46	45,2	13,5	21	25	8,3 (8,7)
Erskine (2017) (12)	Family and friends of those attending ENT outpa- tient clinics and hospital staff	251	47,5		96	143	12 (13,6)
Eisenbach (2019) (13)	Healthy volunteers without nasal pathology	37	48,6	14,8	16	21	9,2 (7,2)
Farhood (2016) ⁽¹⁴⁾	Adults accompanying patients during visits to the Otolaryngology–Head and Neck Surgery clinic at the Medical University of South Carolina	95	53,4	17,3	36	59	14,6 (15,2)
Gregório (2015) (15)	adult healthy volunteers	539	41,91	16,36	253	286	9,83 (8,16)
Gillett (2009) (16)	Local hospital and tennis club	116	40		54	62	9,3 (IC 95% 7,5–11,1)
Jalessi (2013)(17)	Healthy volunteers	30	33	6,7	11	19	7,6 (9,1)
Koskinen (2021) (18)	Hospitals' personnel or close circle of the research team members	89	40,4		22	67	8,9
Kosugi (2011) (19)	Medical university staff and patient companions	113	23.35	8,13	49	64	11,42 (9,46)
Lachanas (2014) ⁽²⁰⁾	Members of the medical staff, residents, hospital staff, students and accompanying persons/rela- tives of our patients	120	40.5		65	55	13 (11,68)
Lange (2016) (21)	Respondents to postal questionnaire	268	41,7		126	142	10,5 (IC95%l: 9,1–11,9)
Lumyongsatien (2017) ⁽²²⁾	Normal volunteers	30	46,43	11,138	17	13	7,70 (7,39)
Marambaia (2013) (23)	Patients without sinonasal disease.	98	37,8	12,9	40	58	8 (10)
Maningding (2018)	Controls	48	44		21	27	11,9 (10,6)
Plaas (2019) (25)	Healthy volunteers were recruited from the medi- cal student body and faculty	25	38,56	15,5	11	14	13,1 (9,2)
Riedl (2021) (26)	Patient without CRS treated in the hospital for other reasons	36	33,8	15,9	23	13	15,1 (10,9)
Shapira Galitz (2016) ⁽²⁷⁾	Hospital personnel, medical and nursing students, and visitors to the medical center or patients' companions	73	44,2	15,14	35	38	13,15 (14,2)
Schalek (2009) (28)	Patients admitted to the ENT clinic with non- sinonasal disease	50	44,9		24	26	13,68
Schalek (2009) (28)	Healthy students of the Faculty of Medicine	50	24,1		22	28	10,22
Thakur (2021) (29)	Hospital staff, medical and nursing students	110	27	10,23	72	38	07,58 (6,772)
Yeolekar (2013) (30)	Participants from medical institution	230	21		97	133	8,07
Chen (2023) (31)	Healthy individuals	43	26.5	6	20	23	7.2 (9.7)
Palth (2023) (32)	Healthy participants	1000	44.3	14.2	500	500	20.2 (19.44)

SD (standard deviation).

sinonasal conditions. Specifically, we observed higher values in patients with OSA and those suffering from anxiety/depression. Notably, other authors have also reported variations in SNOT-22 scores with different medical conditions.

While our study found no difference concerning asthma diagnosis, Farhood et al. ⁽¹⁴⁾ observed that the presence of asthma was associated with increased scores. However, conflicting results were reported by other authors, such as de Dorlodot et al. ⁽¹¹⁾ and Lange et al. ⁽²¹⁾, who found no interaction between asthma and their respective cohorts.

The observed differential SNOT-22 scores concerning the diagnosis of anxiety/depression come as no surprise, given the well-established negative impact of these conditions on various QoL assessments. In the context of CRS, Farhood et al. (14) conducted a systematic review and reported significant differences in SNOT-22 scores between patients with and without depression (34.1 and 15.0, respectively; p=0.001). Similarly, in line with these findings, anxiety has been associated with poorer baseline SNOT-22 scores, and patients with anxiety have shown less improvement in their scores after undergoing surgery ⁽³³⁾. These results highlight the interconnected nature of psychological well-being and sinonasal health. Individuals experiencing anxiety or depression may have heightened symptom burden, leading to a more substantial impact on their daily functioning and overall QoL. The assessment of psychological factors alongside sinonasal symptoms becomes crucial for a comprehensive understanding of the patient's health status and tailoring effective treatment strategies.

In our cohort, we made a notable discovery, as we found a statistically significant association between a diagnosis of OSA and increased SNOT-22 scores. Interestingly, the OSA cohort of patients was also studied by Farhood et al. (14), but their findings differed from ours, as they did not identify any statistically significant difference between the groups with and without OSA. One intriguing hypothesis that warrants attention is related to how patients interpret and respond to the sleep-related questions in the SNOT-22 questionnaire. While patients are specifically instructed to attribute their responses to sinonasal disorders, many find it challenging to discern whether their symptoms originate from the nose or other factors, such as sleep-related issues. Consequently, some patients may inadvertently provide inaccurate responses on the questionnaire, leading to an artificial inflation of their SNOT-22 scores. Indeed, the study conducted by Lachanas et al. (34) examined patients with CRSwNP and those with OSA who completed the SNOT-20 questionnaire. The study revealed that both groups obtained similar scores, but the intriguing difference arose in how they attributed their symptoms. OSA patients tended to attribute their symptoms

to the "wellness" section of the questionnaire, while CRSwNP patients linked their symptoms to the "rhinologic" section. This discrepancy in attribution is of paramount importance and must be duly considered in daily clinical practice.

Finally, in our cohort, we observed no difference in SNOT-22 scores among smokers, which aligns with the findings published by De Dorlodot ⁽¹¹⁾. However, it is worth noting that other studies, such as Lachanas et al. ⁽³⁵⁾, reported significantly higher SNOT-22 values in smoking control group participants (15.75 \pm 1.68) compared to non-smoking controls. Similarly, Hopkins et al. ⁽⁴⁾ found that the group of patients with CRS who were smokers had significantly higher SNOT-22 scores than non-smokers, although they did not evaluate the same in the control group.

Conclusion

Determining SNOT-22 scores in a population without CRS holds considerable importance as it provides a valuable starting point in the assessment of sinonasal health in the general population. For patients with CRS, the utilization of SNOT-22 aids in defining treatment guidelines and identifying individuals with scores close to our meta-analysis mean value (10.5), indicating a possible lack of clinical improvement. Moreover, the questionnaire enables healthcare providers to establish treatment strategies that align with the specific expectations of the patient, ensuring a patient-centered approach to medical care.

Acknowledgement

This work has been the winner of the second prize for the best master's thesis "Advanced Rhinology and Anterior Skull Base" from the International University of Andalucia.

Authors' contributions

LMP: Literature review, statistical analysis and creation of the manuscript; NIGS: Creation of the instrument, informed consent, and study database. Data collection and statistical analysis, literature review and manuscript elaboration. MJRL: Creation of the database and data collection; CCH: Statistical analysis, elaboration of the meta-analysis, development and revision of the manuscript; IA: creation and review of the study; JM and CH: review of the study.

Funding

None

Conflicts of interest

CCH have been remunerated for research activities by Cinfa, Medtronic, Sanofi; and conferences for GSK, Sanofi, Mylan, Organon, Astrazeneca. IA has received advisory board fees and consultation fees from Viatris, Menarini, GSK, MSD, AstraZeneca, Novartis, Sanofi, Cinfa, Olympus, Storz, Metronic, and Roche. CH has received advisory board fees and consultation fees from GSK, AstraZeneca, Sanofi and Lilly. The rest of the authors declare not to have any conflict of interest.

Data availability

Not applicable.

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