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Rhinology

Normative data for interpreting the SNOT-22

Valori di riferimento per interpretare lo SNOT-22

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SUMMARY

Objectives. The Sino-Nasal Outcome Test 22 (SNOT-22) is a validated patient-reported outcome instrument to evaluate the health-related quality of life (HRQoL) in patients with chronic rhinosinusitis (CRS). There are no published normative SNOT-22 scores, limiting its interpretation.

Methods. Symptom scores from 1,000 SNOT-22 questionnaires were analysed by principal component analysis (PCA) and exploratory factor analyses. Data were derived from a survey with 1,000 healthy Europeans (reference cohort) who were recruited using the Respondi panel for market and social science research. This subsample was quoted to the population distribution of the German Microcensus and selected from a non-probability panel.

Results. The overall normative SNOT-22 score can be detected to be 20.2 ± 19.44. Male (18.49 ± 19.15) and older (> 50 years old; 18.3 ± 17.49) participants had overall lower SNOT-22 mean results than females (21.8 ± 19.6) and younger (21.4 ± 20.55) participants, indicating higher levels of satisfaction. PCA proposed two SNOT-22 domains ("physiological well-being" and "psychological well-being"), which explained 65% of the variance.

Conclusions. These are the first published (German) normative scores for the SNOT-22 and provide a clinical reference point for the interpretation of data.

KEY WORDS: Sino-Nasal Outcome Test 22, normative score, functional endoscopic sinus surgery, chronic rhinosinusitis, patient-reported outcome measures

RIASSUNTO

Obiettivi. *Il Sino-Nasal Outcome Test 22 (SNOT-22) è uno strumento validato per valutare la qualità della vita nei pazienti affetti da rinosinusite cronica (CRS). Tuttavia, non esistono in letteratura punteggi di riferimento per lo SNOT-22, limitandone l'interpretazione.*

Metodi. *I punteggi dello SNOT-22 di 1.000 individui sani sono stati analizzati mediante l'analisi delle componenti principali (PCA) e l'analisi fattoriale esplorativa. I dati sono stati ricavati da un'indagine su cittadini dell'Europa centrale, reclutati utilizzando il pannello Respondi per le ricerche di mercato e di scienze sociali.*

Risultati. *Il punteggio di riferimento complessivo dello SNOT-22 è stato in media pari a 20,2 ± 19,44. I partecipanti maschi (18,49 ± 19,15) e oltre i 50 anni (18,3 ± 17,49) avevano risultati complessivamente inferiori rispetto ai partecipanti di sesso femminile (21,8 ± 19,6) e giovani (21,4 ± 20,55), indicando livelli più elevati di soddisfazione. La PCA ha proposto due domini SNOT-22 ("benessere fisiologico" e "benessere psicologico"), che spiegavano il 65% della varianza.*

Conclusioni. *Questi sono i primi punteggi normativi pubblicati (in Germania) per lo SNOT-22 e possono fornire un riferimento clinico per l'interpretazione del questionario.*

PAROLE CHIAVE: *Sino-Nasal Outcome Test-22, valori di riferimento, chirurgia funzionale endoscopica dei seni paranasali, rinosinusite cronica, patient-reported outcome measures*

Introduction

Chronic rhinosinusitis (CRS) is a common and debilitating condition with significant economic impact [1], which poses a considerable burden to healthcare providers and patients. Patients with worse sinus-specific quality-of-life (QoL) impairment are more likely to pursue functional endoscopic sinus sur-

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gery (FESS), whereas those with less symptomatic burden are more likely to continue medical therapy alone [2].

There is a growing acceptance that the patient's opinion is essential in providing high-quality health care. The European position paper on rhinosinusitis and nasal polyps (EPOS) 2020 recommends subjective assessment of chronic rhinosinusitis symptoms in research and in clinical practice using validated questionnaires [3].

The Sino-Nasal Outcome Test 22 (SNOT-22) is a well-validated [4], disease-specific instrument that combines rhinologic issues (physical problems and functional limitations) with general health issues (e.g., emotional domains) [5]. Because of its reliability, validity, responsiveness and easy application [6], the SNOT-22 is considered to be the most suitable patient-reported outcome measure (PROM) for evaluating patients with CRS. The 4-subdomain structure for SNOT-22 (reflecting sleep, nasal, otologic/facial pain, and emotional symptoms of CRS) was validated as the most appropriate for a total of 800 patients with CRS from eastern and western United States by using confirmatory factor analysis (CFA) [7].

There are still no normative scores for the SNOT-22 questionnaires. It is not yet known how the QoL of CRS patients undergoing FESS compares with that of a meaningful control population. Normative scores have been published for disease-specific questionnaires before and after septorhinoplasty, which allow rhinosurgeons to predict and evaluate the outcome of rhinosurgery [8]. Previous studies have proposed different tools to evaluate the effect of CRS on the patient's quality of life. Obviously, baseline SNOT-22 seems to be one of the most important factors affecting outcomes [9] and several studies have suggested its prognostic role in terms of achievement of improvement and risk of revision surgery [10]. Thus, measurements of the proportion of CRS patients receiving a minimal clinically important difference (MCID) [11-14] and the percentage of relative improvement (RI) [13,14] after FESS based on their pre-operative QoL level have been performed. However, pre-operative CRS patients are not "normal" because they carry the physical and psychological burdens caused by CRS. Thus, normative SNOT-22 scores may provide a clinical reference point for the interpretation of data. Therefore, the main aim of our study was to provide the first normative values for the SNOT-22 as an additional decision-making tool after FESS by performing a systematic prospective study on 1,000 healthy participants. Moreover, the secondary objective of the study was to simplify the previously common four-component model for the SNOT-22 by using principal component and exploratory factor analysis.

Materials and methods

Recruitment and patient data

1,000 German individuals (reference cohort) were recruited via a non-probabilistic online panel. The subset of the panel used for this study was quoted to relevant population distributions of the German Microcensus (an annual 1% probability sample of the German population) [15]. Relevant parameters were age, gender, region and education. Migration was also considered but not quoted for. The reference cohort was recruited from September 2018 using the Respondi panel, an international organisation for standardisation (ISO)-certified online access panel for market and social science research. The participation was voluntary but compensated with an expense allowance. Due to the nature of a cohort derived from the general public, the sample size was decided on to ensure a small sampling error and smaller confidence intervals, since the presence of participants with low (or high) QoL-measures was expected to be less pronounced. Sociodemographic questions were asked first. Second, the SNOT-22 questionnaire was completed by the study participants. Raw data were cleaned and converted into a labeled Statistical Package for Social Sciences (SPSS) dataset before checking that questions were complete and relevant quotas were distributed. Test groups were screened to make sure the right questions had been asked. Statistical analysis was conducted by GESIS (Leibniz Institute for Social Sciences).

Disease-specific QOL questionnaire

We used the German validated version of the Sino-Nasal Outcome Test-22 (SNOT-22) [16,17] to measure health-related quality of life (HRQoL) in patients with CRS [4]. SNOT-22 is the modified version of SNOT-20, which has been validated by Piccirillo et al. [18], and to which two cardinal CRS symptoms, "stuffed nose" and "difficulty to feel smells or tastes", have been added [19]. The resulting SNOT-22 was validated in English by Hopkins and colleagues [4]. SNOT-22 covers a broad range of health-related QoL problems, including physical problems, functional limitations and emotional consequences [19]. The questionnaire is converted into a score of 0-110, with higher scores indicating a greater impact on QoL. All questions are based on a 0-5 scale, where 0 defines no problems with the given symptom and 5 defines the maximum problems. According to Feng et al., the outcomes it measures can be divided into four different clinical subscales: sleep, nasal, otologic/facial pain, and emotional symptoms (Cronbach's alpha > 0.7) [7]. The translation and cultural adaptation of the SNOT-22 questionnaire was carried out in accordance with the guidelines and standards for the translation and cultural adaptation of PROMs as recom-

mended by the ISPOR Task Force [20]. For the questionnaire all rights are reserved; Copyright 2006, The Washington University in St. Louis, Missouri.

Statistical analysis

The data were analysed using the statistical software R (version 3.5.2). Utilising the libraries *psych, nFactor and FactoMineR,* Principal Component Analyses (PCA) and Exploratory Factor Analyses (EFA) were conducted. To determine the number of main components, graphical and non-graphical PCAs were used, including Scree Plots and the analyses of the models Eigenvalues, Parallel Analysis and the determination of optimal coordinates using the methods suggested by Kaiser [21] and Cattell [22]. For the latter EFA, we used the "standard" regression estimation suggested by Thomson [23], while the Varimax procedure was chosen for rotation (although we cannot be certain that the main components are actually independent). Generally, this assumption can be expected to be met, when variables only (significantly) load on one particular factor (above |0.3|) while having "zero-loadings" on any other factor. Furthermore, factors are expected not to be described by all existing variables, if there is more than one factor. If the assumptions are not met, the influence of particular variables on any factor may be over- or underestimated, which may lead to false conclusions. The underlying results show that the assumption is met for most variables, while there are some that load on more than one particular factor. However, in those cases, the difference in loadings is distinctive enough to assume that the decision for a particular variable to load on a factor may still be valid.

After the initial PCAs and EFAs, the two main components indicating a physical and a psychological constituent were identified. Since our interest was also to explore which demographics contribute to which part of these components, a subdivision of the SNOT-22 into two sub-indices was performed and regression analyses as well as students t-tests and tests for correlations of key-characteristics were conducted. For that purpose, we rescaled the sub-indices to a range from 0-110 to have a better comparability towards the total outcomes of SNOT-22. Aside from the coefficients, residual standard errors, results of the students' t-statics and p-values are reported below. A p-value less than 0.05 was considered statistically significant.

Results

Clinical characteristics

1,000 participants (500 males and 500 females) were sampled. The mean age of the participants was 44.3 ± 14.2 years. The response rate is not reported since participants belong to a non-probabilistic open access panel with quoted parameters and a fixed sample size. Participants were sampled from an existing (opt-in) access panel until a particular quota was filled.

Influence of sociodemographic aspects on the overall, psychological and physiological assessment

Regarding the influence of the sociodemographic aspects on the overall, psychological and physiological assessment measured by SNOT-22, age and female gender significantly affected the overall and psychological component ($p < 0.01$), whereas the physiological component was only influenced by age. Tests for correlation showed only a low, but significant linear relationship in case of age (overall: $r = -0.09$; $p = 0.006$; physical: $r = -0.09$; $p = 0.006$; psychological: $r = -0.07$; $p = 0.02$), however, the regression analysis (Tab. I) showed a significant effect on the magnitude of the SNOT-22 values. Old age is defined as older than 50 years and young age as less than 50 years. There was a negative linear relationship between the age and the SNOT-22 score: as the age increased, the SNOT-22 score decreased, indicating higher levels of satisfaction (Fig. 1A). Young and old participants differed significantly in results of SNOT-22 overall score (21.4 [± 20.6] *vs* 18.3 [± 17.5]), psychological (27 [± 27.2] *vs* 23.5 [± 23.4] and physiological (17.6 [± 19.1] *vs* 14.6 [± 15.8]) ($p < 0.01$). Moreover, male participants had lower SNOT-22 questionnaire results than female participants (Fig. 1B). Comparing men (n = 500) and women (n = 500) by t-test, they differed highly significantly from each other regarding the SNOT-22 overall (18.5 [± 19.2] *vs* 21.8 [± 19.6]) and psychological components (22.6 [± 25.3] *vs* 28.7 [± 27.3]) ($p < 0.01$), but not concerning the SNOT-22 physiological aspect (15.7 [± 17.7] *vs* 17.1 [± 18.1]) ($p = 0.20$). No influence of marital status, residence state, educational level, or employment status was ascertainable.

PCA of the SNOT-22 and EFA of the identified two-domain SNOT-22 structure

In this study, the 22 items were methodologically reduced into subsets of symptoms by using PCA. The PCA proposed at least two SNOT-22 domains ("physiological well-being" and "psychological well-being"), which explained 65% of the total variance. All factor loadings were > 0.5.

Graphical (Scree and Biplot; Fig. 2), as well as non-graphical attempts (Fig. 3), were used (Parallel Analysis and Optimal Coordinates) to distinguish the number of major components contributing to the overall SNOT-22-Score. The graphical analysis suggested three major components, whereas non-graphical suggested only two. Therefore, the EFA was calculated separately for two and three components. However, the inclusion of a third component did lit-

Table I. Regression-Table of overall SNOT-22 values, physical and psychological well-being by sociodemographic characteristics.

	SNOT-22	Physical well-being	Psychological well-being
Constant	29.483***	17.633**	46.601***
	(7.933)	(7.333)	(10.732)
Age	-0.170***	-0.131**	-0.227***
	(0.057)	(0.053)	(0.077)
Gender: female	3.555***	1.935	5.894***
	(1.307)	(1.209)	(1.769)
Marital status: married	0.651	1.485	-0.554
	(1.513)	(1.398)	(2.046)
Marital status: divorced	2.216	1.067	3.876
	(2.156)	(1.993)	(2.917)
Marital status: widowed	-2.995	-1.822	-4.690
	(4.162)	(3.847)	(5.630)
State: Bavaria	-4.916*	-3.966	-6.287
	(2.861)	(2.645)	(3.871)
State: Berlin	-2.038	-2.451	-1.441
	(4.390)	(4.058)	(5.939)
State: Brandenburg	-2.114	-0.750	-4.083
	(4.545)	(4.201)	(6.148)
State: Bremen	-2.915	-3.646	-1.859
	(5.160)	(4.770)	(6.981)
State: Hamburg	-5.244	-5.243	-5.244
	(3.463)	(3.201)	(4.684)
State: Hess	-6.583**	-7.607***	-5.104
	(3.077)	(2.845)	(4.163)
State: Mecklenburg Western Pomerania	-5.483	-5.566	-5.363
	(5.164)	(4.774)	(6.986)
State: Lower Saxony	-2.395	-1.642	-3.482
	(3.067)	(2.835)	(4.149)
State: Northrhine-Westphalia	-2.139	-2.868	-1.086
	(2.798)	(2.587)	(3.786)
State: Rhineland Palatinate	-2.008	-1.310	-3.016
	(3.154)	(2.916)	(4.267)
State: Saarland	-1.826	0.660	-5.418
	(4.119)	(3.808)	(5.572)
State: Saxony	-3.165	-2.900	-3.548
	(3.569)	(3.299)	(4.828)
State: Saxony-Anhalt	-6.640	-5.700	-7.997
	(4.363)	(4.033)	(5.903)
State: Schleswig-Holstein	-0.954	-2.623	1.457
	(3.321)	(3.069)	(4.492)
State: Thuringia	-2.772	-3.014	-2.422
	(3.860)	(3.568)	(5.222)
Migration (if true) within EU	-0.120	-1.853	2.384
	(4.528)	(4.185)	(6.125)
Migration (if true) outside EU	-2.082	1.277	-6.934
	(4.205)	(3.887)	(5.689)

continues ▶

Table I. Regression-Table of overall SNOT-22 values, physical and psychological well-being by sociodemographic characteristics (*follows).*

	SNOT-22	Physical well-being	Psychological well-being
Education: low	-3.545	4.501	-15.168*
	(6.316)	(5.839)	(8.544)
Education: mid	-4.426	3.785	-16.286*
	(6.340)	(5.860)	(8.576)
Education: high	-5.259	4.238	-18.976**
	(6.364)	(5.883)	(8.609)
Employment: not/no longer employed	5.573	2.727	9.684*
	(4.246)	(3.925)	(5.744)
Employment: sometimes	2.895	0.415	6.478
	(4.643)	(4.292)	(6.281)
Employment: part-time	0.138	-1.533	2.552
	(4.358)	(4.029)	(5.896)
Employment: full-time	3.690	2.698	5.123
	(4.182)	(3.866)	(5.658)
Observations	1,000	1,000	1,000
Log likelihood	-4,367.375	-4,288.756	-4,669.524
Akaike's information criterion	8,794.751	8,637.513	9,399.048

*Significance: * p < 0.05; ** p < 0.01; *** p < 0.001.*

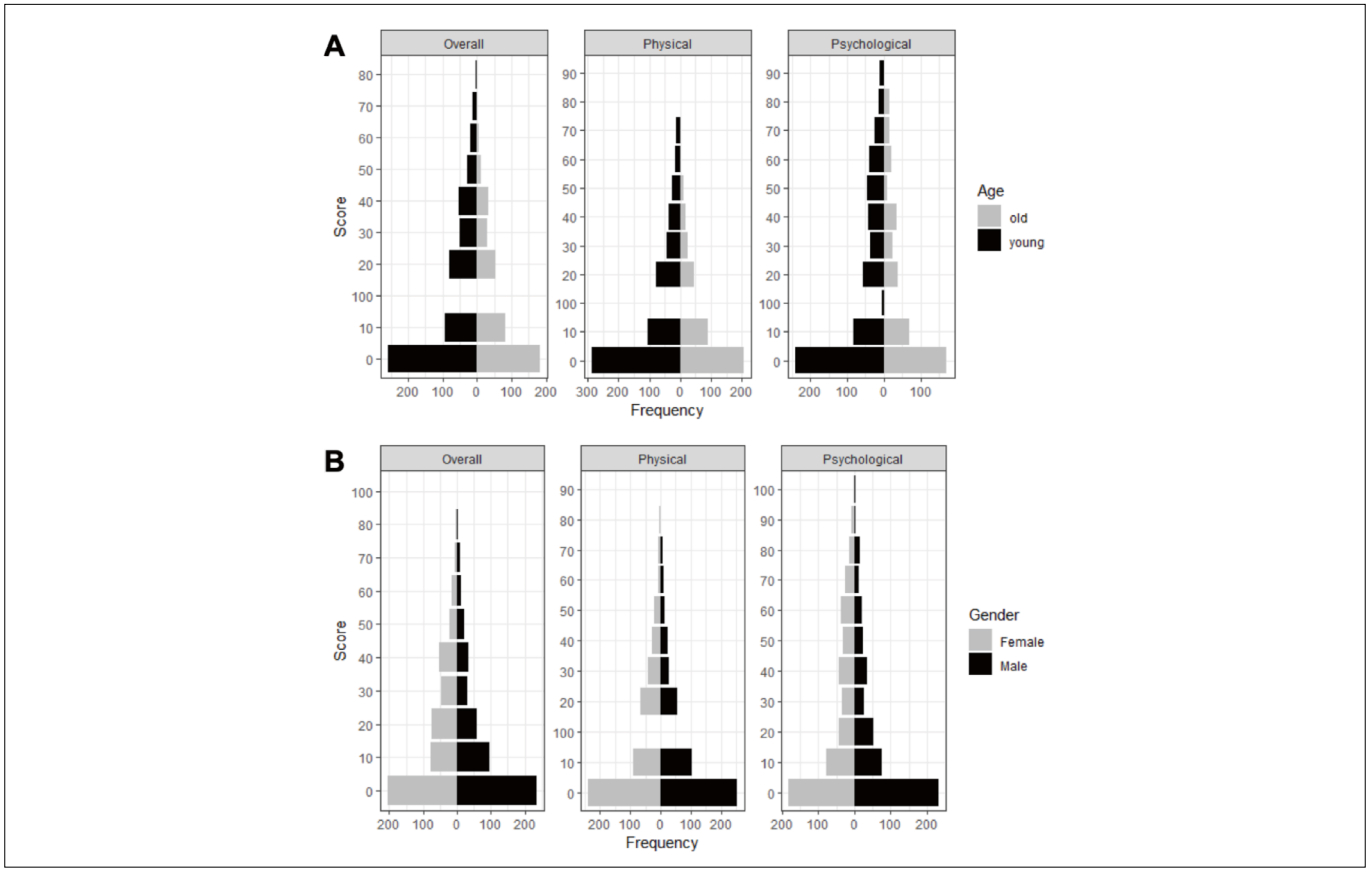

Figure 1. Forest plot showing the association of the SNOT-22 with age (**A**) and gender (**B**). The questionnaire score is plotted on the y-axis, the frequency of score responses on the x-axis. Lower scores of SNOT-22 signify a more positive rating indicating higher levels of satisfaction.

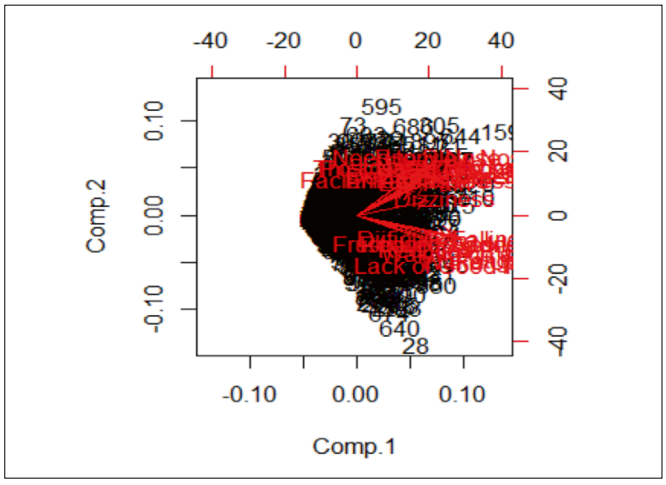

Figure 2. Biplot figure of our two-factor Principal Component Analysis. It is clearly visible that the participant cohort is divided in two groups concerning the SNOT-22 questionnaire. Comp. 1 and Comp. 2 are the first two Components that will later be used as the sub-indices physiological and psychological well-being. The "cloud" of numbers reflects the observations and their respective case number, whereas the different variable names are represented in red. The arrow that stems from the graphs centroid and joins the variable name can be used to determine the relatedness between the variables. The closer they are, the higher the (positive) correlation between these variables. Arrows that oppose each other in a 90°-angle can be considered as uncorrelated. Arrows that go into a different direction are negatively correlated.

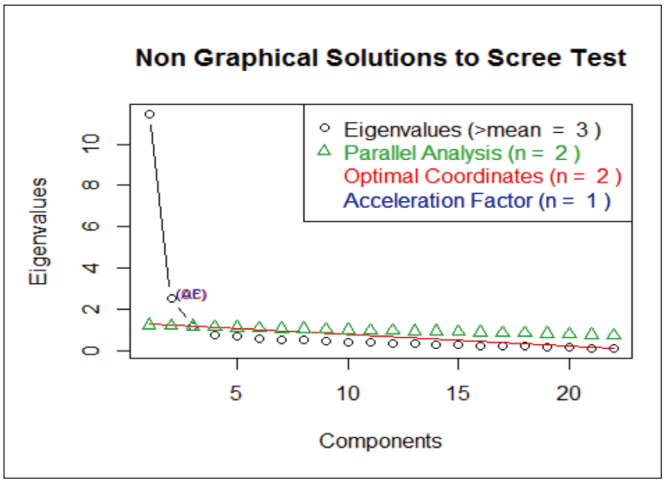

Figure 3. Non-graphical analysis as elbow figure. The black curve, illustrating the Eigenvalues in descending order, would suggest the inclusion of 3 main components, since any further Eigenvalues are below one. However, the parallel analysis (green), comparing the actual matrix of Eigenvalues to a Monte-Carlo-simulated matrix of the same size, shows that only the EVs of two main-components are above the 95th percentile. The same number of components is suggested in regard of the EVs' gradients and the optimal coordinates (red), whereas the Acceleration Factor (blue) shows that the major shift in the slope of this curve can be seen after the first component.

tle to improve the overall analysis. Indeed, using the third component by individual and variable PCA factor map, a clear assignment of test score categories could not be produced, while the joint distributions of the factor loadings seemed rather heterogeneous for all main components that included the third one. In contrast to this, an individual and variable two-components-factor analysis showed a clustering of variables on two main components. This makes PCA of utmost importance as 'hypothesis generating' tool creating a simple and clear two-factor construct including items of physical well-being (factor 1) and items of psychological well-being (factor 2), as shown in Table II.

Discussion

To assess the HRQoL in CRS, the SNOT-22 has become the reference questionnaire [4]. At present, the literature still lacks normative values of SNOT-22 in a European general population with an adequate sample size. Previous major fields of studies using SNOT-22 was rather on comparing pre- and postoperative HRQoL outcome of patients undergoing FESS [4,5]. Hopkins et al., who were the first to validate the SNOT-22 in the United Kingdom, employed the questionnaire in 2,077 surgical patients and obtained a preoperative score of 41.7 [4] and an overall SNOT-22 score of 9.3 in 116 healthy participants. A first cross-sectional study on normative values with an adequate sample size of 539 healthy volunteers, selected according to gender and age, was performed in Brazil by Gregorio et al. who concluded that the range of 0-8 points seemed to be more suitable as a "normal" value for the SNOT-22 instrument [24]. Whether this is also true for Europeans needed to be ascertained.

In our study, a SNOT-22 score of 20.2 ± 19.4 has been detected in 1,000 healthy Europeans, who were quoted to relevant population distributions of the German Microcensus. That our normative values are higher than previously reported [4,24-28] could be due to the fact that the questionnaire had general health domains such as "fatigue" or "difficulty to sleep", which may be associated with other non-reported or not-investigated medical conditions. Moreover, the different SNOT-22 standard scores can be associated with the difference in life and culture between the diverse nations. Additionally, we considered this reference cohort to be a "healthy" cohort. Thus, the medical history of comorbidities (allergy, asthma and aspirin sensitivity) or previous operations/trauma was not queried as our priority in recruiting participants for the study was to obtain an adequate population group that corresponded to the German Microcensus in terms of characteristics such as age, gender, level of education and region. However, the presence of comorbidities

Table II. SNOT-22 divided by two main components: depending on the higher value, the variable was assigned to the respective factor 1 (physical well-being item) or factor 2 (psychological well-being item) after explorative factor analysis.

SNOT-22	Factor 1 (physical well-being items)	Factor 2 (psychological well-being items)
Need to blow nose	0.63	
Nasal blockage	0.58	0.34
Sneezing	0.64	
Runny nose	0.69	
Cough	0.64	
Postnasal discharge	0.75	
Thick nasal discharge	0.78	
Ear fullness	0.70	0.32
Dizziness	0.56	0.44
Ear pain	0.71	
Facial pain or pressure	0.73	
Decreased sense of smell/taste	0.62	
Embarrassed	0.67	
Difficulty falling asleep	0.35	0.69
Waking up at night		0.72
Lack of good night's sleep		0.82
Wake up tired		0.85
Fatigue		0.88
Reduced productivity	0.31	0.82
Reduced concentration	0.34	0.78
Frustrated, restless, irritable	0.35	0.76
Sad	0.32	0.70

known to affect SNOT-22 results could play a role as potential confounders**.** Here, we used a well-established study design with a large sample size of 1,000 participants that were recruited by an international organisation for standardisation (ISO)-certified online access panel for market and social science research. We assumed that the decision to participate in the Respondi panel was not correlated to anything that may affect SNOT-22 scores. Our reference cohort thus corresponds to a patient cohort most closely approximating a probabilistic patient cohort compared with control cohorts used in other studies. The way the healthy subjects were selected in further studies, only by the response of the subjects, may have included possible bearers of CRS who did not have their formal diagnosis and carries the risk of bias.

Regarding the sociodemographic aspects, we could show that age and female gender significantly affected the overall and psychological component, whereas the physiological component was only influenced by age. Old and male participants had lower SNOT-22 results than young female volunteers, indicating a higher level of satisfaction. This is in line with previous studies [24,29]. Older people may be more likely to experience facility in adapting psychologically to major changes in functional disabilities than younger patients do. From a sociologic standpoint, women have historically been considered more likely to report symptoms, seek medical care, and give poorer self-evaluation of health, which may bias data toward a greater effect of CRS on QoL in women [30]. Further QoL studies reported that women have significantly lower QoL for the same objective level of disease [31], whereas other studies found no difference when controlling for depression or analysing only disease-specific variables [32]. Gender differences in CRS are poorly understood [33], strongly paced and merit further study.

Because groupings of highly correlated symptoms were apparent from the SNOT-22 questionnaires, nowadays numerous PCA and EFA, proposing four SNOT-22 domains, "nasal symptoms", "otologic symptoms", "sleep symptoms", and "emotional symptoms", have already been carried out [7,19,34]. Nevertheless, ambiguous factor loadings and problematic item-domain assignments remained. "Facial pain or pressure" was allocated to the "otologic symptoms"-domain, however, this may better fit into the "nasal symp-

toms". "Reduced productivity", "reduced concentration" and "frustrated/restless/irritable" as cardinal symptoms of depression [35] assigned to "sleep symptoms", although these domains assigned better to "emotional symptoms" [34]. Feng et al. validated the subdomain structure of the SNOT-22 in an American patient collective by CFA and underlined that the use of PCA and EFA has resulted in inconsistent clustering patterns of CRS symptoms throughout the literature [7]. Since we intended to initially explore how data for the SNOT-22 are related and which dimensions could be determined, we preferred PCA together with EFA over CFA. However, a CFA may have been useful if we had had a particular model on how the data are structured. Moreover, the majority of such factor analyses have mainly been performed in non-European CRS patients [7,19], while European data are lacking [34]. Here, we are pursuing different goals than our predecessors by exploring the SNOT-22's underlying factorial structure in a healthy middle-European reference cohort. Since the third factor only provided about 5% more of explained overall variance, we suggested a two-principal factor concept divided into "physiological well-being" and "psychological well-being". A plausible explanation for disparately reported SNOT-22 subdomain structures could be the presence of confounding variables such as environment, socioeconomic status, cultural differences, or climate (United States *vs* Europe) [7]. Moreover, it might also be possible for the healthy reference cohort to differ in that case from a patient cohort as well. The 22 items of the SNOT-22 can be logically assigned to the respective two subdomains, except for "difficulty falling asleep" loading on the "psychological" factor and feeling "embarrassed", which fitted into the "physical" component. However, we can share these assignments. Patients with impaired psychological well-being might have difficulty falling asleep because they feel stressed, sluggish, anxious, and sad. Feeling "embarrassed" causes not only psychological, but also physiological stress reactions. Indeed, CRS has a substantial negative health impact, adversely affecting mood, physical functioning and social functioning [36].

A weakness of our study is that the sample was a non-probabilistic quota sample, so the data is more suited to descriptive analysis; inference cannot be calculated. Therefore, we have to assume that SNOT-22 scores are independently distributed between those that opt-in and those that do not. Another limitation of our study is the homogeneity of the European reference cohort presented here, which may not be comparable to a more diverse or ethnic patient population. Minimising this demographic influence, a proportion of persons with a migration background was included in our participant recruitment. In addition, influential factors such as allergy, previous operations, nose/facial trauma, affective disorders, or asthma were not included in our SNOT-22 analysis, which is a further weakness of our study. Our primary aim was to include presumed healthy study participants in our study who, because they were not affected by symptoms and did not know our study objective (type of blinding), had no incentive to bias the SNOT-22 results or to complete the SNOT-22 responses in a directional manner. This should avoid a confounding factor of selection bias or response shift bias phenomenon, that often occur in patient-reported outcome measures [37,38]. Our study has several strengths. This is the first study measuring the impact of CRS symptoms in healthy volunteers by using SNOT-22. In addition to the Lund-Mackay score > 1 and SNOT-22 value > 20 after a cycle of medical therapy appropriating indications to FESS according to the EPOS guideline [3], normative SNOT-22 scores can also be used as an additional decision-making tool. Comparing SNOT-22 of CRS patients with normative values explains any differences in scores better than simply comparing scores before and after surgery. Indeed, preoperative CRS patients are not "normal" because they carry the physical and psychological burdens of CRS. Normative scores advance the understanding of expected patient outcomes, improve the patient-physician shared decision-making process, and may help to reduce the risk of unwarranted practice variation in the future.

Conclusions

According to the EPOS guidelines [3], outcomes in patients undergoing FESS should be evaluated with PRO instruments, such as the SNOT-22. PRO instruments generate useful data regarding satisfaction and FESS-related QoL. This study presents the first known normative values for the SNOT-22, which will be useful for head and neck surgeons and researchers in providing a clinical context to interpret SNOT-22 data.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

MP: designed and coordinated the study, participated in data acquisition and analysis, interpreted the data and drafted the manuscript; MS: participated in data interpretation and statistical analysis; CC: interpreted data and revised the manuscript; PKP: revised the manuscript; IB: participated

in data interpretation and revision of the manuscript; KZ: designed and coordinated the study, participated in data acquisition and analysis, critically revised the manuscript for important intellectual content.
The authors made substantial contributions to the study.

Ethical consideration

This study was approved by the Ethics Committee of the Medical Faculty at the University of Heidelberg (project no. S-143/2020).
The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.
All patients were informed about the study aims and protocol, and participants were enrolled after giving informed written consent.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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