Multi-institutional minimal clinically important difference of the 22-item Sinonasal Outcome Test in medically managed chronic rhinosinusitis*

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Abstract

Background: With a rapid proliferation of clinical trials to study novel medical treatments for CRS, the objective of this study was to study the minimal clinically important difference (MCID) of the 22-item Sinonasal Outcome Test (SNOT-22) in medically-managed CRS patients.

Methods: A total of 183 medically-treated CRS patients were recruited. All patients completed a SNOT-22 at enrollment and subsequent follow up visit. Distribution and anchor-based methods were used for MCID calculation. These data were combined with data from a previously published study on SNOT-22 MCID in 247 medically managed CRS patients to determine a final recommended MCID value using the combined cohort of 430 patients.

Results: In our cohort, distribution- and anchor-based methods—using both sinus-specific and general health anchors—provided greatest support for a 12-point SNOT-22 MCID, which had approximately 55% sensitivity but 81% specificity for detecting patients explicitly reporting improvement in their sinus symptoms and general health. In the combined cohort of 430 patients, we also found greatest support for a 12-point SNOT-22 MCID, which had approximately 57% sensitivity and 81% specificity for detecting patients explicitly reporting improvement in their sinus symptoms and general health. We also find evidence that the MCID value may be higher in CRS patients without nasal polyps compared to those with nasal polyps.

Conclusions: Our results - which include data from patients from two different institutions and regions - confirm a SNOT-22 MCID of 12 in medically managed CRS patients. The SNOT-22 MCID was specific but not sensitive for identifying CRS patients experiencing improvement in symptoms or general health.

Key words: chronic rhinosinusitis, SNOT-22, MCID, minimal clinically important difference, quality of life, patient-reported outcomes

Introduction

Chronic rhinosinusitis (CRS) is an inflammatory disorder of the paranasal sinuses that has the primary negative impact of significantly reducing quality of life (QOL) in affected patients and which has a tremendous cost to society [1-4]. While several distinct and independent mechanisms have been identified for how CRS affects patients to reduce QOL [5-8], the chronic symptomatology associated with CRS is the primary driver of decreased QOL [9,10]. Chronic symptoms associated with CRS include not only the classic sinonasal symptoms that are diagnostic and most perceived by patients [1,2,11], but also extra-nasal symptoms in the domains of craniofacial pain, poor sleep quality and mood disturbance [12-14].

The central role of patient-experienced symptoms and QOL in CRS position these disease manifestations as the primary targets for treatment. Moreover, patient-reported outcome measures

(PROMs) have become critical to quantifying CRS disease (e.g. symptoms and QOL) burden and to judging whether a treatment has had a meaningful impact. However, the central role of PROMs in the assessment and study of CRS has rightfully called attention to the distinction between statistically significant differences versus clinically meaningful differences in PROM scores. Apropos to this discussion is the concept of the minimal clinically important difference (MCID), which has been defined for PROMs as "a difference [in] score that is large enough to have an implication for the patient's treatment or care" [15]. Over time, various methodologies have been developed for the calculation of the MCID, although anchor-based methods remain preferred [16].

The 22-item Sinonasal Outcome Test (SNOT-22) is a validated PROM that assesses CRS-specific QOL, which serves to quantify the burden of symptoms in the domains of nasal symptoms, craniofacial discomfort, poor sleep quality, and mood disturbance [17,18]. The SNOT-22 is a frequently used PROM for the assessment of outcomes after treatment for CRS [19]. As is the case with all PROMs, the MCID of the SNOT-22 is dependent on patient expectations in relation to the treatment that is being given [16]. As expected, divergent values of the SNOT-22 MCID have been reported in CRS patients treated with the distinct treatment modalities of endoscopic sinus surgery (ESS) [17,20] vs. medical management [21]. Given the recent proliferation of clinical trials studying novel medical therapies for CRS [22,23], an understanding of the MCID for medically managed CRS patients is now greater than ever. Although the MCID of the SNOT-22 in medically-managed CRS patients has been previously reported as 12 [21], the objective of our study was to determine whether this result held true in an independent, geographically and culturally distinct cohort of patients. Moreover, by combining our data with the data from this previous study of SNOT-22 MCID in medically managed CRS patients [21], we sought to determine an MCID value of the SNOT-22 for medically managed CRS patients that would be broadly generalizable.

Materials and methods

Study participants

This study was approved by the University of Cincinnati College of Medicine Institutional Review Board (2019-0397). Adult patients of age 18 years or older with consensus guideline criteria for CRS [24] were recruited prospectively and provided informed consent for inclusion in this study. In order to remove the confounding effect of recent ESS, patients who had ESS within the previous 6 months were also excluded from enrollment.

Study design and data collection

This is a prospective observational study and data were combined with those of a previously published prospective longitudinal study. For this study, all patients who were enrolled were managed medically during the study period. Medical management uniformly included intranasal corticosteroids (spray or irrigations) and at least daily saline irrigation, which are both supported by level 1 evidence in the long-term medical management of CRS [1,2]. Other elements of medical management included short courses of systemic antibiotics or corticosteroids, and biologics as needed based on patient-specific basis and consistent with the recommended use of these medications for CRS patients [1,2]. Participants were assessed at two time points - enrollment and the next follow up visit, which was between one and twelve months after enrollment. A follow up time period of up to twelve months was allowed in order to include real world follow up times and also to mirror the prior study by Phillips et al. [21]. The length of time between enrollment and the next follow up visit was determined on a patient-by-patient basis, but no participant underwent ESS during the study period.

At enrollment, the age, gender and smoking history of all participants were recorded. Any participant who reported current or former tobacco use was considered to be a smoker [25,26]. All participants completed a SNOT-22. All participants were also assessed by the evaluating rhinologist for a history of 1) aeroallergen hypersensitivity based on formal allergy testing, 2) asthma, and 3) nasal polyps at the time of enrollment based on nasal endoscopy. At the next follow up, participants completed another SNOT-22 but also answered two additional questions, which were used as anchors for the subsequent MCID calculation as previously described [17,21]. The first anchor question was a sinus-specific anchor which asked patients to compare their sinus symptoms at the follow up visit compared to the time of enrollment. The next anchor question asked participants to compare their general health at the follow up visit compared to the time of enrollment. Participants answered both anchor questions on the same 5-item scale: "Much worse", "A little worse", "About the same", "A little better", and "Much better" [10].

Statistical analysis

All analyses were performed with the statistical software package R (www.r-project.org). All differences in SNOT-22 are reported as post-treatment minus pre-treatment SNOT-22 score, such that a negative change in the SNOT-22 score indicates improvement while positive change indicated worsening. Descriptive statistics, including the use of unpaired t-test and analysis of variance (ANOVA) were performed. This study was powered to detect differences of large effect size (d=0.8) in the change of SNOT-22 scores in participants answering their anchor questions as "About the same" compared to "A little better" with a power of 0.8 at a significance level of 0.05, reflecting an anchor-based method of MCID calculation. Data from our study participants were also combined with those of the 2018 study Phillips et al, which previously investigated the MCID of the SNOT-22 in medically managed CRS patients using the same experimental design [21].

Table 1. Clinical and demographic characteristics of study participants at enrollment.

	All study participants (N = 430)	Our study participants (N = 183)	Phillips et al participants (N = 247)	P value*
Demographics				
Age, mean in years, (SD)	52.0 (15.9)	49.5 (15.5)	53.9 (16.0)	0.004
Gender				0.205
Male	51.9%	48.1%	54.7%	
Female	48.1%	51.9%	45.3%	
Smoking	30.2%	27.3%	32.4%	0.289
Comorbidities				
Aeroallergen hypersensitivity	56.5%	67.2%	48.6%	< 0.001
Asthma	28.6%	23.5%	32.4%	0.052
Aspirin sensitivity	4.0%	2.7%	4.9%	0.323
CRS characteristics				
Nasal polyps	44.0%	36.6%	49.4%	0.002
Previous sinus surgery	38.8%	37.2%	40.1%	0.278
SNOT-22 score, mean (SD)				
Pre-treatment	40.5 (22.4)	45.1 (20.5)	37.1 (23.2)	< 0.001
Post-treatment	32.6 (20.7)	37.6 (20.9)	28.9 (19.8)	< 0.001
Sinus-specific anchor response				0.518
Much worse	4.2%	2.7%	5.3%	
A little worse	13.0%	12.6%	13.4%	
About the same	40.0%	38.3%	41.3%	
A little better	21.2%	24.0%	19.0%	
Much better	21.6%	22.4%	21.1%	
General health anchor response				0.037
Much worse	1.9%	1.1%	2.4%	
A little worse	9.8%	7.1%	11.7%	
About the same	45.6%	43.7%	47.0%	
A little better	22.8%	29.5%	17.8%	
Much better	20.0%	18.6%	21.1%	

*Comparison between our cohort and Phillips et al. [21].

The SNOT-22 MCID was calculated using three different methods [16]. The first method was the distribution-based method that was calculated as half of the standard deviation of participants' SNOT-22 scores at enrollment. The second method was an anchor-based method whereby the MCID was calculated as the difference in mean SNOT-22 score change between participants responding with "About the same" compared to those responding with "A little better" [16,27,28]. The third method for calculating MCID used Receiver Operator Characteristic (ROC) curve analysis [16,27]. The ROC method identified the change in SNOT-22 score, which maximized the sum of sensitivity and specificity of identifying participants who reported an improvement ("A little better" or "Much better") in their sinus symptoms or general health. The area under the ROC curve (AUC) was calculated with the trapezoid rule and the 95% confidence interval of the AUC was calculated by performing 2000 bootstraps of the data. The 95% confidence interval around threshold changes in SNOT-22 score maximizing the sum of sensitivity and specificity was performed by bootstrapping the data 1000 times.

Results

Study participants

A total of 183 participants were recruited and their baseline clinical and demographic characteristics are described in Table 1, along with the characteristics of participants from the 2018 Phillips et al. study [21] and the overall cohort of patients from both of these studies. In comparison to participants from Phillips et al. [21], our participants were younger, had more aeroallergen hypersensitivity, lower prevalence of polyp disease, and higher pre-treatment and post-treatment SNOT-22 scores. The mean time between enrollment and follow up visits was 69 days (standard deviation [SD]: 39 days) for our participants, 167 days (SD: 97 days) for the Phillips et al. cohort and 125 days (SD: 92) for all study participants. The mean change in SNOT-22 score between study time points was -7.4 points (SD: 16.7) for our participants, -8.2 (SD: 19.7) for the 2018 Phillips et al. cohort and -7.9 (SD: 18.4) for all study participants.

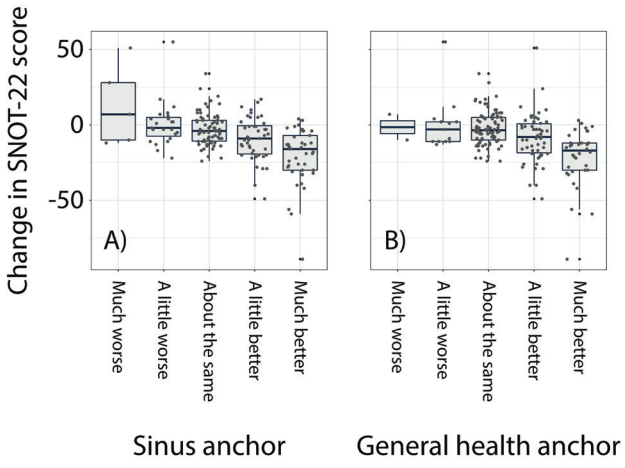

Figure 1. Boxplot with individual data points overlaid showing the distribution of changes in SNOT-22 score for each corresponding (A) sinus-specific and (B) general health anchor response for our study participants.

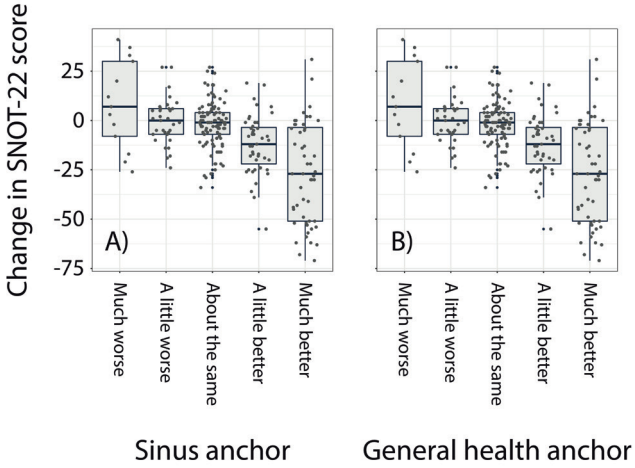

Figure 2. Boxplot with individual data points overlaid showing the distribution of changes in SNOT-22 score for each corresponding (A) sinus-specific and (B) general health anchor response for the 2018 Phillips et al. [21] study participants.

Determining the MCID of the SNOT-22 using a distribution-based method

In our participants, the SD of baseline SNOT-22 scores was 20.5 so the distribution-based MCID (0.5×SD) is calculated to be 10.3, which effectively translates to an MCID of 11 that had 56.4% sensitivity and 75.5% specificity for detecting patients who reported improvement in sinus symptoms and 54.5% sensitivity and 74.7% specificity for detecting patients who reported improvement in general health. The distribution-based MCID of the SNOT-22 in the 2018 Phillips et al. cohort was previously reported to be 11.6, which had 59.6% sensitivity and 81.8% specificity for detecting patients who reported improvement in sinus symptoms and 57.3% sensitivity and 79.5% specificity for detecting patients who reported improvement in general health. In combining our study participants with those of the 2018 Phillips et al. cohort, the distribution-based MCID is calculated to be 11.2, effectively translating to an MCID of 12, which had 58.2% sensitivity and 81.7% specificity for detecting patients who reported improvement in sinus symptoms and 56.0% sensitivity and 80.1% specificity for detecting patients who reported improvement in general health.

Determining the MCID of the SNOT-22 using an anchor-based method: differences between anchor responses

The changes in SNOT-22 scores reported by patients for each sinus-specific anchor response and general health-specific response are shown in Figures 1-3 and Table 2. Across the responses of the sinus-specific anchor and general health-specific anchor, there were statistically significant differences in SNOT-22 change for our participants, the 2018 Phillips et al. participants and all participants combined ($p<0.001$ in all cases by ANOVA). As a reflection of the SNOT-22 MCID, we then calculated the mean differences in SNOT-22 change between patients who reported their sinus symptoms and their general health to be "a little better" compared to "about the same". In our cohort, this difference was -6.5 points (95%CI: -1.5 to -11.5, $p = 0.011$) using the sinus anchor response (Figure 1a) and -6.3 points (95%CI: -1.2 to -11.4, $p = 0.015$) using the general health anchor response (Figure 1b). This translated to a 65.9% sensitivity and 64.3% specificity to detect patients experiencing improvement on the sinus anchor-based MCID and 63.6% sensitivity and 63.2% specificity to detect patients experiencing improvement on the general health anchor-based MCID. For the 2018 Phillips et al. participants, these differences were -10.5 (95%CI: -1.7 to -12.2, $p<0.001$) using the sinus anchor response (Figure 2a) and -8.3 (95%CI: -1.7 to -10.1, $p=0.002$) using the general health anchor response (Figure 2b), which translated to a 59.6% sensitivity and 80.4% specificity for the sinus anchor-based MCID and 59.4% sensitivity and 74.8% specificity for the general health anchor-based MCID to detect patients experiencing improvement. For all the participants (ours combined with the 2018 Phillips et al. participants), these differences were -8.7 (95%CI: -5.2 to -12.1, $p < 0.001$) using the sinus anchor response (Figure 3a) and -7.3 (95%CI: -1.9 to -9.2, $p < 0.001$) using the general health anchor response (Figure 3b), which translated to a 61.4% sensitivity and 73.6% specificity for the sinus anchor-based MCID and 61.4% sensitivity and 69.9% specificity for the general health anchor-based MCID to detect patients experiencing improvement.

Determining the MCID of the SNOT-22 using an anchor-based method: receiver operating characteristic curve analysis

We next used ROC curve analysis on anchor responses from our participants to calculate the SNOT-22 MCID. Using the sinus-specific anchor question, a change in SNOT-22 score of -11.5 points (95%CI: -6.5 to -17.5 points) maximized the sum of sensitivity

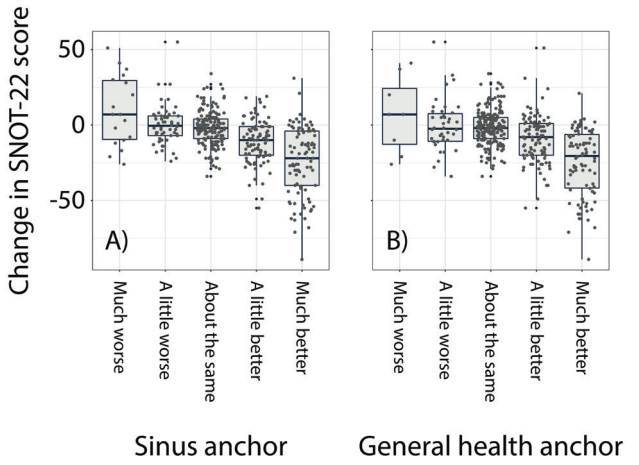

Figure 3. Boxplot with individual data points overlaid showing the distribution of changes in SNOT-22 score for each corresponding (A) sinus-specific and (B) general health anchor response for all study participants (our study participants and the 2018 Phillips et al. [21] study participants combined).

(56.5%) and specificity (81.6%) for identifying patients experiencing improvement (AUC=0.727, 95%CI: 0.653 – 0.801, p<0.001). Using the general health anchor, a change in SNOT-22 score by -11.5 points (95%CI: -6.5 to -16.5 points) also maximized the sum of sensitivity (54.5%) and specificity (81.1%) for identifying patients experiencing improvement (AUC=0.706, 95%CI: 0.631 – 0.782, p<0.001).

In the 2018 Phillips et al. participants, using the sinus-specific anchor, a change in SNOT-22 score of -12.5 points (95%CI: -3.5 to -23.0 points) maximized the sum of sensitivity (57.6%) and specificity (83.8%) for identifying patients experiencing improvement (AUC=0.768, 95%CI: 0.706 – 0.830, p<0.001). Using the general health anchor, a change in SNOT-22 score of -17.5 points (95%CI: -5.5 to -23.5 points) maximized the sum of sensitivity (49.0%) and specificity (88.7%) for identifying patients experiencing improvement (AUC=0.741, 95%CI: 0.676 – 0.806, p<0.001). In the combined group of participants (ours and the 2018 Phillips et al. participants), using the sinus-specific anchor, a change in SNOT-22 of -11.5 points (95%CI: -6.5 to -16.5 points) again maximized the sum of sensitivity (58.2%) and specificity (81.7%) for identifying patients experiencing improvement (AUC=0.751, 95%CI: 0.704 – 0.798, p<0.001). Using the general health anchor, a change in SNOT-22 score of -11.5 points (95%CI: -6.5 to -18.5) also maximized the sum of sensitivity (56.0%) and specificity (80.1%) for identifying patients experiencing improvement (AUC=0. 725, 95%CI: 0.676 – 0.774, p<0.001).

MCID of the SNOT-22 in chronic rhinosinusitis patients with and without polyps

Because it identifies an MCID value which maximizes the sum of sensitivity and specificity, we used the anchor-based, ROC method to determine a SNOT-22 MCID value in medically managed CRS patients with and without polyps (CRSwNP and CRSsNP, respectively) using all 430 study participants. Using the sinus-specific anchor in the CRSwNP group, a change in SNOT-22 score of -11.5 points (95%CI: -2.5 to -15.5 points) maximized the sum of sensitivity (60.5%) and specificity (85.1%) for identifying patients experiencing improvement (AUC=0.778, 95%CI: 0.707 – 0.849, p<0.001). Using the general health anchor in the CRSwNP group, a change in SNOT-22 score of -11.5 points (95%CI: -3.5 to -15.0 points) again maximized the sum of sensitivity (58.5%) and specificity (86.3%) for identifying patients experiencing improvement (AUC=0.765, 95%CI: 0.694 – 0.836, p<0.001). Using the sinus-specific anchor in the CRSsNP group, a change in SNOT-22 score of -14.5 points (95%CI: -9.5 to -18.5 points) maximized the sum of sensitivity (50.5%) and specificity (87.1%) for identifying patients experiencing improvement (AUC=0.732, 95%CI: 0.667 – 0.798, p<0.001). Using the general health anchor in the CRSsNP group, a change in SNOT-22 score of -16.5 points (95%CI: -6.5 to -19.5 points) maximized the sum of sensitivity (44.3%) and specificity (88.9%) for identifying patients experiencing improvement (AUC=0.700, 95%CI: 0.631 – 0.769, p<0.001). The difference in calculated SNOT-22 MCID between CRSwNP and CRSsNP patients was not statistically significant using the sinus-specific anchor (p=0.122) but was statistically significant using the general health anchor (p = 0.022).

Discussion

The SNOT-22 is a validated, high-quality PROM which reflects CRS symptom burden and CRS-specific QOL, and it is a preferred instrument for the measurement of CRS outcomes after treatment, whether medical or surgical [19]. The last several years has seen a proliferation of novel medical treatments for CRS [22,23,29]. Assessment of the safety and efficacy of these medications has required clinical trials and the subsequent cost-effectiveness determination of these medications has depended on their abilities to provide clinically meaningful improvements for patients. In this setting, PROMs—including the SNOT-22 in particular—have been absolutely necessary, with interpretation of PROM score changes needed with respect to their MCIDs. The MCID of a PROM is very dependent on the clinical context and the associated patient expectations, in which it is given [16]. While the MCID of the SNOT-22 has been well accepted as 8.9 for patients undergoing ESS [17], it has only been recent since an MCID for the SNOT-22 was reported as 12 points in medically managed CRS patients by Phillips et al. in 2018 [21]. In this study, we sought to more comprehensively determine and characterize the MCID of the SNOT-22 using an independent cohort of medically managed CRS patients. In our study participants, in the 2018 Phillips et al. [21] participants, and after combining our data with those of the 2018 Phillips et al. study (in order to provide a results from a more diverse multi-institutional, multi-regional and multi-cultural population), we again find that the

Table 2. Anchor-based changes in SNOT-22 score.

Our study participants					
Sinus-symptom anchor	Much worse	A little worse	About the same	A little better	Much better
Change in SNOT-22 score, mean (SD)	12.8 (26.7)	0.6 (15.1)	-2.7 (10.8)	-9.2 (14.2)	-20.5 (18.6)
General health anchor	Much worse	A little worse	About the same	A little better	Much better
Change in SNOT-22 score, mean (SD)	-1.5 (12.0)	0.5 (18.1)	-2.2 (11.5)	-8.5 (16.3)	-21.6 (19.2)
Phillips et al. participants					
Sinus-symptom anchor	Much worse	A little worse	About the same	A little better	Much better
Change in SNOT-22 score, mean (SD)	8.4 (22.7)	-0.3 (11.6)	-1.7 (11.7)	-12.2 (14.6)	-26.5 (25.4)
General health anchor	Much worse	A little worse	About the same	A little better	Much better
Change in SNOT-22 score, mean (SD)	9.7 (28.5)	-0.7 (16.4)	-1.7 (11.7)	-10.1 (16.0)	-27.3 (24.0)
All study participants					
Sinus-symptom anchor	Much worse	A little worse	About the same	A little better	Much better
Change in SNOT-22 score, mean (SD)	9.6 (23.2)	0.1 (13.1)	-2.1 (11.3)	-10.8 (14.4)	-23.9 (22.7)
General health anchor	Much worse	A little worse	About the same	A little better	Much better
Change in SNOT-22 score, mean (SD)	6.9 (25.0)	-0.3 (16.7)	-1.9 (11.6)	-9.2 (16.1)	-25.0 (22.3)

MCID of the SNOT-22 in medically managed CRS patients to most consistently be calculated as 12 points.

The MCID of the SNOT-22 has been previously investigated in CRS patients treated with ESS. In the 2009 study by Hopkins et al., which first described the psychometric validity of the SNOT-22 in over two thousand CRS patients undergoing ESS [17], the MCID of the SNOT-22 determined to be 8.9 using an anchor-based method. This study had strengths including the large sample size as well as the use of an anchor-based method, which is a preferred strategy for calculation of MCIDs. Moreover, although Hopkins et al. did not specify the use of distribution-based methods, the variance of pre-ESS SNOT-22 scores in their study participants suggests that distribution-based methods would have supported their estimate of 8.9, further lending support to their MCID estimate for CRS patients treated with ESS.

A subsequent and more recent study of 276 patients undergoing ESS used distribution-based methods solely also to find a SNOT-22 MCID of 9.0 [20]. The MCID of the SNOT-22 in medically managed CRS patients has also been previously studied. Phillips et al. studied 247 CRS patients who were treated medically and used distribution-based as well as anchor-based methods, using both sinus-specific and general health anchors to determine the SNOT-22 MCID as 12 points. A subsequent study by Chowdhury et al. used distribution-based methods only to study the MCID of the SNOT-22 in 120 CRS patients with medically recalcitrant CRS who elected to continue medical treatment rather than pursue ESS and reported the SNOT-22 MCID to be 8 in this population [30]. However, interpretation of these results was constrained by small sample size, inclusion limited to only medically recalcitrant CRS patients, and sole reliance on distribution-based methods. Distribution-based methods for MCID calculation are limited by dependence on the patient population being studied [31] and not accounting for patient-perceived improvement [32], and as a result, they are generally used to support the results of anchor-based methods rather than being used as primary methods for determining MCID [16].

In our study, we use a distribution-based method as well as two anchor-based methods to calculate the MCID of the SNOT-22 in a population of patients presenting with CRS who were treated with appropriate medical management. We found the greatest support for a SNOT-22 MCID of 12 points in these medically managed CRS patients from distribution-based and the anchor-based ROC methods, using both sinus-specific and general health-specific anchor questions. This support for the 12-point SNOT-22 MCID came from our cohort, the 2018 Phillips et al. cohort, as well as when we combined both of these cohorts, which originated from two culturally distinct geographic regions. In contrast, when we looked at the difference in the change in SNOT-22 scores in patients from our cohort reporting no difference in comparison to a little improvement in sinus symptoms or general health - another anchor-based method for MCID calculation - we calculated a 7-point MCID. However, this value had considerably lower specificity and only marginally better sensitivity compared to the 12-point MCID value, which was identified through multiple methods including the anchor-based ROC method which calculates MCID using a balanced approach to optimizing sensitivity and specificity. This variation in MCID calculation that we observed highlights the necessity of using different methods for calculating an MCID so that a spurious value is not identified by chance selection of one method and instead, an MCID value is determined through the convergence of results from multiple methods. Moreover, our results

also highlight the need for transparency in MCID calculation, including the reporting of different MCID calculations as well as their accuracy (e.g. sensitivity and specificity) for identifying patients experiencing clinically meaningful improvement, so that results can be fully interpreted and judged.

In light of our results, quantitative interpretation of change in SNOT-22 score in medically-managed CRS patients should be done so differently than in surgically-managed CRS patients based on different MCID values (12 vs. 8.9 respectively). While our underlying hypothesis was that differences in patient expectations may drive different MCID values in medically - vs. surgically-managed CRS patients, it is unclear why the MCID of medically-managed has consistently been found to be higher than surgically-managed patients. It is possible that patients who decide to undergo surgery and its inherent risks may be personally incentivized to feel improved after the experience. However, any explanation is conjecture at this point and more study is needed to understand why this MCID difference exists.

Although our results indicate that changes in SNOT-22 score, should be differentially interpreted in medically- vs. surgically-managed CRS patients with respect to MCID, it is also important for practitioners and researchers to be aware of the general limitations of MCIDs [16]. Our results also confirm previous findings that an MCID tends to be more specific than sensitive (21,33), and underscores the need to interpret PROMs scores in relation to an MCID with the understanding that there will be many patients who may not necessarily demonstrate an MCID in PROM score improvement but still experience clinically meaningful improvement [34].

Finally, our results also indicate the possibility that the SNOT-22 MCID in medically managed CRS patients may be slightly higher in CRSsNP compared to CRSwNP patients, for whom we also found support for a 12-point SNOT-22 MCID. Specifically, while we did not find a significant difference in SNOT-22 MCID using the sinus-specific anchor between CRSsNP and CRSwNP, we did find a significant difference using the general-health anchor. Previous studies have shown that CRSsNP and CRSwNP patients experience different profiles in CRS-associated symptoms, with CRSsNP experiencing more craniofacial discomfort symptoms and mood disturbance symptoms than CRSwNP [14,35]. Moreover, we have previously found evidence for the possibility that CRSwNP patients are more sensitive to changes in CRS symptoms with respect to how they judge their CRS symptom control, which may translate to smaller SNOT-22 score changes needed to experience clinically meaningful improvement [35].

Our results should be interpreted within the constraints of our study. Follow-up times in our study were up to 1 year (implemented to include real world follow up periods and to mirror the design of the 2018 Phillips et al. study), which could introduce recall bias in anchor responses. Although we have specifically studied this issue in the past and not found evidence of recall bias in anchor responses for follow-up time periods of up to 1 year [36], this is nevertheless a caveat of our study. Additionally, while all patients were treated with a regimen deemed to be reflective of appropriate medical management that was based on saline irrigations and intranasal corticosteroids, there was variability in exact medical treatment regimens. While different medical regimens could be associated with different patient expectations (which could impact MCID calculation), we anticipate that differences in patient expectations (and hence MCID calculation) would be much larger in comparing medically- vs. surgically-managed CRS patients.

Conclusion

Multiple MCID calculation methods, applied to patients from two different regions and treated at two different institutions, support a 12-point SNOT-22 MCID in medically managed CRS patients. This MCID value, like MCID values reported for other PROMs, is specific but not sensitive for detecting CRS patients who have experienced clinically meaningful improvement. Interpretation of SNOT-22 score changes in the context of this MCID should be considered with the caveat that a significant fraction of patients experiencing clinically meaningful improvement may have less than an MCID of improvement. Finally, the SNOT-22 MCID may be slightly higher in CRSsNP compared to CRSwNP but this distinction requires further study.

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Authorship contribution

KMP: concept of study, collection of data, analysis of results, write up of manuscript, critical review of all contents; FAH: collection of data, write up of manuscript, critical review of all contents; LMB: collection of data, write up of manuscript, critical review of all contents; KWS: collection of data, write up of manuscript, critical review of all contents; DTL: analysis of results, write up of manuscript, critical review of all contents; ARS: concept of study, collection of data, analysis of results, write up of manuscript, critical review of all contents.

Conflict of interest

The authors declare that there are no conflicts of interests regarding the publication of this paper.

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