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den Heijer, Marc C.; Joustra, Gonneke E.; Vermeulen, Karin M.; Korsten-Meijer, Astrid G.W.; Feijen, Robert A.

Published in:
Clinical Otolaryngology

DOI:
10.1111/coa.14158

Received: 13 July 2023 | Accepted: 17 March 2024

DOI: 10.1111/coa.14158

ORIGINAL ARTICLE

WILEY

Sinonasal inverted papilloma and predictors of health-related quality of life after endonasal endoscopic surgery: A prospective cohort study

Marc C. den Heijer[1,2] | Gonneke E. Joustra[1,2] | Karin M. Vermeulen[3] | Astrid G. W. Korsten-Meijer[1] | Robert A. Feijen[1]

[1]Department of Otorhinolaryngology – Head and Neck Surgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

[2]Graduate School of Medical Sciences, University of Groningen, Groningen, The Netherlands

[3]Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Correspondence
Marc C. den Heijer, Department of Otorhinolaryngology – Head and Neck Surgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
Email: m.c.den.heijer@umcg.nl

Abstract

Objectives: Existing knowledge on health-related quality of life (HRQoL) after surgical removal of sinonasal inverted papilloma (IP) is limited. Moreover, predictors for a better or worse post-operative HRQoL outcome are not known. Our aim was to assess HRQoL in all three health domains (physical, psychological, and social), track its post-operative trajectory, investigate if pre-operative observations could predict distinct post-operative HRQoL outcomes, and evaluate whether physicians' interventions could contribute to improved post-operative HRQoL.

Design: Prospective cohort study.

Setting: Tertiary referral hospital.

Participants: Seventy-four patients who underwent surgery for an IP were included. They were asked to fill in the Endonasal Endoscopic Sinus and Skull-Base Surgery Questionnaire (EES-Q) pre-operatively, and then 2 weeks, 3 months, and 1 year post-operatively.

Main Outcome Measures: Linear mixed models analyses were performed to evaluate the overall post-operative HRQoL and the separate health domains, as well as the impact of specific variables (sex, age, American Society of Anaesthesiologists [ASA] classification, smoker, Krouse staging, pre-operative EES-Q score, type of surgery, and post-operative antibiotics) on HRQoL improvement.

Results: The total EES-Q score ($p < .001$) as well as the physical ($p < .001$), psychological ($p = .049$), and the social ($p = .002$) domains significantly improved post-operatively. ASA classification ($p = .049$), pre-operative EES-Q score ($p < .001$) and post-operative antibiotics ($p = .036$) were significant variables.

Conclusions: Overall HRQoL, as well as each of the three health domains, improved significantly. A higher ASA score, a higher pre-operative EES-Q score, and the

administration of post-operative antibiotics were significant predictors for better HRQoL recovery post-operatively. Further research is necessary to confirm these results.

KEYWORDS
EES-Q, health-related quality of life, patient-reported outcome measure, prospective cohort study, sinonasal inverted papilloma

1 | INTRODUCTION

Sinonasal inverted papillomas (IP) are benign tumours accounting for 0.4%–7% of all tumours of the sinonasal tract.[1] It primarily affects patients in their fifth to sixth decades of life, with a male-to-female ratio ranging from 2 to 3:1. While they can occur across a wide range of ages, these conditions are generally rare in children.[2] Despite the benign character there are three main reasons to remove the tumour. First, there is a risk of malignant transformation.[3] Second, because of the clinical presentation of the patients.[4] And last, aggressive growth can lead to the destruction of local anatomical structures.[5] After surgery, patients will need to recover physically, process the event psychologically and gradually restart their daily activities. These factors can have a major impact on patients' health-related quality of life (HRQoL).

To date, only few studies examined the HRQoL in patients with an IP. These studies found that patients with a benign sinonasal tumour have a better post-operative HRQoL compared with those with a malignant tumour. They also found that the HRQoL returned to normal after surgical removal of an IP.[6–8] However, this has not been explored with the Endonasal Endoscopic sinus and skull-base Surgery Questionnaire (EES-Q), which has the three obligate health domains (physical, psychological, and social), but mainly in the physical health domain. Moreover, predictors for a better or worse post-operative HRQoL outcome are not known.

Because there is an increasing need to comprehensively evaluate the effects of diseases and treatment, the objectives of our study were threefold. First, we aimed to assess the pre-operative HRQoL and subsequently examined the post-operative trajectory. Second, we sought to investigate whether pre-operative observations can serve as predictors for distinct post-operative HRQoL outcomes. Additionally, we aimed to evaluate whether interventions carried out by physicians can contribute to improve post-operative HRQoL. By achieving these objectives, we hope to enhance the counselling process for patients with IP and gain novel insights into the outcome of actions performed by the physician.

Key points

- To date, only few studies examined the health-related quality of life (HRQoL) in patients with a sinonasal inverted papilloma (IP). Moreover this is mainly limited to the physical domain.
- The endoscopic endonasal sinus and skull-base surgery questionnaire (EES-Q) does assess all three health domains: physical, psychological, and social.
- Post-operatively, we observed a temporary decline in HRQoL, primarily attributed to patients' social limitations, but over the total examined post-operative period, all three health domains and consequently, the overall HRQoL significantly improved.
- We found that a higher American Society of Anaesthesiologists score, a higher pre-operative EES-Q score, and the administration of post-operative antibiotics were significant predictors for better HRQoL recovery post-operatively.

2 | MATERIALS AND METHODS

2.1 | Ethical considerations

The study was authorised by the local institutional ethical review board of our tertiary referral centre.

2.2 | Inclusion

From 2013 onward, we asked all our patients undergoing surgery for an IP at our department of Otorhinolaryngology – Head and Neck Surgery to participate in this study if they met the inclusion criteria.

These criteria were: (1) endoscopic endonasal surgery for a histologically proven IP; (2) ≥18 years old; (3) capable of reading and writing in the Dutch language.

After informed consent, patients received the EES-Q by (e-)mail and were asked to complete the questionnaire pre-operatively, and then at 2 weeks, 3 months, and 1 year post-operatively. These questionnaire moments coincided with the regular controls in the outpatient clinic.

A pre-operative EES-Q and at least one follow-up EES-Q were prerequisites for data analysis.

2.3 | Surgical techniques

Patients underwent endonasal endoscopic surgery by a skilled surgeon in a tertiary care centre. Depending on the tumour location and extension different surgical procedures were performed. All

TABLE 1 Krouse staging for inverted papilloma.

Krouse staging by J. H. Krouse	
T1	Tumour totally confined to the nasal cavity, without extension into the sinuses. The tumour can be localised to one wall or region of the nasal cavity, or can be bulky and extensive within the nasal cavity, but must not extend into the sinuses or into any extranasal compartment. There must be no concurrent malignancy
T2	Tumour involving the ostiomeatal complex, and ethmoid sinuses, and/or the medial portion of the maxillary sinus, with or without involvement of the nasal cavity. There must be no concurrent malignancy
T3	Tumour involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus, with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasal cavity. There must be no concurrent malignancy
T4	All tumours with any extranasal/extrasinus extension to involve adjacent, contiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space. All tumours associated with malignancy

procedures were carried out with image-guided surgical navigation (Kick® EM, Brainlab, Heimstetten, Germany).

As most IPs grow into the maxillary sinus, most interventions consist of a modified endoscopic Denker's procedure (inferior turbinectomy and removal of the medial wall of the maxillary sinus).[9] In this study, we distinguish in our modified endoscopic Denker's procedures between a medial maxillectomy type 2 and type 3. Where in a medial maxillectomy type 2 the lacrimal duct is spared and in a type 3 it is tangentially cut and extracted for better view on the anterior wall of the maxillary sinus.

With a tumour outside of the maxillary sinus, endoscopic excision with or without functional endoscopic sinus surgery was performed.

All patients received perioperative one gift of intravenous prophylactic antibiotics and intramuscular corticosteroids. After the surgery, all patients were instructed to thoroughly rinse their noses with a saline solution, and a corticosteroid nasal spray was prescribed.

2.4 | Design of the study

In this prospective cohort study, we used the EES-Q as the HRQoL instrument. This is a validated instrument for assessing the HRQoL in all three health domains (physical, psychological, and social) during the surgery period.[10,11] A total of 30 items (10 per domain) describe activities or complaints with a 5-point Likert response scale ranging from 'not at all' (1), 'mildly' (2), 'moderately' (3), 'severely' (4), to 'very severely' (5) to indicate the degree of inconvenience. Note that higher scores correspond with lower HRQoL.

2.4.1 | EES-Q score and domain scores

To obtain an easily interpretable score, the sum of scores in one domain was recalculated into a *domain score* ranging from 0 (not at all) to 100 (very severe inconvenience). *Domain scores* were calculated by summing the 10-item score of each domain, subtracting 10 points from this total and multiply this by 2.5. *Domain scores* were corrected for the missing answers by adjusting the subtracted value and the multiplication factor accordingly.[11] The maximum number of missing answers was three per subject per domain, otherwise it was filed as missing data. The *EES-Q score*, ranging from 0 (not at all) to 100 (very severe inconvenience), was calculated by summing the three *domain scores* and dividing the total score by three.

TABLE 2 Patient characteristics and treatment.

Characteristic	Number (%)
Total	74
Sex	
Male	51 (69)
Female	23 (31)
Age at surgery (years)	
Mean ± standard deviation	60 ± 13
Median (interquartile range)	63 (55–67)
Range	21–92
ASA classification	
1	19 (26)
2	48 (65)
3	7 (9)
4	0 (0)
Krouse staging	
T1	7 (10)
T2	35 (47)
T3	32 (43)
T4	0 (0)
Surgical procedure	
Median maxillectomy type 2	17 (23)
Median maxillectomy type 3	38 (51)
Other (endoscopic excision ± FESS)	19 (26)
Post-operative systemic antibiotics	
No	33 (45)
Yes	41 (55)

Abbreviations: ASA, American Society of Anaesthesiologists; FESS, functional endoscopic sinus surgery.

2.4.2 | Variables

Data on *sex* and *age* were collected by the medical records.

The extension of tumour was defined by pre-operative *Krouse staging*,[12] see Table 1.

Comorbidity of the patients was defined by the American Society of Anaesthesiologists (ASA) classification, ranging from *ASA 1* to *ASA 6*.[13] *Smoking* was added as a separate variable.

To assess whether the pre-operative EES-Q score could be a predictor for post-operative HRQoL, three equal groups were made

TABLE 3 linear mixed models of the EES-Q score and domain scores separately.

Score (baseline)	Coefficient	SE	95% confidence interval		*p*
EES-Q score (20)	−10	1.6	−16	−7	**<.001**
Physical domain (23)	−11	1.9	−15	−7	**<.001**
Psychological domain (8)	−2	1.1	−4	−0.003	**.049**
Social domain (23)	−10	3.1	−17	−4	**.002**

Note: $p < .050$ means a significant decrease in score over time, that is, a significant better HRQoL post-operatively. Bold indicates significant results.
Abbreviations: EES-Q, Endonasal Endoscopic Sinus and Skull Base Surgery Questionnaire; SE, standard error.

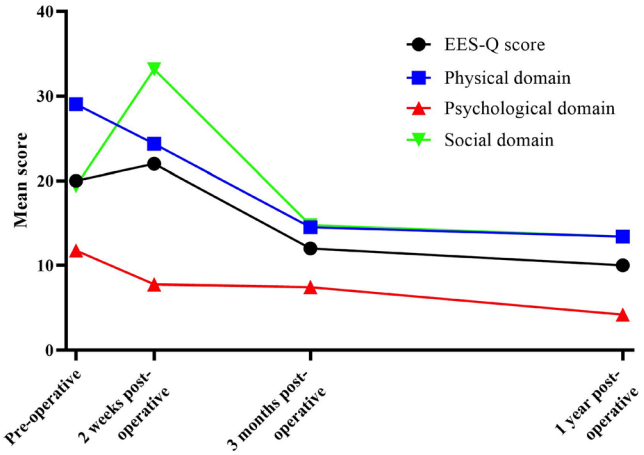

FIGURE 1 Mean Endonasal Endoscopic Sinus and Skull-Base Surgery Questionnaire (EES-Q) and mean domain scores. Two weeks post-operatively, there is a decline in health-related quality of life (HRQoL), as indicated by the increase in the mean EES-Q score, which can be largely attributed to the social limitations patients experience shortly after surgery. This is reflected in the rise of the social domain score. Nevertheless, over time, the EES-Q score and scores of each health domain show a significant decrease, signifying a significant improvement in post-operative HRQoL.

based on the pre-operative EES-Q score. These were obtained by the 33⅓ and 66⅔ percentile of the pre-operative scores. These groups were defined as *low pre-operative EES-Q score*, *middle pre-operative EES-Q score*, and *high pre-operative EES-Q score*.

Surgical procedures (as mentioned above) were defined as *medial maxillectomy type 2*, *medial maxillectomy type 3*, and *other*.

If during the surgery, patients were found to have sinusitis (inflamed mucosa and/or pus), we administered oral antibiotics following standard prophylactic antibiotics, after surgery for 1 or 2 weeks. We examined the effect of these *post-operative antibiotics* on the post-operative HRQoL.

2.5 | Statistical analysis

Descriptive statistics were used to describe patient characteristics. Mean EES-Q score and mean domain scores were calculated. To examine if there was a relationship between the *pre-operative EES-Q score* and the other variables a descriptive exploratory analysis (Pearson's chi-square) was performed.

2.5.1 | Linear mixed models

To assess the HRQoL outcome we performed linear mixed models (LMMs) analyses on our data.

The course in *time* was adjusted for the irregularly spaced post-operative surveys and squared if this resulted in a better model of fit. To determine best model of fit −2 Log Likelihood (−2LL), Akaike's Information Criterion (AIC) and Schwarz's Bayesian Information Criterion (BIC) were used.

For the analysis on predictors the variables *sex*, *age*, *Krouse staging*, *ASA*, *smoker*, *pre-operative EES-Q score*, *type of surgery*, and *post-operative antibiotics* were included as fixed effects. The variable *age* was mean-centred.

Covariance type was set at *unstructured* and calculation was based on *repeated measures*. This was also determined by using −2LL, AIC, and BIC. Estimation method was set to *maximum likelihood*. Coefficient, standard error, 95% confidence interval and *p*-value are displayed.

All statistical analyses were performed with IBM SPSS Statistics version 22.0 (SPSS IBM, Inc., Armonk, NY, USA).

3 | RESULTS

3.1 | Baseline characteristics and treatment

Between 2013 and 2021 a total of 74 patients met the inclusion criteria and were enrolled in this study. Mean age was 60 years and 69% was male. Baseline characteristics and treatment are presented in Table 2.

Mean follow-up was 3.2 years. In this population no patients had a malignant transformation of the tumour.

In five patients, there was a small defect of the lamina papyracea (with the peri-orbit still intact) and in two patients there was a small cribriform plate defect without liquorrhea. All other procedures were without complications.

Post-operatively, one patient experienced bleeding, which was successfully treated with a tamponade. Another patient had bleeding that eventually required unilateral clipping of the sphenopalatine artery. Additionally, two patients developed infected wound beds in the post-operative period, which required oral antibiotic treatment.

TABLE 4 linear mixed models of the EES-Q score with the variables.

Variable	Coefficient (β)	SE	95% CI		p
Sex					
Baseline	.08	1.9	−3.7	3.9	.967
*Time	−7.7	13.6	−34.9	19.5	.573
Age					
Baseline	.01	0.08	−0.2	0.2	.877
*Time	−.9	0.61	−2.2	0.3	.128
ASA classification					
Baseline	−2.1	1.7	−5.5	1.2	.209
*Time	−25	12	−50	−0.1	**.049**
Smoker					
Baseline	−2.1	2.1	−6.3	2.2	.335
*Time	−15	17	−49	19	.378
Krouse staging					
Baseline	.54	1.5	−2.4	3.5	.715
*Time	7.6	10	−13	28	.469
Pre-operative EES-Q					
Baseline	15	1.1	13	18	**<.001**
*Time	−44	8.3	−61	−27	**<.001**
Type of surgery					
Baseline	.53	1.1	−1.7	2.8	.637
*Time	−9.5	8.1	−26	6.8	.248
Post-operative AB					
Baseline	.37	1.9	−3.4	4.1	.846
*Time	−30	14	−57	−2.0	**.036**

Note: $p < .050$ at *baseline* means a statistically significant different estimated baseline status for that variable. $p < .050$ at *variable*. **Time* means a significant effect of that variable on the post-operative HRQoL. Bold indicates significant results.
Abbreviations: AB, antibiotics; ASA, American Society of Anaesthesiologists; CI, confidence interval; EES-Q, Endonasal Endoscopic Sinus and Skull Base Surgery Questionnaire; SE, standard error.

3.2 | EES-Q score and domain scores

Results of the LMM are given in Table 3. Mean EES-Q scores and mean domain scores were plotted in a graph (Figure 1).

3.3 | Variables and HRQoL

The cut-off values for the 33⅓ and 66⅔ percentiles of the pre-operative EES-Q scores were 12 and 26, respectively.

LMM results of the variables and the post-operative HRQoL are given in Table 4 and the mean ESS-Q scores for the different groups of the variables are plotted in a graph (Figures 2 and 3).

In exploratory analysis, we found no significant correlation between the pre-operative EES-Q score and the other variables (Table 5). In this analysis, age was dichotomised by the median (63 years).

4 | DISCUSSION

To our knowledge, this is the first prospective cohort study examining the HRQoL in all three health domains in patients undergoing surgery for a sinonasal IP. Besides, it is the first study seeking predictors for a more complete HRQoL outcome in this population.

4.1 | Key findings

Due to the social complaints, there is a remarkable decline in HRQoL 2 weeks post-operative. Eventually, patients will have a significant improvement in their HRQoL 3 months and 1 year post-operatively.

We found that a higher ASA score, a higher pre-operative EES-Q score and the use of post-operative antibiotics resulted in a more distinct improvement of post-operative HRQoL. Tumour extent was not a significant predictor of post-operative HRQoL. Neither was surgical invasiveness, nor the other measured variables.

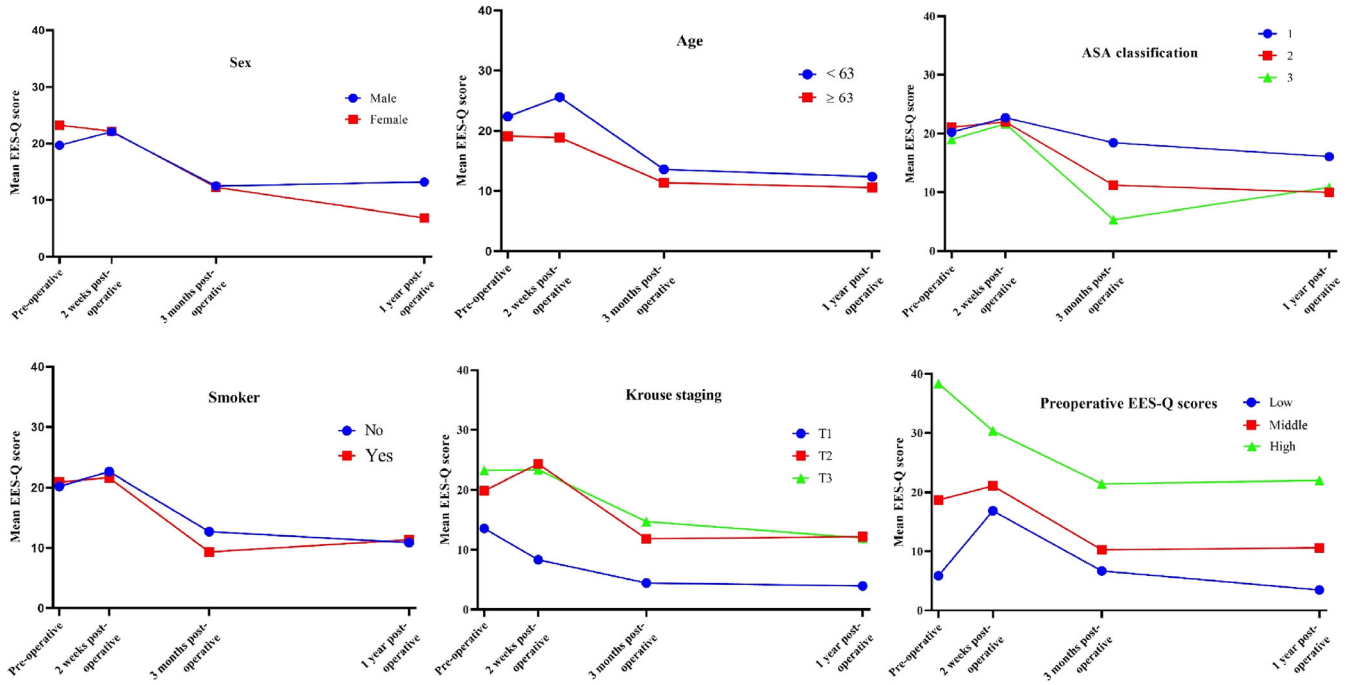

FIGURE 2 Pre-operative observations. Pre-operatively, the mean scores for the different American Society of Anaesthesiologists (ASA) groups are nearly identical. Post-operatively, however, the ASA 1 group exhibits less health-related quality of life (HRQoL) improvement than the ASA 2 and 3 groups. The group with a high pre-operative Endonasal Endoscopic Sinus and Skull-Base Surgery Questionnaire (EES-Q) score shows remarkable HRQoL improvement compared with the other two groups, especially in comparison to the group with a low pre-operative EES-Q score. The low pre-operative EES-Q score group does however improve in HRQoL compared with pre-operative.

These results may lead the surgeon to discuss these issues pre-operatively. Moreover, it suggests a better healing process with post-operative antibiotics. Finally, it questions whether surgical conservatism should be pursued indiscriminately in this disease, as we do not measure a difference in HRQoL outcome.

4.2 | Comparison to other studies

Our IP cohort has a better pre-operative HRQoL compared with the pre-operative HRQoL of the chronic rhinosinusitis (CRS) patients from our recently published study.[14] The CRS patients had a mean EES-Q score of 37 (only median scores are published); in this population, the mean pre-operative score was 20. The biggest difference was in the physical domain, followed by the social domain. Our IP cohort does have a worse HRQoL than the healthy individuals of that same study (20 vs. 14, respectively). The EES-Q score of the IP cohort 1 year post-operatively is similar to the EES-Q score of healthy individuals, suggesting that HRQoL will return to normal. Van Samkar and Georgalas[8] support this outcome by showing that the SNOT-22 score after removal of an IP at follow-up (median 6 years) is similar as in healthy individuals. Whether the social domain was influential in their outcome is not known because the SNOT-22 cannot differentiate between these, unlike the EES-Q. In addition, they had no pre-operative data and their population was rather small ($n = 37$). Deckard et al.[6] included 18 IP in their analysis on HRQoL after endoscopic treatment of sinonasal neoplasms ($n = 71$) and concluded that patients with benign tumours have a better HRQoL outcome than patients with malignant tumours. Harrow and Batra[7] reported similar results in their study including IP patients ($n = 19$), who accounted for only 20% of their total population (benign and malignant). Both performed no sub-analysis on IP alone.

Pre-operatively, patients of the different ASA groups score similar. However, the post-operative HRQoL is better in patients with a higher ASA score. We hypothesize that this can be explained by the fact that chronically diseased patients are known to accommodate to their illness, which results in better HRQoL measures.[15] Moreover, the group with the high pre-operative EES-Q score shows the biggest improvement in HRQoL post-operative compared with the other groups. This is in line with CRS studies where patients with a higher pre-operative SNOT-22 score show a greater improvement post-operative compared with patients with a lower pre-operative SNOT-22 score.[16–18]

In the pre-operative assessment, it is usually not evident whether the patient has post-obstructive sinusitis caused by the tumour obstruction. Intraoperative findings of sinusitis (inflamed mucosa and/or pus) resulted in the initiation of broad-spectrum antibiotic therapy for 1 or 2 weeks, depending on the operator's preference. To our knowledge, there are no articles available on this topic in combination with an IP. The existing body of literature presents divergent findings regarding the benefits of post-operative antibiotics after endoscopic endonasal sinus surgery for CRS. While certain studies demonstrate positive outcomes associated with their use,[19–21] other studies do not report

significant advantages.[22,23] Systematic reviews on this topic therefore do not provide a comprehensive recommendation.[24,25] In our cohort, antibiotics were administered for the treatment of post-obstructive sinusitis, that is, secondary sinusitis. Notably, the forementioned studies do not differentiate between primary and secondary sinusitis, although this distinction could potentially influence the outcome. To the best of our knowledge, there are no existing studies investigating the use of post-operative antibiotics specifically for secondary CRS. Our hypothesis is that if antibiotics contribute to improved long-term HRQoL, it may be attributed to enhanced healing of the sinonasal mucosa. Further research is necessary to explore this in greater detail.

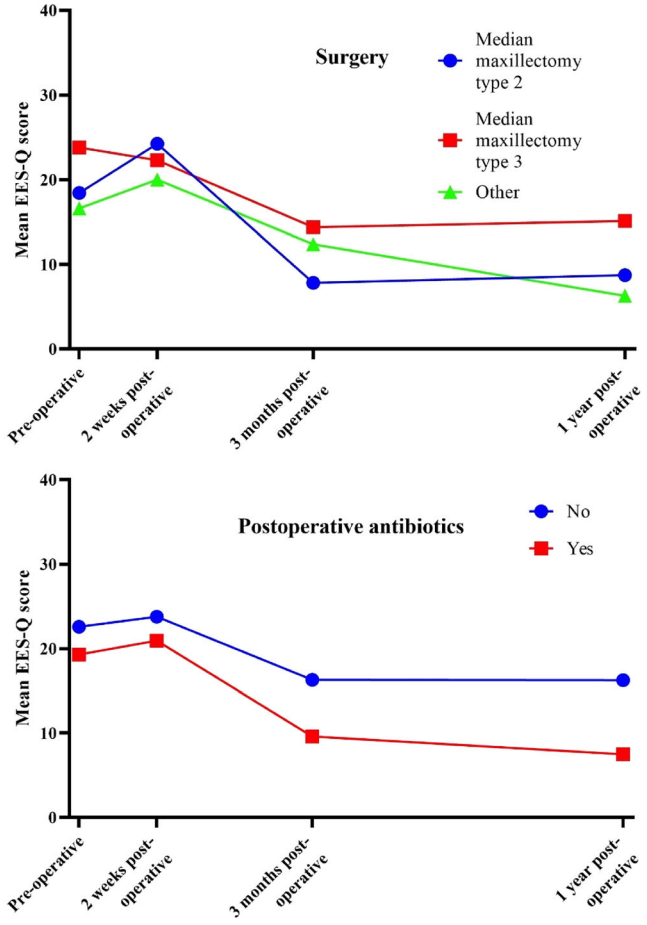

FIGURE 3 Interventions. All surgical groups have similar pre-operative mean Endonasal Endoscopic Sinus and Skull-Base Surgery Questionnaire (EES-Q) scores, and there is no significant difference in their post-operative health-related quality of life (HRQoL). While the patients who received post-operative systemic antibiotics had a similar pre-operative EES-Q score compared with the group without post-operative antibiotics, they did demonstrate a significantly better improvement in HRQoL.

4.3 | Strengths and limitations

The EES-Q is a relatively new instrument; therefore, most of the comparisons made are with the SNOT-22. The primary distinction between these instruments lies in their domains. While the SNOT-22 primarily focuses on the physical domain, the EES-Q examines all three essential health domains. We deliberately chose to use only the EES-Q because it not only measures like other instruments, but also includes additional mandatory aspects.

Since IP is a relatively rare disease, research in this field with a big cohort is a big challenge. Nevertheless, our cohort appears to be relatively large compared with the other clinical IP studies. For more support of evidence of our results, more studies (with greater numbers) should be performed. Furthermore, the retrospective nature of the intervention analyses does not provide conclusive evidence for the future. Finally, to date, there is no minimal clinically important difference (MCID) known of the EES-Q.

4.4 | Future perspectives

First, we want to examine whether patients who received post-operative antibiotics maintain a higher level of HRQoL in comparison to the non-antibiotics group. To accomplish this, we will administer the EES-Q questionnaire once again, 5 years after the surgical intervention.

Second, it is our goal to determine the MCID of the EES-Q for better interpretation of the results.

Third, there is no significant difference in HRQoL between patients who underwent a median maxillectomy 2 (MMT) and those who underwent a MMT 3 procedure. The assessment of long-term recurrence was not within the scope of this study. Exploring the potential association between surgical invasiveness and recurrent rates of IP offers a valuable subject for future research.

Finally, there is a growing trend to thoroughly assess the impact of diseases and treatment. We therefore ask all our patients who undergo endoscopic endonasal sinus and/or anterior skull-base surgery to contribute to our research by filling in the EES-Q at predetermined times. We aspire to use questionnaires for patient monitoring, disease screening, counselling for treatment and for clear communication between the physician and the patient.

5 | CONCLUSION

In this first prospective cohort study on HRQoL after surgical removal of a sinonasal IP, we observed a temporary decline in HRQoL shortly

TABLE 5 Pearson chi-square, *p*-value.

	Sex	Age	ASA classification	Smoker	Krouse staging	Type of surgery	Post-operative antibiotics
Pre-operative EES-Q score	.101	.65	.984	.787	.059	.423	.233

Abbreviations: ASA, American Society of Anaesthesiologists; EES-Q, Endonasal Endoscopic Sinus and Skull Base Surgery Questionnaire.

after the surgery, primarily attributed to the social limitations encountered by patients. In the total examined post-operative period, all three health domains, and consequently, the overall HRQoL improved significantly. Moreover, we found that a higher ASA score, a higher pre-operative EES-Q score, and the administration of post-operative antibiotics were significant predictors for better HRQoL recovery post-operatively. Further research is necessary to confirm these results.

AUTHOR CONTRIBUTIONS

Marc C. den Heijer: Concept and design, data collection, statistical analysis, article writing. **Gonneke E. Joustra:** Review article. **Karin M. Vermeulen:** Data analysis support, review article. **Astrid G. W. Korsten-Meijer:** Concept and design, review article. **Robert A. Feijen:** Concept and design, review article.

ACKNOWLEDGEMENTS

The authors thank the participants, without them our health-related quality of life studies would not be possible.

FUNDING INFORMATION

The authors have no financial or other conflicts to report.

CONFLICT OF INTEREST STATEMENT

The authors have no financial or other conflicts to report.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/coa.14158.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available upon request from the authors. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was authorised by the local institutional ethical review board of our tertiary referral centre.

ORCID

Marc C. den Heijer https://orcid.org/0000-0002-0425-613X
Gonneke E. Joustra https://orcid.org/0000-0001-8171-0546
Karin M. Vermeulen https://orcid.org/0000-0001-9257-2791
Astrid G. W. Korsten-Meijer https://orcid.org/0000-0001-5094-7698
Robert A. Feijen https://orcid.org/0000-0002-8568-0847

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: den Heijer MC, Joustra GE, Vermeulen KM, Korsten-Meijer AGW, Feijen RA. Sinonasal inverted papilloma and predictors of health-related quality of life after endonasal endoscopic surgery: A prospective cohort study. Clinical Otolaryngology. 2024;49(4):453–61. https://doi.org/10.1111/coa.14158