Patient preferences for treatment of chronic rhinosinusitis with nasal polyps

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Dear Editor:

Choosing between revision endoscopic sinus surgery (ESS) versus biologic therapy for recurrent chronic rhinosinusitis with nasal polyposis (CRSwNP) is a complex, multifaceted decision that involves not only clinical and financial factors but also patient preferences [1,2]. Currently, there are no quantitative studies investigating patient preferences for CRSwNP treatment options. Increased awareness of patient-centered approaches to treatment warrant further investigation.

We designed a discrete-choice experiment (DCE) to quantitatively assess patient preferences in the setting of recurrent CRSwNP after ESS [3,4]. In a DCE, participants are offered a series of options which are described using combinations of select attributes. Attribute levels are varied experimentally. Preference weights are estimated to quantify the relative importance of each treatment attribute. Latent-class analysis (LCA) can be applied to evaluate heterogeneity of treatment preferences across participants.

Adult patients diagnosed with CRSwNP and evaluated at Duke University Health System between July 2013 and February 2023 with at least one previous ESS at any institution were invited to complete an online survey. The survey included a DCE comprised of 12 choice questions from a pool of 72 experimentally designed questions. In the DCE, participants were asked to suppose their symptoms were as severe as they had been prior to their last sinus surgery and their physician has given them a choice of revision ESS, biologic therapy, or no additional treatment. All treatment choices including benefits and risks were described in patient-friendly language. Treatment descriptions were based on input provided by patients, otolaryngologists, allergists, and methodologists to minimize bias.

Treatment options in each choice question were described by three additional attributes with corresponding levels. These included the number of oral steroid courses in the next year (none, one, two), symptom severity after treatment (no symptoms, mild, moderate), and the probability of disease recurrence within two years (10%, 30%, 40%). Attribute levels were selected based on input from clinician investigators and outcomes reported in published literature, and were of sufficient range to encourage consideration of tradeoffs across the treatment options as observed during qualitative interviews with individuals with CRSwNP [5-7]. An example DCE question is shown in supplemental materials.

151 patients completed the survey. LCA revealed three distinct preference classes. All three classes preferred treatment over no treatment. Class 1 (57.0%) had no discernable preference regarding treatment type. Rather, symptom severity after treatment was the most important factor influencing choices, and chance of recurrence was the second most important. The number of oral steroid courses was relatively less important. The two other classes strongly preferred a particular treatment type over the other attributes: Class 2 (24.3%) preferred biologic therapy and Class 3 (18.6%) preferred revision ESS (Figure 1). Nearly all patients had a membership probability of ≥90% for one class and <10% for the other two, demonstrating the strength of separation of the preference classes. Age, education, and previous experience with biologic therapy were independently associated with class membership. Patients with higher membership probabilities to Class 2 were older and more likely to have a previous prescription for a biologic therapy (p=0.038). Patients with higher membership probabilities to Class 2 and Class 3 were also less likely to have a four-year college degree or higher than those in with higher membership probabilities to Class 1 (83.2%) (p=0.036, p=0.007, respectively).

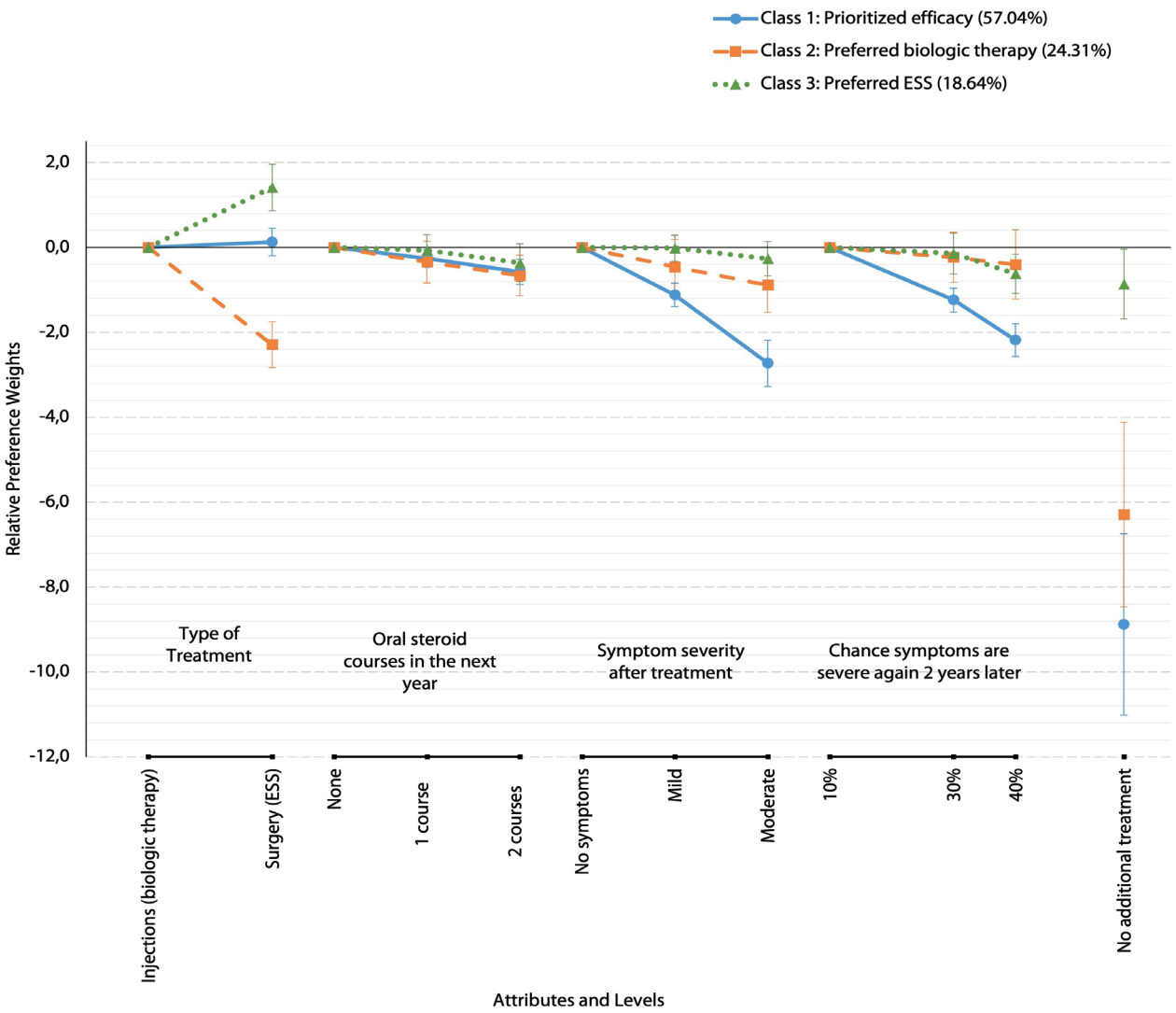

Figure 1. Relative Preference Weights by Class. This figure depicts preference weights for each of the four treatment attributes across three classes. The classes were distinct in their preferences for the first attribute (type of treatment). Class 1 did not prefer either treatment type, but rather prioritized treatment efficacy in terms of reduced symptom severity and lower chance of recurrence at two years. Class 2 preferred injections, and Class 3 preferred ESS. Error bars show the 95% confidence interval around the mean value. ESS = endoscopic sinus surgery.

In conclusion, this quantitative analysis of patient preferences for recurrent CRSwNP reveals that while efficacy was the most important treatment attribute for most patients, distinct subsets of patients preferred either surgery or biologic therapy, regardless of efficacy. Age, education, and previous experience with biologic therapy were associated with preference patterns. Our findings have clinical implications for shared-decision making, informed consent, and treatment adherence.

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Authorship contribution

JSu: contributed to study conduct, concept and design, data acquisition, data analysis and interpretation, and first draft of the manuscript; SO: contributed to data acquisition, interpretation, presentation of the research, and first draft of the manuscript; SDR: contributed to the study conduct, concept and design, data acquisition, data analysis and interpretation; AD, JSi: contributed to the study conduct, concept and design; MJW:

contributed to the study conduct, data acquisition, data analysis and interpretation; J-CY: contributed to data analysis and interpretation; RAH: contributed to study concept, design and data acquisition; DWJ: contributed to the study conduct, concept and design, data acquisition, interpretation, and first draft of the manuscript; All authors reviewed and revised the manuscript critically for important intellectual content, agreed to submit to the current journal, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Conflict of interest

AD is a GSK employee and hold GSK stocks and shares. JSi was a GSK employee at the time of the study. JSu, SDR, and MJW received salary support for work related to this project through a contract research agreement between Duke University and GSK. J-CY reports receiving consulting fees from Duke University during the conduct of the study. RAH and DWJ receive research funding from Regeneron. DWJ reports providing consulting and speaking services to Sanofi and Regeneron. SO does not report any conflicts of interest.

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Data sharing

De-identified data are available from the corresponding author.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Materials and methods

Study sample

Subjects were identified from review of medical records with International Classification of Diseases (ICD)-9 and ICD-10 codes for nasal polyposis. Patients with cystic fibrosis, eosinophilic granulomatosis with polyangiitis, ciliary dyskinesia, or isolated antrochoanal polyps were excluded. The study protocol was approved by the Duke University Institutional Review Board for Clinical Investigations (Pro00111902). All participants provided informed consent online, prior to survey administration.

Treatment descriptions

Biologic therapy was described as a monthly subcutaneous injection once every four weeks at a doctor's office or at home by the patient or a caregiver. Possible side effects were described as serious allergic reactions, sore throat, joint pain, and injection-site reaction. Although all patients had previous experience with endoscopic sinus surgery (ESS), a typical outpatient ESS description and associated risks also were provided. Common short-term ESS side effects were described as mild bleeding, facial discomfort, and pain. Patients were reminded that with ESS there is a chance of serious complications including severe bleeding, permanent loss of smell and/or taste, numbness of the face, mouth, or nose, blindness, brain injury, infection, and pain that does not go away. Patients also could choose no additional treatment that was defined as currently having severe symptoms and requiring three courses of oral steroids in the next year. An example DCE question is shown in Figure S1. Before answering the discrete-choice-experiment (DCE) questions, patients received training on the attributes and choice-task layout, followed by comprehension questions to reinforce the material.

Survey design

Ten patients underwent a one-hour pre-testing interview to evaluate each patient's understanding of the survey content, acceptance of the decision context presented, and their approach to choosing among treatment options in the DCE. Improvements were made to the survey instrument based on patient feedback and interviewer observations. The experimental design for the DCE included 72 choice questions generated in SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA). The final survey was programmed and administered using Lighthouse Studio version 9.14 (Sawtooth Software Inc., Provo, UT, USA). Descriptive statistics of self-reported and clinical patient characteristics were summarized using STATA 17 (StataCorp LLC, College Station, TX, USA). Treatment-choice data from the DCE were examined using latent-class analysis (LCA) in Latent GOLD- software (Statistical Innovations Inc., Belmont, MA, USA).

Statistical analysis

The optimal number of latent classes was determined using Akaike and Bayesian information criteria, relative size of the membership probability for each class, and qualitative preference information gained with each additional class. The analysis included an evaluation of models with two to five classes. Preference weights for attribute levels were estimated using a logit model. Multinomial logistic regression was used to test whether pre-selected patient characteristics were associated with class membership. These included previous experience with biologic therapy, comorbidities (aspirin-exacerbated respiratory disease [AERD], allergic fungal sinusitis [AFS], allergic rhinitis, asthma), oral steroid prescriptions in the past year, post-surgery complications, age, gender, education (four-year college degree or more), and time since diagnosis (six or more years).

Results

Recruitment

Clinicians screened 1,676 medical records and identified 896 eligible patients who received invitations to the online survey from June 15, 2022 to February 3, 2023 through a secure patient communication portal. Patients were offered 45 USD for participating. In total, 151 patients completed the survey. Summary statistics for the cohort are provided in Table S1.

Discussion

This is the first DCE to evaluate patients' treatment preferences in chronic rhinosinusitis (CRS). The use of LCA offers a novel way to classify patients into distinct preference groups using their choice patterns. This approach revealed three groups of patients (i.e., "esotypes"; eso meaning within or inward) with distinct treatment preferences. Improvements in symptom severity and reductions in the chance of recurrence at two years were the most important treatment attributes for most patients (57%) while others prioritized treatment type: biologic therapy (24%) or revision ESS (18%).

Age, education, and use of biologics were significant predictors of preference for a specific treatment type over treatment outcomes. Older patients may have more comorbidities leading to higher surgical risk; thus, contributing to a preference for biologic therapy. Additionally, while there is some evidence of sustained benefit after discontinuation of biologic therapy [1,2], younger patients may be reluctant to commit to a treatment of indefinite duration. Patients with less education tended to be classified among the groups prioritizing treatment type. These individuals may have more difficulty evaluating treatment

benefits and risks and might gain from multimodality education to ensure their treatment choices are well informed. Our results demonstrate that esotype membership was not predicted by symptom severity, comorbidities, gender, time since diagnosis, previous surgeries, or previous surgical complications.

Some limitations are noteworthy. First, the study results are based on patients' choices to hypothetical scenarios and accurate recall of symptoms; actual choices may differ, especially based on financial factors, which can be significant [3,4]. Second, the recurrence attribute represents a probability at a specific point in time. In reality, the probability of recurrence generally increases over time. Finally, there are three biologics approved for chronic rhinosinusitis with nasal polyposis (CRSwNP) in the United States, each with its own unique efficacy, dosing frequency and adverse effect profiles [5].

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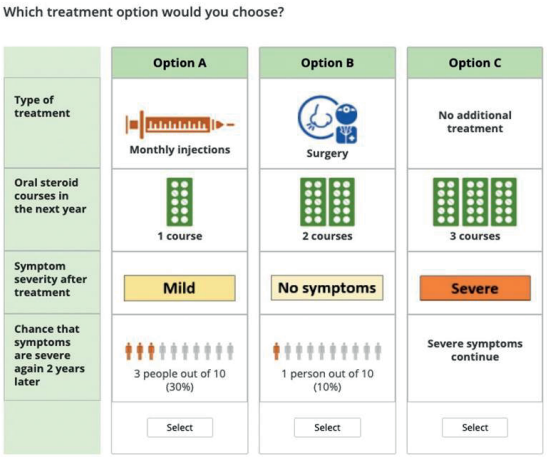

Figure S1. Example DCE question. DCE = discrete-choice experiment.

Table S1. Patient Characteristics (N=151).

Characteristics	n	%
Age (years), Mean (SD)	54.7 (14.5)	
Gender, Female	76	50.3
Ethnicity, Not Hispanic	140	92.7
Race (multiple response options allowed)		
American Indian or Alaskan Native	1	0.7
Asian	5	3.3
Black or African American	22	14.6
White	117	77.5
Other	6	4.0
Prefer not to answer	3	2.0
Highest level of education completed		
High school or equivalent	24	15.9
Technical school or associate's degree	15	9.9
4-year college degree or more	112	74.2
Time since first diagnosed with nasal polyps		
2 years ago or less	13	8.6
3 to 5 years ago	31	20.5
6 or more years ago	107	70.9
Sino-Nasal Outcome Test (SNOT-22) [1] score		
Over the past two weeks (n=143), Mean (SD)	27.9 (18.7)	
Right before prior surgery (n=142), Mean (SD)	51.2 (21.6)	
Number of past surgeries for nasal polyps		
1	67	44.4
2	39	25.8
3 or more	41	27.2
Missing	4	2.7
Time since last sinus surgery for nasal polyps		
Less than a year ago	23	15.2
1 to 2 years ago	22	14.6
3 to 5 years ago	55	36.4
6 to 10 years ago	33	21.9
More than 10 years ago	18	11.9
Lund–Mackay CT score (n=123), Mean (SD)	13.0 (6.1)	
Culture data (n=86)		
Methicillin-sensitive *Staphylococcus aureus*	20	23.3
Methicillin-resistant *Staphylococcus aureus*	2	2.3
Pseudomonas	12	14.0
Coagulase-negative *Staphylococci*	32	37.2
Other	52	60.5
None (no growth)	18	20.9
Indication for biologic medicine (n=46)		
Nasal polyps	32	69.6
Asthma	13	28.3
Other	1	2.2
Biologic prescribed (n=46)		
Dupilumab	42	91.3
Mepolizumab	7	15.2
Omalizumab	8	17.4
Benralizumab	3	6.5
Months since biologic first prescribed (n=46), Mean (SD)	28.2 (35.6)	
Comorbidities		
AERD	37	24.5
AFS	24	15.9
Allergic rhinitis	114	75.5
Asthma	98	64.9
Number of oral steroid prescriptions in the last year, Mean (SD)	0.92 (1.2)	

AERD = aspirin-exacerbated respiratory disease; AFS = allergic fungal sinusitis; CT = computed tomography; SD = standard deviation.

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