Impact of Anosmia Severity on Health Utility Values in Chronic Rhinosinusitis with Nasal Polyps: An Exploratory Analysis from the WAYPOINT Trial

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Introduction

- Chronic rhinosinusitis (CRS) is a common inflammatory condition affecting approximately 9% of the global population.[1]
- Among individuals with CRS, up to 30% present with nasal polyposis (CRSwNP) – a distinct phenotype associated with more severe sinonasal symptoms, including nasal obstruction and olfactory dysfunction.[2,3]
- Olfactory disturbances are well documented to have a substantial negative impact on patients' quality of life.[4]
- However, there is a notable lack of research examining the relationship between olfactory dysfunction and health utility in patients with CRSwNP.

Objective

- To explore the relationship between smell loss severity and health utility estimates in patients with CRSwNP, using data from the WAYPOINT trial – a phase 3, randomized, double-blind, placebo-controlled study evaluating tezepelumab in this population.

Methods

- Analyses were conducted using SAS 9.4, based on data from the WAYPOINT trial (NCT04851964).
- All patients with available data, irrespective of treatment assignment, were categorized by smell loss severity at weeks 4, 12, 24, 36, and 52 using three classification methods:
  - University of Pennsylvania Smell Identification Test (UPSIT)
  - SNOT-22 Item 12: patient-reported severity of smell loss from the 22-item Sino-Nasal Outcome Test
  - Nasal Polyp Symptom Diary (NPSD): patient-reported severity of smell loss
- For each severity category, four utility estimation methods were applied using published algorithms:
  - EQ-5D-3L, crosswalk from EQ-5D-5L (van Hout et al., 2012)[5]
  - SF-6D, mapped from SF-36 (Brazier et al., 2002)[6]
  - EQ-5D-3L, mapped from SF-36 (Rowen et al., 2009)[7]
  - EQ-5D-3L, mapped from SNOT-22 (Crump et al., 2017)[8]
- Utility values were evaluated and modelled at baseline and weeks 4, 12, 24, 36, and 52 using repeated measures.
- The model included covariates for visit, treatment, health state (based on SNOT-22 score: ≤20 = mild; 21–50 = moderate; >50 = severe), and treatment-by-health state interaction.

Results

- The demographics and baseline characteristics of participants in the WAYPOINT trial reflect a clinically relevant population with high disease burden (**Table 1**); over 80% had a baseline SNOT-22 score >50, and 71.3% had a history of prior nasal polyp surgery.
- Patient utility scores at baseline by instrument are shown in **Table 2**; across all instruments, increasing olfactory impairment was associated with lower utility scores, confirming the negative impact on patient quality of life (**Figure 1**).
- The choice of utility estimation method had a quantifiable impact on absolute utility values; across all instruments, the lowest utility scores were consistently observed among EQ-5D-3L estimates mapped from SF-36 scores.

Table 1. Demographics and baseline key characteristics (WAYPOINT)

Baseline Characteristics	Statistics or category	Overall (N=408)
Age (years)	n Mean (SD) Median Min; Max	408 49.7 (13.65) 51.0 18; 81
Gender, n (%)	Male Female	266 (65.2) 142 (34.8)
Comorbid asthma, n (%)	Yes No	245 (60.0) 163 (40.0)
Aspirin/NSAID exacerbated respiratory disease, n (%)	Yes No	71 (17.4) 337 (82.6)
Prior nasal-polyp surgery, n (%)	Yes No	291 (71.3) 117 (28.7)
Baseline EOS count, n (%)	<300 cells/µl ≥300 cells/µl	186 (46.0) 218 (54.0)
Baseline SNOT-22 score, n (%)	≤50 >50	74 (18.1) 334 (81.9)

- The reduction in utility associated with increasing olfactory impairment varied across smell loss classification methods, with SNOT-22 Item 12 and NPSD showing a greater decrease than UPSIT.
- Within each smell loss classification method (UPSIT, SNOT-22 Item 12, and NPSD), the discriminatory power of utility instruments varied; EQ-5D-3L mapped from SF-36 was the least sensitive to differences between mild and severe smell loss, while EQ-5D-3L mapped from SNOT-22 demonstrated the greatest ability to distinguish between severity levels.

Table 2. Baseline utility score by instrument (WAYPOINT)

Baseline Utility	Statistics or category	Overall (N=408)
EQ-5D-3L (crosswalk from EQ-5D-5L)	n Mean (SD) Median Min; Max	408 0.69 (0.245) 0.75 -0.47;1.00
SF-6D (mapped from SF-36)	n Mean (SD) Median Min; Max	408 0.66 (0.111) 0.65 0.30;1.00
EQ-5D-3L (mapped from SF-36)	n Mean (SD) Median Min; Max	408 0.55 (0.117) 0.55 0.14;0.77
EQ-5D-3L (mapped from SNOT-22)	n Mean (SD) Median Min; Max	408 0.49 (0.170) 0.48 0.09;0.91

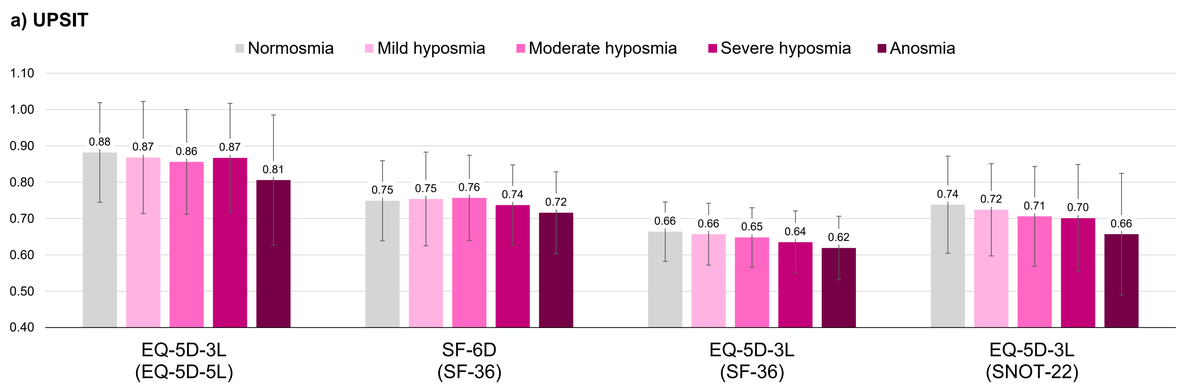

Figure 1. Mean (SD) utility score per instrument by olfactory impairment severity, as categorized by a) UPSIT, b) SNOT-22: Item 12, and c) NPSD self-reported symptom severity.

Conclusions

- This analysis demonstrates a clear association between increasing severity of olfactory dysfunction and declining health utility values in patients with CRSwNP.
- The impact of smell loss on utility was evident across both clinical and patient-reported measures of olfactory dysfunction.
- EQ-5D-3L mapped from SNOT-22 was the most sensitive instrument for detecting utility differences across smell loss severity levels, while EQ-5D-3L mapped from SF-36 was the least.
- These findings highlight the importance of incorporating olfactory function into health-related quality of life assessments where relevant and suggest that preference-based measures derived from disease-specific instruments may better capture the burden of CRSwNP.

Abbreviations:

EOS = Eosinophils; EQ-5D-3L = Euroqol 5-dimensions (3 levels); EQ-5D-5L = Euroqol 5-dimensions (5 levels); Max = Maximum; Min = Minimum; n = Number of participants; NPSD = Nasal Polyp Symptom Diary; NSAID = Non-steroidal anti-inflammatory drug; SD = Standard deviation; SF-36 = 36-Item Short Form Health Survey; SF-6D = Short-Form 6 Dimensions; SNOT-22 = 22-item Sino-Nasal Outcome Test; µl = Microliter; UPSIT = University of Pennsylvania Smell Identification Test.

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