Addressing EQ-5D Ceiling Effects Through a Disease-Specific Symptom Threshold: A Patient-Level Analysis Informing the Cost-Effectiveness of Dupilumab in Chronic Rhinosinusitis With Nasal Polyps in the United Kingdom

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CRSwNP

Conclusions

- **In the TA1134 population (SNOT-22 ≥50), baseline EQ-5D utility was 0.70 (all prior-surgery patients: 0.78) and full-health reports 7% (21%), below the 15% ceiling criterion.**
- **EQ-5D tracked severity and detected a treatment effect; the capped utility gap widened from 0.134 to 0.180, mostly from a larger uncapped gain.**
- **Under the UK EQ-5D-5L value set, the capped gap narrows to 0.142 (illustrative).**

Objective

To assess how the EuroQol 5-dimension (EQ-5D) ceiling and capped utility gain differ between prior-surgery patients and those with a 22-item Sinonasal Outcome Test (SNOT-22) score ≥50, including under the UK 5-level EQ-5D (EQ-5D-5L) value set.

Background

- The reference case of the National Institute for Health and Care Excellence (NICE) for utility calculation is the EQ-5D; departing from it needs peer-reviewed evidence of poor content validity, construct validity and responsiveness.[1]
- In chronic rhinosinusitis with nasal polyps (CRSwNP), burden comes mainly from smell loss, nasal obstruction and poor sleep, none an EQ-5D dimension.[2] In the UK MACRO trial (with or without polyps), surgery improved SNOT-22 by 20 points vs placebo, while EQ-5D-5L and other quality-of-life measures were 'generally quite similar' (some favoured surgery).[3]
- **First committee meeting (July 2025):** trial EQ-5D was preferred to mapped SNOT-22 utilities; after prior surgery, controlled patients' utility (0.925; baseline 0.78) exceeded the UK norm (0.866), so it was capped.[4–6] The committee recognised potential uncaptured benefits related to the EQ-5D's lack of sensitivity.[7]
- **After draft guidance (August 2025):** on clinical advice, the company restricted the population to SNOT-22 ≥50 (459 → 230).[4]
- **Final guidance (February 2026):** the committee accepted this population (§3.3) with capped EQ-5D utilities (§3.12). Noting concerns about the EQ-5D's 'lack of sensitivity', it again concluded that some benefits may not have been captured (§3.16) and weighed this, against high uncertainty, above £20,000 per quality-adjusted life year (QALY) gained (§3.17), while keeping the reference-case EQ-5D.[8] The Scottish Medicines Consortium reached a similar recommendation.[9]

Methods

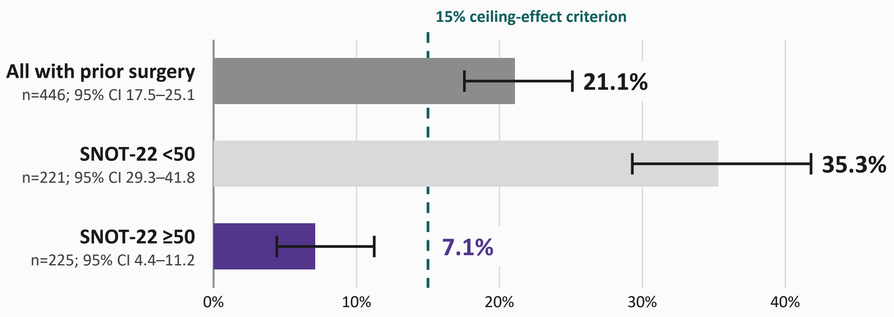
- **Data:** pooled SINUS-24 and SINUS-52, prior surgery: n=459 (446 with baseline EQ-5D); SNOT-22 ≥50: n=230.[5,10] Post hoc, descriptive; Wilson 95% confidence intervals (CIs).
- **Utilities:** EQ-5D-5L (5L)[11] mapped to 3-level (3L; TA1134 Hernández Alava crosswalk)[12] and, illustratively, the UK 5L value set (required for new NICE topics from 27 August 2026).[13,14]
- **Ceilings:** full health (11111; ceiling effect if >15%[15]) and NICE's cap at the UK age–sex norm, multiplying every health state by norm ÷ controlled utility.[4,6,16]
- **Response:** ≥1-point nasal polyp score and ≥8.9-point SNOT-22 improvement; 'controlled' = sustained week-52 responders.[8,17]
- **Severity:** SNOT-22 >50 (Toma & Hopkins)[18]; ≥50 in TA1134 and the British Rhinological Society 2026 statement.[8,19]

Results

The ceiling sat mainly below SNOT-22 50

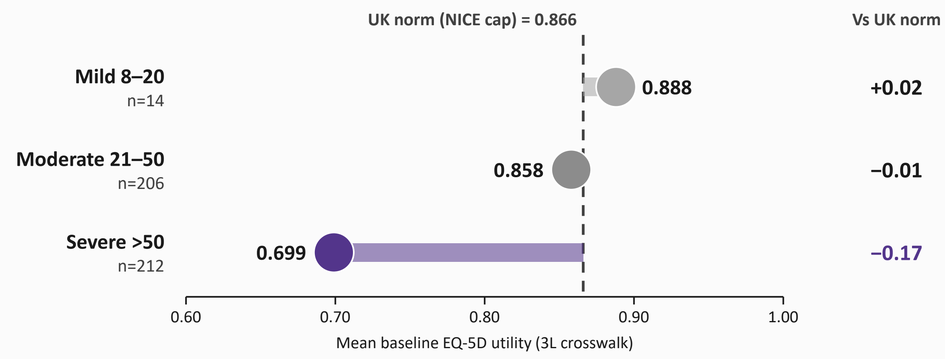
- 21.1% reported full health at baseline (ceiling criterion 15%); 83% of them had SNOT-22 <50 (Figure 1).[5,15]
- Utility fell with severity (0.888 mild to 0.699 severe; Figure 2); SNOT-22 correlated with the UK 5L index (Spearman ρ = −0.54; −0.33 within the range-restricted ≥50 group).[5]

Figure 1. Full health (11111) at baseline: only SNOT-22 ≥50 fell below the 15% criterion[5,15]



Baseline cross-section; whiskers, Wilson 95% CIs.

Figure 2. Mean baseline EQ-5D utility by SNOT-22 band: only the severe band sat well below the UK norm[5,6,18]



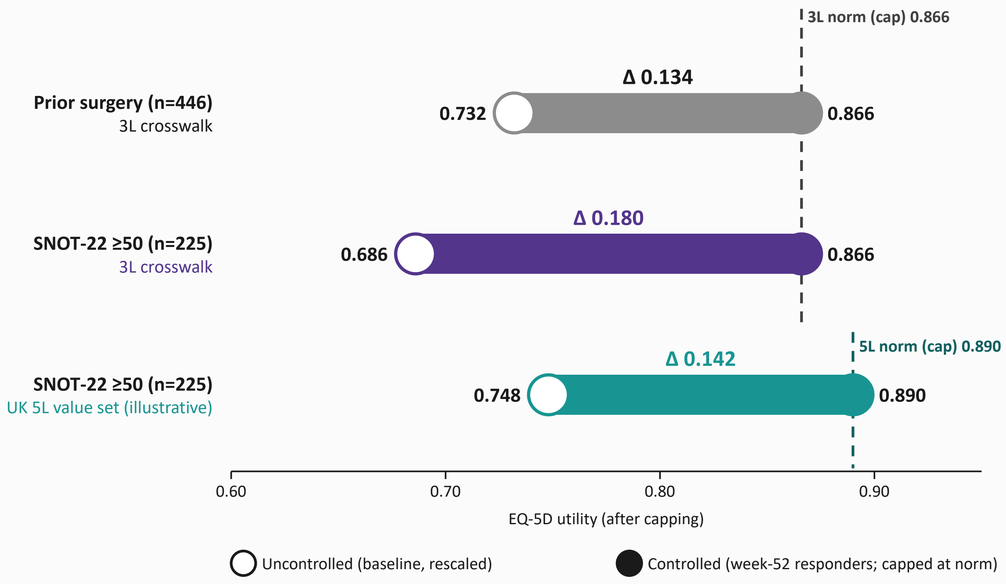
Bars: distance to the UK norm at mean age 51.4.[6] Bands: Toma & Hopkins; both arms; n=432 with week-24 SNOT-22; 3L crosswalk.[12]

EQ-5D detected a treatment effect with or without the SNOT-22 restriction

- Placebo-adjusted week-24 change (least-squares means, analysis of covariance): 0.056 (95% CI 0.031–0.082) after prior surgery; 0.077 (0.036–0.119) at ≥50 (5L: 0.063, 0.022–0.104). The CIs overlap.[5]

Results (continued)

Figure 3. Capped utility gap (controlled minus uncontrolled): wider at SNOT-22 ≥50, narrower under the UK 5L value set[4,6,8,16]



n, patients with baseline EQ-5D. Controlled: baseline plus the week-52 change in sustained responders (original response criteria; SINUS-52; dupilumab every 2 weeks and placebo, inverse-variance pooled; 45 and 25 responders). Point estimates.[4,5] 5L: 0.781 + 0.149 = 0.930, scaled to the 5L norm (age 51, 53% male; unrounded inputs).[4,5,16]

- Before capping, the gap was 0.143 vs 0.183; the cap removed 0.009 vs 0.003 (6% vs 2%), so 0.040 of the 0.046 widening came from the larger uncapped gain. Truncating only the controlled state gives 0.084 vs 0.168.[4]

Under the UK 5L value set, the gap narrows to 0.142

- At ≥50, baseline rises from 0.70 (3L) to 0.78 (5L) and the norm from 0.866 to 0.890; the gain falls from 21% to 16% of controlled utility (Figure 3).[5,6,13,14,16]

Implications for QALY-based appraisal

- Within the clinically defined population (SNOT-22 ≥50), the EQ-5D ceiling fell below 15%: assess instrument performance in the decision population, not the whole trial.
- Report utility gains before and after capping, and state the capping method.
- Restricting on a non-stratified variable breaks randomisation: pre-specify thresholds and report who is excluded.
- Sleep and smell/taste bolt-ons could add sensitivity but sit outside NICE's reference case.[14]

Limitations

- Post hoc subgroup with chance imbalance (baseline 0.72 placebo vs 0.68 dupilumab); NICE judged that breaking randomisation increased uncertainty (§3.3).[4,8]
- NICE's model applied prior-surgery responder rates to the ≥50 population (§3.9).[8]
- 'Controlled' adds responders' change to the cohort baseline, so selection and regression to the mean may inflate it; subgroup responsiveness was not formally compared, and the ceiling was measured at baseline only.
- In the 21–50 band, near-normal utility (0.858) may reflect less quality-of-life loss or limited sensitivity; we did not test between them.[5]
- 5L results are illustrative, outside the NICE model; PMG51 handles 5L values above the norm case by case.[14]

CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; EQ-5D, EuroQol 5-dimension; EQ-5D-5L, 5-level EQ-5D; 3L/5L, 3-/5-level EQ-5D; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; QALY, quality-adjusted life year; SNOT-22, 22-item Sinonasal Outcome Test; UK, United Kingdom.

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Generative AI (Claude, Anthropic) was used to draft and edit text, check references, build the figures and layout, and write code to reproduce the utility calculations (capping and 5L estimates). The authors checked all outputs against the source analyses and take full responsibility for the content.

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