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P3587

Utility scores in chronic spontaneous urticaria: A systematic literature review and statistical analysis

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KEY FINDINGS & CONCLUSIONS

- Utility studies and REMIX trial data show CSU patients have lower utility values than healthy individuals, with greater CSU severity linked to lower scores
- Most published studies used EQ-5D-3L for utility data, while REMIX trials used EQ-5D-5L, indicating better HRQoL for remibrutinib patients due to EQ-5D-5L's lower ceiling effect
- Mean utility analysis from the REMIX cohort suggests remibrutinib may improve HRQoL over placebo, based on incremental differences at weeks 12 and 24 from baseline

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INTRODUCTION

- Chronic spontaneous urticaria (CSU) is a skin condition marked by spontaneous itchy hives and/or angioedema lasting ≥6 weeks[1]
- CSU has a substantial impact on patient health-related quality of life (HRQoL) and productivity[2,3]
- Measuring health-state utility values (HSUVs) is crucial for standardized, objective health state comparisons

OBJECTIVES

- To identify published utility values associated with CSU health states
- To derive new CSU health-state utility scores using recent randomized clinical trial (RCT) data

METHODS

Systematic Literature Review

- A systematic literature review (SLR) was conducted with date limits from January 2013 to May 2023 following PRISMA guidelines[4], using Embase®, MEDLINE®, EconLit, Cochrane Library, NHSEED, and ScHARRHUD databases
- Scientific conference proceedings (e.g., ISPOR, EADV, EAACI, AAD, BAD, WCD, UCRE, AAAAI) and key health agency websites (e.g., NICE, SMC, CADTH) were searched for data from 2021-2023, along with hand searches
- The outcomes included utility outcomes (not limited to EQ-5D. SF-36, SF-12v2, HUI), HRQoL measures, economic models and evaluations with focus on utility outcomes in this paper
- Two independent reviewers initially screened titles and abstracts, followed by full-text reviews to exclude irrelevant records, with any discrepancies resolved by a third reviewer
- One reviewer extracted data, checked for accuracy by another, and quality assessment was performed per NICE recommendations[5]

Utility Analysis

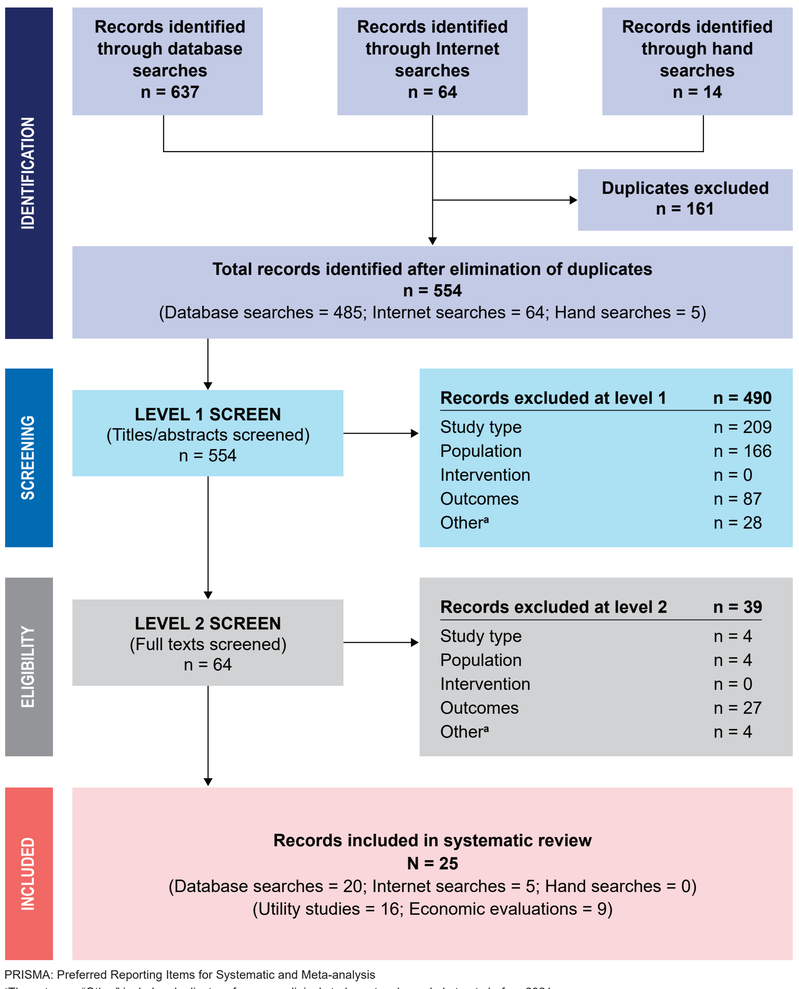
- Pooled EQ-5D-5L utility data from two phase III RCTs (REMIX 1 and 2) were analyzed using descriptive statistics, mixed models, generalized linear mixed models, and the UK value set from the latest NICE guidance[6]
- The EQ-5D-5L has shown better measurement capabilities, fewer ceiling effects (indicating higher sensitivity) and improved discriminatory power and convergent validity compared to the EQ-5D-3L that is currently used in the identified utilities reported in the literature. Also, some studies suggest transitioning to EQ-5D-5L decreases the incremental QALY gain from effective health technologies[7-9]
- CSU health states were defined using the weekly Urticaria Activity Score (UAS7):[10]
  - Urticaria free [UAS7 = 0]
  - Well-controlled urticaria [UAS7 > 0 and ≤ 6]
  - Mild urticaria [UAS7 > 6 and < 16]
  - Moderate urticaria [UAS7 ≥ 16 and < 28]
  - Severe urticaria [UAS7 ≥ 28 and ≤ 42]
- Statistical models used follow-up utility values (weeks 12 and 24) as the dependent variable, with individual patients as random effects and various covariates initially included as fixed effects: baseline utility, baseline UAS7 health state, baseline ISS7, presence of angioedema (baseline and follow-up), CSU duration, previous exposure to anti-IgE biologics; visit week; treatment arm; study; age, weight, sex, and interaction terms between treatment arm and week visit and between the presence of angioedema and the UAS7 health state
- Differences in utility values by health state between treatment arms were also explored through an interaction term in the model
- A parsimonious model was selected using backward elimination, removing variables with the highest P values until all remaining had P < 0.05, with health state forced into the model
- Marginal means with 95% confidence intervals (CIs) were estimated by health state and treatment arm, presented as the means of the model covariates

RESULTS

Systematic Literature Review

- A total of 25 studies were included out of the 554 retrieved publications. Of these, 16 were utility studies (15 real-world evidence studies; 1 RCT) and 9 were economic evaluations (**Figure 1**)

Figure 1. PRISMA flow diagram



PRISMA: Preferred Reporting Items for Systematic and Meta-analysis

[a]The category "Other" includes duplicate references, clinical study protocols, and abstracts before 2021

- Utility estimates were reported in 5 of the 9 economic evaluations: 2 UK-based, 1 each from the US and France, and 1 using values from 3 global studies based on the UK value set (**Table 1**)
- For 4 studies, utilities were derived from pooled values of 3 clinical studies of omalizumab, reported as EQ-5D-3L data
- Primary utility studies showed improved scores with decreased disease activity, while CSU patients had lower values compared to controls and other conditions like psoriasis and atopic dermatitis (**Table 2**)

Table 1. Utility-Weight estimates reported in economic evaluations

Author (year)	Type of economic evaluation, country	Brief description of population	Methods of elicitation	Health state description	Utility estimate
Graham et al. (2016)[11]	CUA Global[a]	Moderate-severe CSU inadequately controlled on SoC	Published mixed-effects regression model constructed from pooled EQ 5D data across the GLACIAL, ASTERIA I, and ASTERIA II trials	Severe urticaria	0.712
				Moderate urticaria	0.782
				Mild urticaria	0.845
				Well-controlled urticaria	0.859
				Urticaria free	0.897
HAS (2014)[12]	CUA France	CSU patients inadequately controlled on SoC	Post hoc analysis of pooled EQ 5D data from the GLACIAL, ASTERIA I, and ASTERIA II trials	Severe urticaria	0.761
				Moderate urticaria	0.799
				Mild urticaria	0.838
				Well-controlled urticaria	0.888
				Urticaria free	0.923
NICE (2015)[13]	CUA UK	CSU patients inadequately controlled on SoC	Pooled EQ 5D scores from the GLACIAL, ASTERIA I, and ASTERIA II trials	Severe urticaria	0.712
				Moderate urticaria	0.782
				Mild urticaria	0.845
				Well-controlled urticaria	0.859
				Urticaria free	0.897
Shaker et al. (2020)[14]	CEA US	CSU patients	Not reported	Chronic urticaria	0.77
				Without urticaria	0.894
SMC (2014)[15]	CUA UK	CSU patients inadequately controlled on SoC	Pooled EQ 5D scores from the GLACIAL, ASTERIA I, and ASTERIA II trials	Severe urticaria	0.712
				Urticaria free	0.897

CEA = cost-effectiveness analysis; CSU = chronic spontaneous urticaria; CUA = cost-utility analysis; HAS = French National Authority for Health; NICE = National Institute for Health and Care Excellence; SMC = Scottish Medicines Consortium; SoC = standard of care; UAS7 = Urticaria Activity Score over 7 days; severe urticaria: UAS7 score of 28–42; moderate urticaria: UAS7 score of 16–27; mild urticaria: UAS7 score of 7–15; well-controlled urticaria: UAS7 score of 1–6 and urticaria free: UAS7 score of 0

[a]Please note the model was UK based, but the utilities were based on results from 3 global clinical trials, with utilities estimated based on the UK value set

Table 2. Utility values by disease severity reported in key primary utility studies identified through the SLR

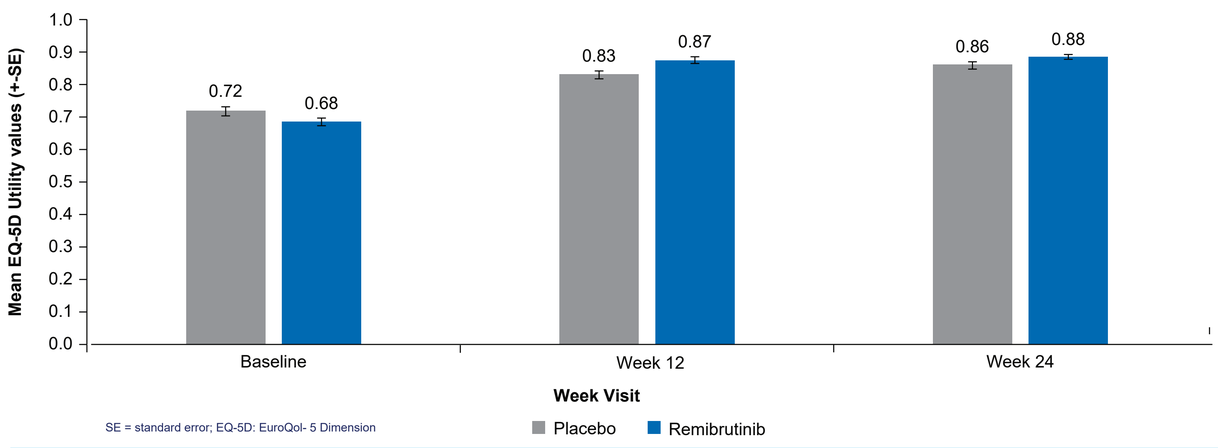
Author (year); sample size	Country	Utility valuation	Health-state description	Utility estimate
Gupta et al. (2013)[16] CSU (N=379)	Multinational*	SF-6D mean (± SE)	Moderate/severe urticaria	0.56 ± 0.012
			Mild urticaria	0.64 ± 0.007
		EQ-5D mean (± SE)	Moderate/severe urticaria	0.56 ± 0.029
			Mild urticaria	0.75 ± 0.017
Hawe et al. (2016)[3] ASTERIA I (N = 318), ASTERIA II (N = 322), and GLACIAL (N = 335)	Global	EQ-5D-3L mean	Urticaria free	0.894
			Well-controlled urticaria	0.862
			Mild urticaria	0.829
			Moderate urticaria	0.78
			Severe urticaria	0.71
Lee et al. (2020)[17] #CU (N=163)	Korea	EQ-5D-5L mean	Urticaria free	0.953
			Well-controlled urticaria	0.913
			Mild urticaria	0.878
			Moderate urticaria	0.86
			Severe urticaria	0.746
Ye et al. (2022)[18] CSU (N=500)	Korea	EQ-5D-5L mean	Well-controlled urticaria	0.93
			Mild urticaria	0.84
			Moderate urticaria	0.79
			Severe urticaria	0.73
Balp et al. (2023)[19] CSU (N=379)	Multinational*	SF-6D mean (± SE)	CSU	0.63 ± 0.01
			PsO	0.68 ± 0.002
			AD	0.68 ± 0.01
		EQ-5D mean (± SE)	CSU	0.69 ± 0.01
			PsO	0.76 ± 0.004
			AD	0.77 ± 0.01
Balp et al. (2015)[20] #CU (N = 369)	Multinational*	SF-6D mean	Currently treated for CU	0.62
			Never experienced CU	0.71
Balp et al. (2017)[21] #CU (N=127; on current CU treatment)	Brazil	SF-6D mean	CU	0.637
			Controls	0.714
Vietri et al. (2015)[22] Currently treated for chronic hives (N=270) Never experienced chronic hives (N=1,080)	US	SF-6D mean	Never experienced chronic hives	0.751
			Currently treated for chronic hives	0.631
Shen et al. (2020)[23] CU (N=716) CSU (N=414)	China	EQ-5D-3L mean (SD)	CU	0.97 (0.14)
			CSU	0.96 (0.14)

*Multinational: France, Germany, Italy, Spain, and the UK; 5EU = France, Germany, Italy, Spain, and the UK; AD = atopic dermatitis; CSU = chronic spontaneous urticaria; CU = chronic urticaria; SD = standard deviation; SE = standard error; SF-6D = Short Form-6 Dimension; EQ-5D: EuroQol- 5 Dimension; UAS = Urticaria Activity Score; UAS7 = Urticaria Activity Score over 7 days; PsO: psoriasis; severe urticaria: UAS7 score of 28–42; moderate urticaria: UAS7 score of 16–27; mild urticaria: UAS7 score of 7–15; well-controlled urticaria: UAS7 score of 1–6 and urticaria free: UAS7 score of 0; #CU is used as a proxy for CSU

Utility Analysis

- Descriptive statistics from the REMIX cohort showed remibrutinib patients had higher utilities than placebo at weeks 12 and 24, despite lower baseline utility vs. placebo (**Figure 2**)

Figure 2. Descriptive statistics of mean EQ-5D utility values by visit week and randomized treatment arm



SE = standard error; EQ-5D: EuroQol- 5 Dimension

- Statistical analysis of the REMIX 1 and 2 data showed an incremental decrease in utility for worse health states (**Table 3)**
- In the well-controlled health state, remibrutinib outperforms placebo in utility values (mean: 0.898 vs. 0.863; p=0.078), with borderline statistical significance
- Sensitivity analysis further confirmed the robustness of the results

Table 3. Mean utility values estimated from the mixed-effects model

UAS7 health state	Mean (SE)	95% CI
Urticaria free	0.928 (0.008)	0.913–0.943
Well controlled	0.889 (0.009)	0.871–0.906
Mild	0.866 (0.007)	0.851–0.880
Moderate	0.833 (0.009)	0.815–0.853
Severe	0.749 (0.011)	0.727–0.770

CI = confidence interval; SE = standard error; UAS7 = Urticaria Activity Score over 7 days

Note: Following backward elimination, the final model included only the significant covariates of sex, baseline utility, weight, UAS7 category, ISS7 at baseline, and presence angioedema on the visit day

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Disclosure

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