The Use of Disease-Specific Health-Related Quality of Life (HRQoL)/Patient Reported Outcomes (PROs) Scales in Rare Inflammatory Conditions (RICs).

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Introduction

BACKGROUND

- HRQoL/PRO endpoints are heavily weighed by patients and payer bodies.
- Disease-specific scales may be less available and not validated in rare conditions, making the accurate determination of HRQoL in these patients difficult.

Objective

- **To understand how frequently disease-specific scales are used in RIC trials and how HRQoL outcomes are incorporated in National Institute for Health and Care Excellence (NICE) health technology assessments (HTAs) in these populations.**

Methods

- Rare inflammatory conditions were identified in a review of medicinal products across all rare conditions.[1]
- For twenty-four identified RICs, a review of ClinicalTrials.gov from the last five years was undertaken using indication names and “quality of life” search terms. Data regarding the HRQoL/PRO scales were used and the frequencies of disease-specific HRQoL scales were extracted. HTAs from NICE were reviewed for each indication to understand if and how payers incorporate HRQoL assessments in their submissions and comments on the use of scales were collected. A targeted search was performed in MEDLINE to identify disease-specific scales in selected RICs.

Results

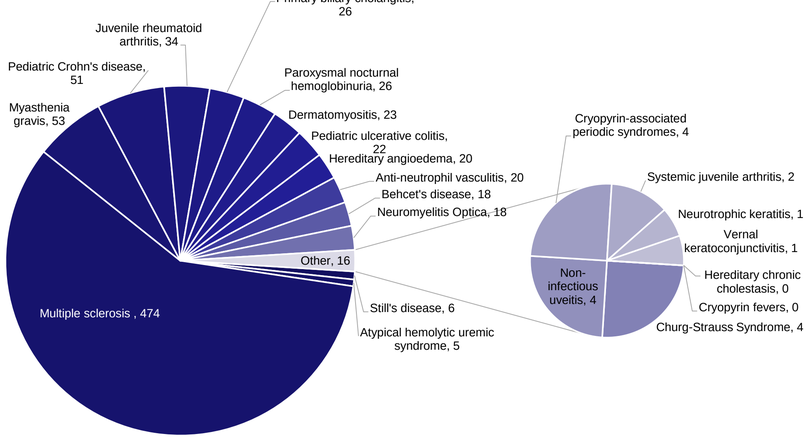
- Twenty-four rare inflammatory conditions were identified (**Table 1**) with prevalence ranging from 1-9/100,000 to 1-5/10,000 population. A total of 839 unique trials in 22 RICs were identified and reviewed (**Figure 1**). No clinical trials reporting HRQoL were identified for two RICs (hereditary chronic cholestasis, cryopyrin fevers).

Table 1. Rare Inflammatory Conditions

Table	Worldwide prevalence*
Multiple sclerosis	NR
Myasthenia gravis	1-9/100,000
Pediatric Crohn's disease	NR
Juvenile rheumatoid arthritis	1-5/10,000
Primary biliary cholangitis	1-5/10,000
Paroxysmal nocturnal hemoglobinuria	1-9/100,000
Dermatomyositis	1-9/100,000
Pediatric ulcerative colitis	NR
Anti-neutrophil vasculitis	1-5/10,000
Hereditary angioedema	1-9/100,000
Behcet's disease	1-9/100,000
Neuromyelitis Optica	1-9/100,000
Wegener’s granulomatosis	1-9/100,000
Familial Mediterranean fever	1-5/10,000
Still's disease	1-9/100,000
Atypical hemolytic uremic syndrome	1-9/100,000
Non-infectious uveitis	1-5/10,000
Churg-Strauss Syndrome	1-9/100,000
Cryopyrin-associated periodic syndromes	Unknown
Systemic juvenile arthritis	1-9/100,000
Neurotrophic keratitis	1-5/10,000
Vernal keratoconjunctivitis	1-5/10,000
Hereditary chronic cholestasis	NR
Cryopyrin fevers	NR

***Prevalence estimates from https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN**
European estimations if a worldwide estimation is not available

Figure 1. Number of clinical trials within last 5 years for RICs



Over half of clinical trials report disease-specific scales as secondary endpoint

- HRQoL/PRO scales were reported in 689 trials (82.1%) and the majority (58.9%) of clinical trials listed at least one disease-specific scale as a secondary outcome (**Figure 2**).
- Among the 22 RICs, ≥50% of clinical trials reported at least one HRQoL scale as a secondary endpoint for 21 RICs; only one RIC (pediatric ulcerative colitis) had less than 50% of its clinical trials reporting HRQoL as a secondary endpoint (**Figure 2**).
- Fourteen of 22 RICs had a least one clinical trial including a disease-specific scale. Excluding indications not reporting any disease-specific scales, of these 14 RICs, the percentage of clinical trials reporting disease-specific scales ranged from 7% to 100%.
- Conditions that frequently used disease-specific scales were hereditary angioedema (100%), systemic juvenile arthritis hereditary (100%), vernal keratoconjunctivitis (100%), primary biliary cholangitis (87%), myasthenia gravis (81%) and multiple sclerosis (71%) (**Table 2**).

Table 2. Conditions using disease-specific scales and list of scales

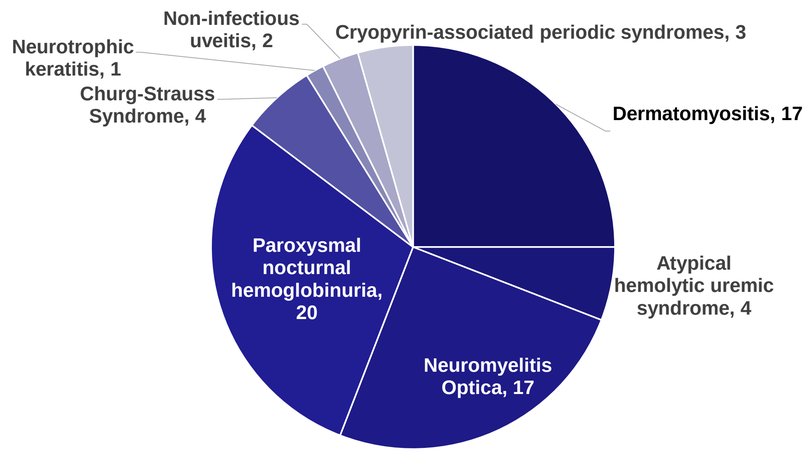
Condition	% of trials using disease-specific scales	Disease-specific scales
Hereditary angioedema	100%	AE-QoL
Systemic juvenile arthritis	100%	ACR Component: CHAQ: Functional Ability Score
Vernal keratoconjunctivitis	100%	QUICK
Primary biliary cholangitis	87%	PBC-40
Myasthenia gravis	81%	MG QOL-15, MG-ADL
Multiple sclerosis	71%	AMSQ-SF, CAREQOL-MS, DIDA-Q, FAMS, FSIQ-RMS, GLTEQ, HAQUAMS, MFIS, SymptoMScreen, MSWS-12, MSFIS, MSIS, MSIS-29, MSISQ-15, MSNQ, MSQLI, MSQOL-54, MS-TAQ, MSWDQ-23, Multiple sclerosis-59 French scale, MusiQoL, NFI-MS, Qualiveen, WPAI-MS
Pediatric ulcerative colitis	47%	IBD-DI, Pediatric IBD Intermed, IBD-KID2, IBD-SES-A, IBD-Q, SIBDQ
Behcet's disease	47%	BDCAF2006, BD QoI,
Juvenile rheumatoid arthritis	44%	JAQQ, CHAQ-DI, Peds-QL Arthritis module, Peds-QL Rheumatology module, CASE, Scoliosis Research Society Scale-22, SUPERKIDZ
Pediatric Crohn's disease	36%	Pediatric IBD Intermed, IBD-KID2, IBDQ-32, IBD-SES-A, IBD-DI, SIBDQ
Still's disease	25%	ACR Component: CHAQ: Functional Ability Score
Wegener’s granulomatosis	14%	BVAS, SNOT-22
Anti-neutrophil vasculitis	11%	AAV-PRO
Familial Mediterranean fever	8%	FMF-QoL

ACR, American College of Rheumatology; AE-QOL, angioedema quality of life; AMSQ-SF, Arm function in multiple sclerosis-short form; AAV-PRO, ANCA-associated vasculitis patient-reported outcomes; BDCAF, Behcet’s disease current activity form; BD, Behcet’s disease; BVAS, Birmingham vasculitis activity score; CARE, Caregiver health-related quality of life in multiple sclerosis; CHAQ, childhood health assessment questionnaire; DI, disability index; DIDA-Q, dual-task impact on daily living activities questionnaire; FAMS, functional assessment of multiple sclerosis; FMF-QOL, Familial Mediterranean fever; FSIQ-RMS, full scale intelligence questionnaire – relapsing multiple sclerosis; GLTEQ, Godlin-Shephard leisure-time physical activity questionnaire; HAQUAMS, Hamburg quality of life questionnaire multiple sclerosis; IBD, inflammatory bowel disease; IBD-Q, IBD questionnaire; JAQQ, juvenile arthritis quality of life questionnaire; KID2, IBD knowledge inventory devise; MFIS, modified fatigue impact scale; MG QOL-15, myasthenia gravis quality of life; MG-ADL, myasthenia gravis activity of daily living; MSFIS, multiple sclerosis modified fatigue impact scale; MSIS, multiple sclerosis impact scale; MSISQ, multiple sclerosis Minnesota satisfaction questionnaire; MSNQ, multiple sclerosis neuropsychological screening questionnaire; MSQL1, multiple sclerosis quality of life index; MSQOL, multiple sclerosis quality of life; MS-TAQ, multiple sclerosis treatment adherence questionnaire; MSWS, multiple sclerosis walking scale; Musi-QOL, multiple sclerosis international quality of life; NFI-MS, neurologic fatigue index; PBC, primary biliary cholangitis; QUICK, quality of life in children with vernal keratoconjunctivitis; SES-A, self-efficacy scale; SIBDQ, short IBD questionnaire; SUPERKIDZ, standardized universal pain evaluations for rheumatology providers for children and youth; WPAI, work productivity and activity impairment

Not all RICs report disease-specific scales

- Eight of 22 RICs did not report any disease-specific scales in the clinical trials, 3 of which included more than 10 clinical trials (dermatomyositis, neuromyelitis optica, paroxysmal nocturnal hemoglobinuria) (**Figure 3**).
- From targeted searches, disease-specific scales were not identified for 7 of the 8 RICs. For these RICs, either disease-specific scales for similar conditions or generic scales were used in the clinical trials.
- For the 8th RIC, paroxysmal nocturnal hemoglobinuria, two disease-specific scales have recently been developed but have not yet been incorporated into clinical trials: QLQ-AA/PNH and PNH-SQ.[2,3]

Figure 3. Number of trials per RICs not reporting disease-specific scale in clinical trials



NICE appraisals rarely incorporate disease-specific scales among submissions for RICs

- Despite the relatively high frequency of disease-specific scales seen in clinical trials, of 24 NICE appraisals in the 22 identified RICs, only 11 submissions included disease-specific scales; two submissions mapped disease-specific scales to EQ-5D (**Figure 4**).
- Disease-specific scores were not translated into utilities in 5 submissions due to absence of validated mapping methods and/or evaluators’ concerns with the validity of results.

Figure 2. Percentage of clinical trials in RICs reporting HRQoL scales and disease-specific scales

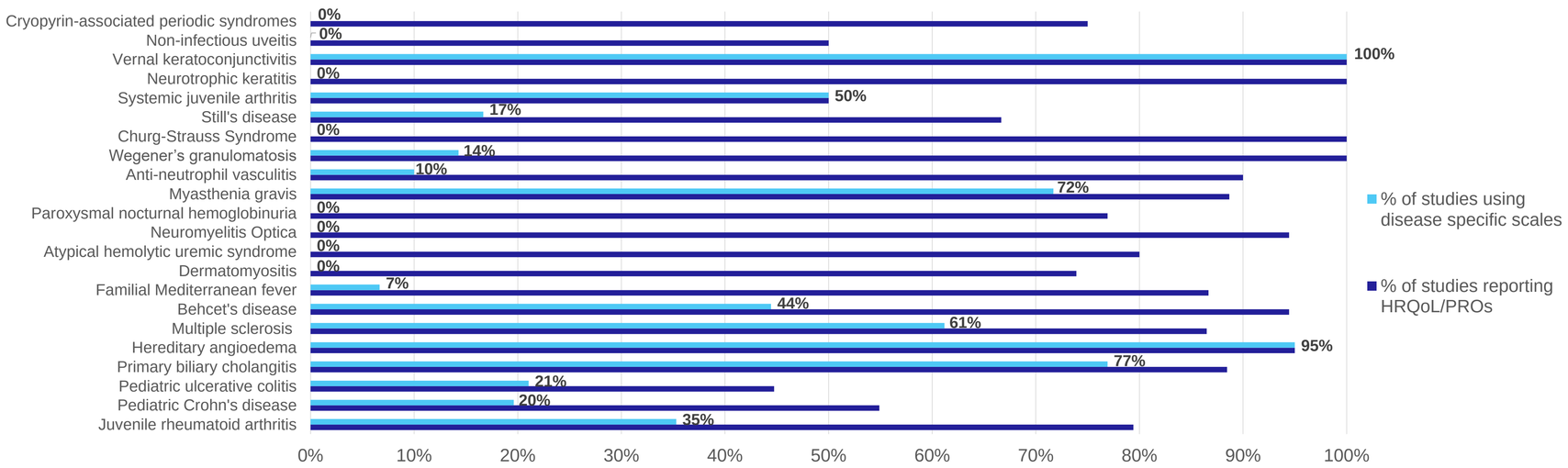
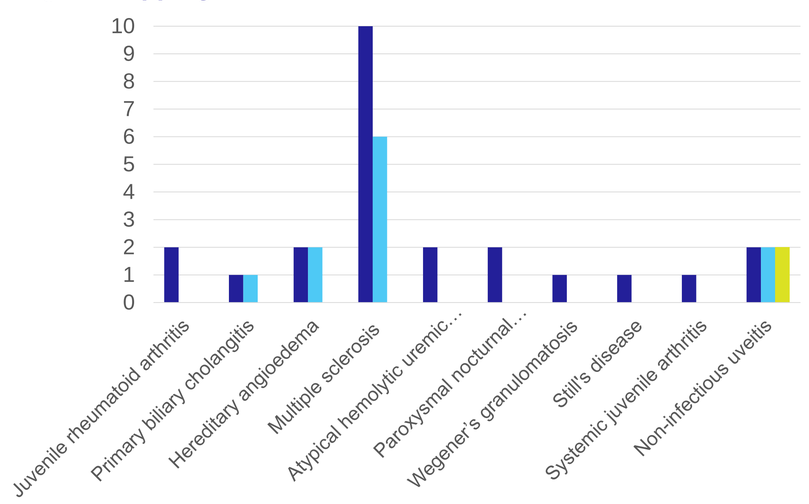


Figure 4. RICs NICE appraisals using disease-specific scales and EQ-5D mapping



Conclusions

- **Of 22 RICs, the majority of identified clinical trials included at least one disease-specific scale as a secondary endpoint.**
- **In RICs not including a disease-specific scale, these scales were not available for the majority of these indications.**
- **Few NICE appraisals reported incorporation of disease-specific scales in their assessment. Future studies should assess how use of disease-specific scales in ongoing clinical trials are incorporated into future HTA assessments.**
- **Disease-specific scores were not translated into utilities in 5 submissions due to absence of validated mapping methods and/or evaluators’ concerns with the validity of results.**
- **Patients with RICs may suffer from poor HRQoL; its assessment is crucial for designing a patient-centric approach to assessment of outcomes in clinical trials.**

Abbreviations

HRQoL, health-related quality of life; HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; PNH-SQ, Paroxysmal Nocturnal Hemoglobinuria Symptom Questionnaire; PRO, patient-reported outcome; QLQ-AA/PNH, Quality of Life Questionnaire-Atypical Anemia/Paroxysmal Nocturnal Hemoglobinuria; RIC: rare inflammatory condition

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References

1. Gahl et al, Orphanet J Rare Dis. 2021 Jul 13;16(1):308. doi: 10.1186/s13023-021-01923-0.
2. Niedeggen C, Singer S, Groth M, et al. Design and development of a disease-specific quality of life tool for patients with aplastic anaemia and/or paroxysmal nocturnal haemoglobinuria (QLQ-AA/PNH)-a report on phase III. Ann Hematol. 2019;98(7):1547-1559. doi:10.1007/s00277-019-03681-3
3. Daly, R.P., Jalbert, J.J., Keith, S. et al. A novel patient-reported outcome instrument assessing the symptoms of paroxysmal nocturnal hemoglobinuria, the PNH-SQ. J Patient Rep Outcomes 5, 102 (2021). https://doi.org/10.1186/s41687-021-00376-0