HTA77

How to best model caregiver quality of life in health technology assessments? Lessons from NICE submissions in multiple sclerosis

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SUMMARY

OBJECTIVES

- Multiple sclerosis (MS) is a chronic, autoimmune-mediated neurological disease which often involves progressive deterioration and increased dependence on informal caregivers over time.
- Caregiver burden is increasingly being considered in NICE health technology assessments (HTAs). This study aimed to identify instances where caregiver burden was modelled in or incorporated into NICE technology appraisals (TAs) for MS interventions.

METHODS

- TAs in MS published from the inception of the NICE HTA process until 5th June 2024 were systematically identified and reviewed. Final appraisal documents and committee papers were obtained and searched for the terms: ‘carer’, ‘caregiver’, ‘family’, and ‘informal care’.
- TAs in which carer QoL was directly considered by NICE evaluation committees were also included.

FINDINGS

- NICE have published 15 recommendations in MS: 14 TAs (**13 STAs** and **1 MTA**) which modelled caregiver QoL and 1 TA which was a fast-track appraisal.
- In every submission identified, carer disutilities were modelled based on patient disease severity classified by Expanded Disability Status Scale (EDSS), meaning they were easily comparable. In addition, all submissions used **1 caregiver**.
- The NICE committee preferred assumptions where carer utility decrements rose with worsening patient EDSS health state. Carer QoL was accepted and included in the committee base-case in all 14 TAs.

RECOMMENDATIONS

- Carer HRQoL is best modelled employing **(dis)utilities as a function of the patient’s disease severity or health state**.
- Carer HRQoL should be derived from **EQ-5D**/ generic measure in indication (**primary data if possible**) > EQ-5D/ other generic measure in proxy indication with justification > Vignette study with justification > modified Delphi using vignette methodology with justification.
- Justification when modelling >1 caregiver for indications in the adult population.

BACKGROUND & AIMS

- Multiple sclerosis (MS) is a complex, is an autoimmune-mediated neurodegenerative disease that affects approximately 2.3 million people worldwide and is often diagnosed between the ages of 20 and 50 years, with females experiencing it more often than males.[1]
- Despite recent advances in treatment i.e., disease-modifying therapies (DMTs), many people with multiple sclerosis (MS) require ongoing care and support due to the progressive nature of the disease. Informal carers provide much of the everyday support and can experience significant burden because of their role, with relevant implications on quality of life (QoL).[2]
- While health technologies aim to improve patients’ health, health technology assessment (HTA) agencies have increasingly identified health-related quality-of-life effects (HRQoL) for caregivers and family members of ill patients (i.e., spillover effects), as important considerations in health economic (HE) modelling.[3]
- In 2022, the updated National Institute for Health and Care Excellence (NICE) methods guide suggested that “evidence should be provided to show that the condition is associated with a substantial effect on carer's health-related quality of life and how the technology affects carers.” However, did not provide further guidance on how effects on informal carers or other family members should be included.[4]
- Therefore, this study aimed to investigate and identify instances where informal carer burden was modelled in or incorporated into NICE technology appraisals (TAs) for DMTs for MS, and to understand how carer HRQoL can be measured and included in HE models.

METHODS

- A document analysis of final appraisal documents (FADs), appraisal consultation documents (ACDs) and committee papers of single TAs (STA), multiple TAs (MTA), and highly specialised technologies (HSTs) in MS published on the nice.org.uk website from its inception until 5th June 2024 was undertaken. Documents were retrieved and screened for the keywords: ‘carer’, ‘caregiver’, ‘family’, and ‘informal care’ (Table 1).
- Information about carer HRQoL as considered by the manufacturer, evidence assessment group (EAG) and NICE committee, was extracted from eligible submissions. The reference lists of eligible submissions were checked for previously published STAs/MTAs.

RESULTS

- NICE have published 15 recommendations in MS: 14 TAs (**13 STAs** and **1 MTA**) which modelled carer QoL and 1 TA which was a fast-track appraisal.
- In every submission identified, carer (dis)utilities were modelled based on patient disease severity classified by Expanded Disability Status Scale (EDSS), meaning they were easily comparable. In addition, all submissions used **1 carer**.
- The NICE committee preferred assumptions where carer utility decrements rose with worsening patient EDSS health state. Carer QoL was accepted and included in the committee base-case in all 14 TAs.

Table 1. Eligibility criteria.

Criteria	Inclusion	Exclusion
Population	Individuals with any type of multiple sclerosis (MS) including clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS)	Any other indication
Intervention	Any disease-modifying therapy	Any intervention not for MS
Outcomes	Caregiver/ carer/ family/ sibling AND HRQoL/ utilities/ burden	Not applicable
Study design	NICE technology appraisals or NICE highly specialised technologies	Not applicable

RECOMMENDATIONS

- In organising HE modelling for submissions, manufacturers should consider 1) dossier discourse concerning the qualitative burden of the disease; 2) source of caregiver HRQoL values; 3) number of caregivers modelled; 4) suitability of modelling approach adopted; 5) position within the cost-utility analysis.

Table 2. Recommendations for modelling caregiver HRQoL in HTA submissions.

Category	Suggestion	Reasoning
Qualitative burden	▪ ***De novo* caregiver surveys if caregiver burden or extent of patient dependence on informal caregivers has not been well established in clinical practice and/or literature** ▪ **Published qualitative surveys of family/ caregiver burden in condition or proxy indication** ▪ **Caregiver HRQoL reviews using systematic methodology**	▪ **HTA committees require sufficient evidence to justify including consideration of caregiver HRQoL e.g., NICE TA748** ▪ **Demonstrate the nature of the condition and its burden on informal, primary caregivers** ▪ **Highlight patient’s dependence on informal caregivers** ▪ **Discuss impact of caregiving e.g., emotional burden, productivity impact, time spent on round-the-clock care, etc.**
Source of HRQoL estimates	**In hierarchal order:** ▪ ***De novo* ED-5D estimates from clinical trials** ▪ **ED-5D values from published literature (cited in previous appraisals, if possible)** ▪ **Other HRQoL measures in trial mapped to EQ-5D** ▪ **Other generic measures from proxy indication** ▪ **Vignette study**	▪ **SHEER guidelines #6 recommends the use of primary data[5]** ▪ **Justification in departure from HTA reference case is necessary** ▪ **Follow best practice for vignette development as final option.[6] Include justification for paucity of other robust options**
Number of caregivers	▪ **1 caregiver if adult population** ▪ **≥1 caregiver for paediatric population possible with justification**	▪ **>50% of NICE submissions modelled 1 caregiver** ▪ **Validation on number of carergiver is imperative**
Modelling approach	▪ **Disutilities as a function of patient health state/ disease severity/ treatment/ adverse events, preferable methodology** ▪ **Utility as a function of patient health state/ treatment** ▪ **QALY loss due to bereavement** ▪ **Cap on utilities/ disutilities, with justification** ▪ **Combination of techniques listed above**	▪ **Consider the possibility of double-counting QALY loss by combining caregiver disutility by patient severity + QALY loss upon patient death** ▪ **Consider applying caregiver disutilities to most severe patient health states only** ▪ **Consider clinician validation to support inclusion**
Position within manufacturer submission	▪ **Preferred in base-case analysis** ▪ **Consider placement in scenario analysis only if there are notable methodological concerns** ▪ **Consider placement in both base-case and scenario analysis by exploring different modelling approaches and/or different utility sources**	▪ **>80% of NICE submissions included carer HRQoL in base-case analyses** ▪ **Exploring different approaches i.e., utility vs disutility in submissions for indications without a precedent case, is advisable** ▪ **Consider previous submissions in similar or proxy indications**

References

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2. *Wittenberg (2019). Spillover effects on caregivers’ and family members’ utility: a systematic review of the literature. Pharmacoeconomics, 37, 475-499.*
3. *Pennington (2020). Inclusion of carer health-related quality of life in National Institute for Health and Care Excellence appraisals. Value in Health, 23(10), 1349-1357.*
4. *Dawoud (2022). Capturing what matters: updating NICE methods guidance on measuring and valuing health. Quality of Life Research, 31(7), 2167-2173.*
5. *Henry (2024). Recommendations for emerging good practice and future research in relation to family and caregiver health spillovers in health economic evaluations: a report of the SHEER task force. Pharmacoeconomics, 42(3), 343-362.*
6. *Rowen (2020). Measuring And Valuing Health-Related Quality Of Life When Sufficient EQ-5D Data Is Not Available.*

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