Can Carer Quality Adjusted Life Year (QALY) Shortfall Help Us Quantify the Caregiving Burden in Health Technology Assessment (HTA)? Learnings From a Case Study in Amyotrophic Lateral Sclerosis (ALS)

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Background

- QALY shortfall is sometimes used by HTA bodies to apply additional weighting for the most severe conditions in economic evaluations.
- HTA bodies may consider absolute QALY shortfall (the future health lost by people living with a condition, compared with expected future health without the condition over the remaining lifetime of the patients) and proportional QALY shortfall (the proportion of future health lost by people living with the condition)
- Carer health effects may be included in QALY calculations but are not typically included in calculations of QALY shortfall. [1]
- Including caregiver health effects in economic evaluations would more fully capture overall population health benefits, but there is no standard method. In some cases where carer health effects are modelled by directly applying a caregiver disutility, there may be an incremental QALY loss for carers if an intervention extends life but does not reduce caregiver burden – which does not match societal preferences. [2]
- This study aimed to explore a method of including caregiver burden in cost effectiveness analysis by weighting QALY gains according to modelled health lost from providing informal care (carer QALY shortfall) – and how this may affect decision making in HTA.
- We chose ALS as a case study as it is associated with a significant caregiving burden, there are potential new therapies available, and model structures are well established.

Methods

- We built a Markov model evaluating the cost effectiveness of edaravone as an add on to standard of care (SoC) in ALS over a lifetime horizon (35 years), from a UK NHS perspective.
- Model health states were based on the King's clinical staging system. Transition probabilities, patient utilities and the method for calculating carer disutility were taken from previous economic analyses in ALS.[3,4]
- We assumed that the effect of edaravone on progression was fixed (hazard ratio=0.665, 95% CI 0.41 to 1.08); effectiveness estimation was based on survival data from an unpublished manufacturer report[5].
- 1 carer per patient was included in the base case, assumed to be the same age as the patient at 65. Carer disutility was calculated using the formula:

  *Carer disutility = (Patient utility – general population utility)*0.5*

- QALY shortfall for SoC was calculated for patients and for carers – over both patient and carer lifetimes (including bereavement effects for caregivers on patient death), as shown in Figure 1.

Figure 1: Method for calculating patient and carer QALY shortfall
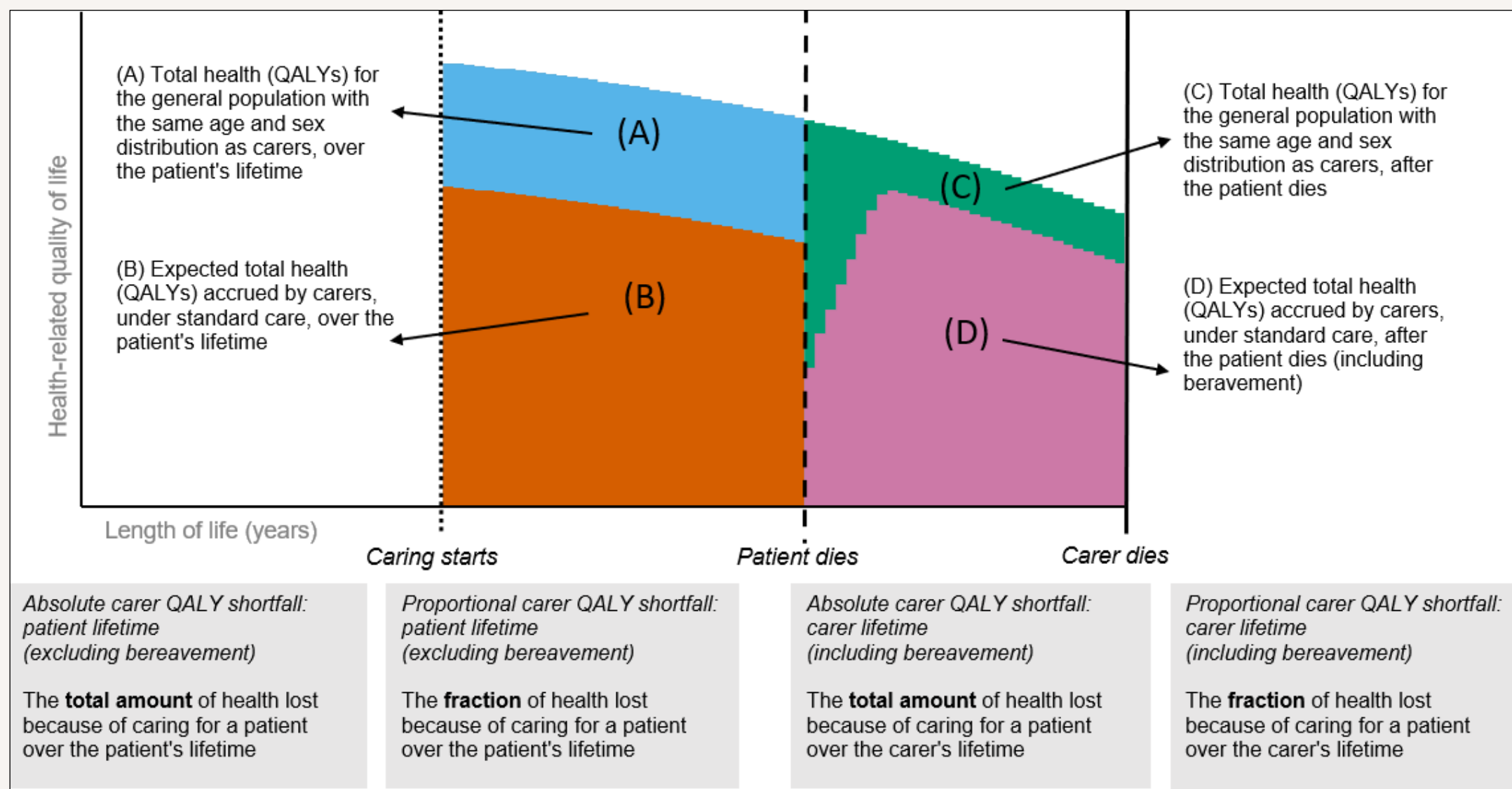
- A QALY weighting was applied to incremental patient QALYs according to the size of the combined QALY shortfall – in line with NICE's severity thresholds and weightings (Table 1).
- Uncertainty was explored including varying age of patients or carers, number of carers and increased carer disutility.

Table 1: NICE severity modifier thresholds

QALY weight	Proportional shortfall	Absolute shortfall
X1	<0.85	<12
X1.2	0.85 to 0.95	12 to 18
X1.7	>0.95	>18

Results

- The incremental QALY gain for edaravone plus standard care was 0.17 with patient QALYs alone and decreased to 0.14 when carer QALY loss was included.
- **Absolute and proportional QALY shortfall was smaller for carers than patients in the base case and all scenarios**. When patient and carer QALY shortfall were combined, absolute QALY shortfall *increased* and proportional QALY shortfall *decreased* compared to patient QALY shortfall alone (shown in Figures 2 and 3)
- Proportional patient QALY shortfall was high enough to meet the severity modifier threshold for a 1.2x QALY weighting, but **carer QALY shortfall alone or inclusion of carer QALY shortfall in combined QALY shortfall did not lead to an additional QALY weighting**.
- The **carer QALY shortfall was sensitive to carer age, number of carers and increased carer disutility** (Figures 2 and 3)

Table 2: Estimated patient and carer QALY shortfall for SoC in model

	Absolute	Proportional
Patient QALY shortfall	9.60	0.879
Carer QALY shortfall (patient lifetime)	0.308	0.102
Carer QALY shortfall (carer lifetime)	0.448	0.041

Table 3: Combined patient and carer QALY shortfall for SoC in model

	Absolute	Proportional
Combined QALY shortfall (patient lifetime)	9.91	0.711
Combined QALY shortfall (carer lifetime)	10.05	0.458

Figure 2: Scenario analyses exploring the effect of changes in carer characteristics on absolute QALY shortfall

Patient, carer and combined absolute QALY shortfall - scenario analysis

- Base case: Absolute patient QALY shortfall 9.6, Absolute carer QALY shortfall (carer lifetime) 0.448, Absolute combined QALY shortfall (carer lifetime) 10.05
- Multiple carers: 9.6, 0.896, 10.5
- Carer age 30: 9.6, 0.448, 10.05
- Carer and patient age 55: 13.02, 0.491, 13.51
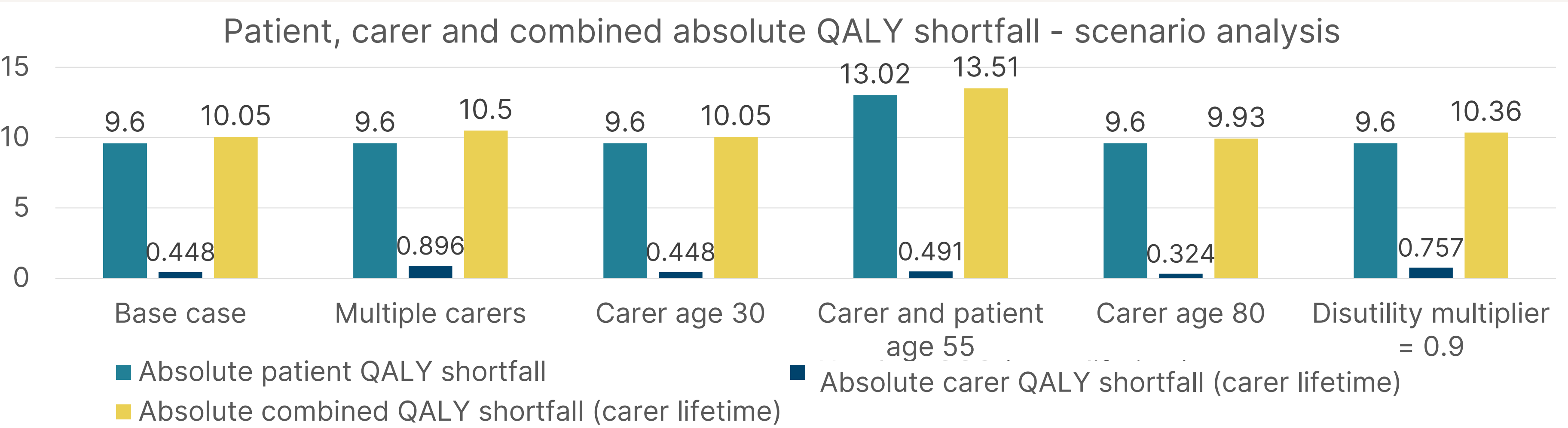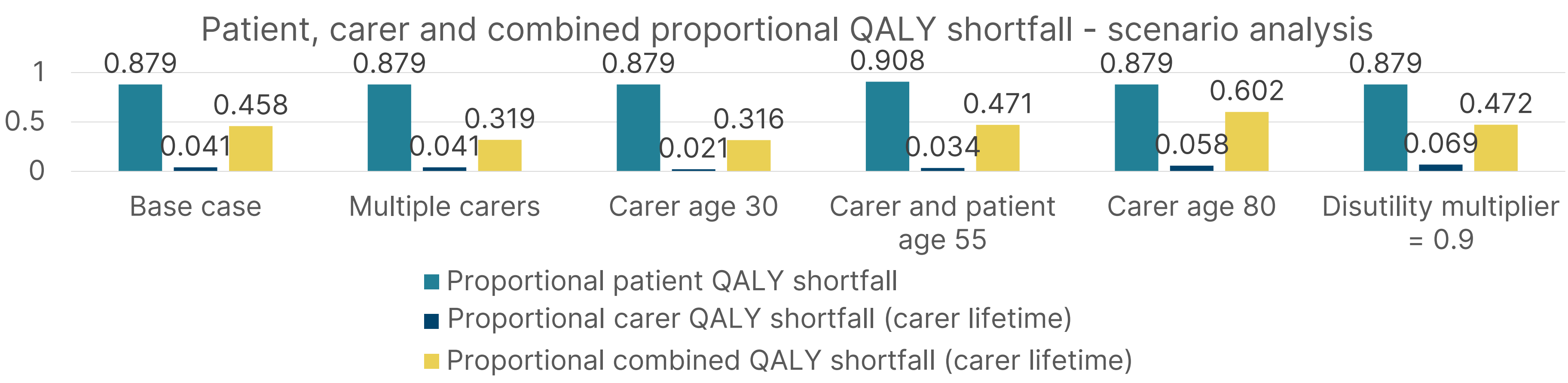- Carer age 80: 9.6, 0.324, 9.93
- Disutility multiplier = 0.9: 9.6, 0.757, 10.36

Figure 3: Scenario analyses exploring the effect of changes in carer characteristics on proportional QALY shortfall

Patient, carer and combined proportional QALY shortfall - scenario analysis

- Base case: Proportional patient QALY shortfall 0.879, Proportional carer QALY shortfall (carer lifetime) 0.041, Proportional combined QALY shortfall (carer lifetime) 0.458
- Multiple carers: 0.879, 0.041, 0.319
- Carer age 30: 0.879, 0.021, 0.316
- Carer and patient age 55: 0.908, 0.034, 0.471
- Carer age 80: 0.879, 0.058, 0.602
- Disutility multiplier = 0.9: 0.879, 0.069, 0.472

Conclusions

- It has been possible to calculate carer QALY shortfall from carer disutility - the approach outlined in this study makes it possible to indirectly include carer HRQoL in economic evaluations and avoids the paradoxical QALY loss for carers that can occur when an intervention prolongs life but does not reduce caregiver burden.
- Inclusion of carer QALY shortfall in QALY shortfall calculations did not increase the incremental patient QALY weighting in this case study because of its small size - a larger impact on carer QALYs would be needed for carer QALY shortfall to affect incremental patient QALY weighting.
- Further research is needed into whether directly combining patient and carer QALY shortfall is appropriate and what time period should be used (carer or patient lifetime), the value that should be placed on carer HRQoL, and the appropriate thresholds and weightings to apply when considering carer health effects.

References
1. Wailoo, A. A guide to calculating burden of illness for NICE Evaluations: Technical Support Document 23, 2024 [Available from https://www.sheffield.ac.uk/nice-dsu/tsds/severity-shortfall-tsd]
2. Al-Janabi H, Wittenberg E, Donaldson C, Brouwer W. The relative value of carer and patient quality of life: A person trade-off (PTO) study. Social Science & Medicine. 2022 Jan 1;292:114556
3. Balendra R, Al Khleifat A, Fang T, Al-Chalabi A. A standard operating procedure for King's ALS clinical staging. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration. 2019
4. Thakore NJ, Lapin BR, Kinzy TG, Pioro EP. Deconstructing progression of amyotrophic lateral sclerosis in stages: a Markov modeling approach. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration. 2018 Oct 2;19(7–8):483–94
5. CADTH Common Drug Review Pharmacoeconomic Review Report for Radicava. Canadian Agency for Drugs and Technologies in Health; 2019 Apr. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542526/pdf/Bookshelf_NBK542526.pdf

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