

# Can We Mitigate the Caregiver QALY Trap in Economic Evaluations? A Case Study in Duchenne Muscular Dystrophy



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## Background

- The provision of informal care can be associated with a multitude of adverse health effects, including impairment to emotional, social, financial, physical, and spiritual functioning, and even premature death<sup>1</sup>
- Incorporating caregiver burden in economic evaluations for treatments that also extends life can have a negative impact on the incremental cost-effectiveness ratio
- This arises for treatments that prolong survival in diseases with significant informal care demands, thereby accruing losses in caregiver utilities (stemming from the provision of informal care) during the life-years gained with a high caregiver burden
- In this scenario, strictly maximizing QALYs introduces a trade-off between extending the life of the patient and reducing the burden of the caregiver, a phenomenon referred to as the “caregiver QALY trap”<sup>2,3</sup> (Figure 3, panel A)
- A solution that has been proposed in the literature to help manage the caregiver QALY trap in economic evaluations involves the explicit modeling of a ‘bereavement effect’, that is, a disutility experienced by caregivers following the death of the patient<sup>2</sup> (Figure 1)

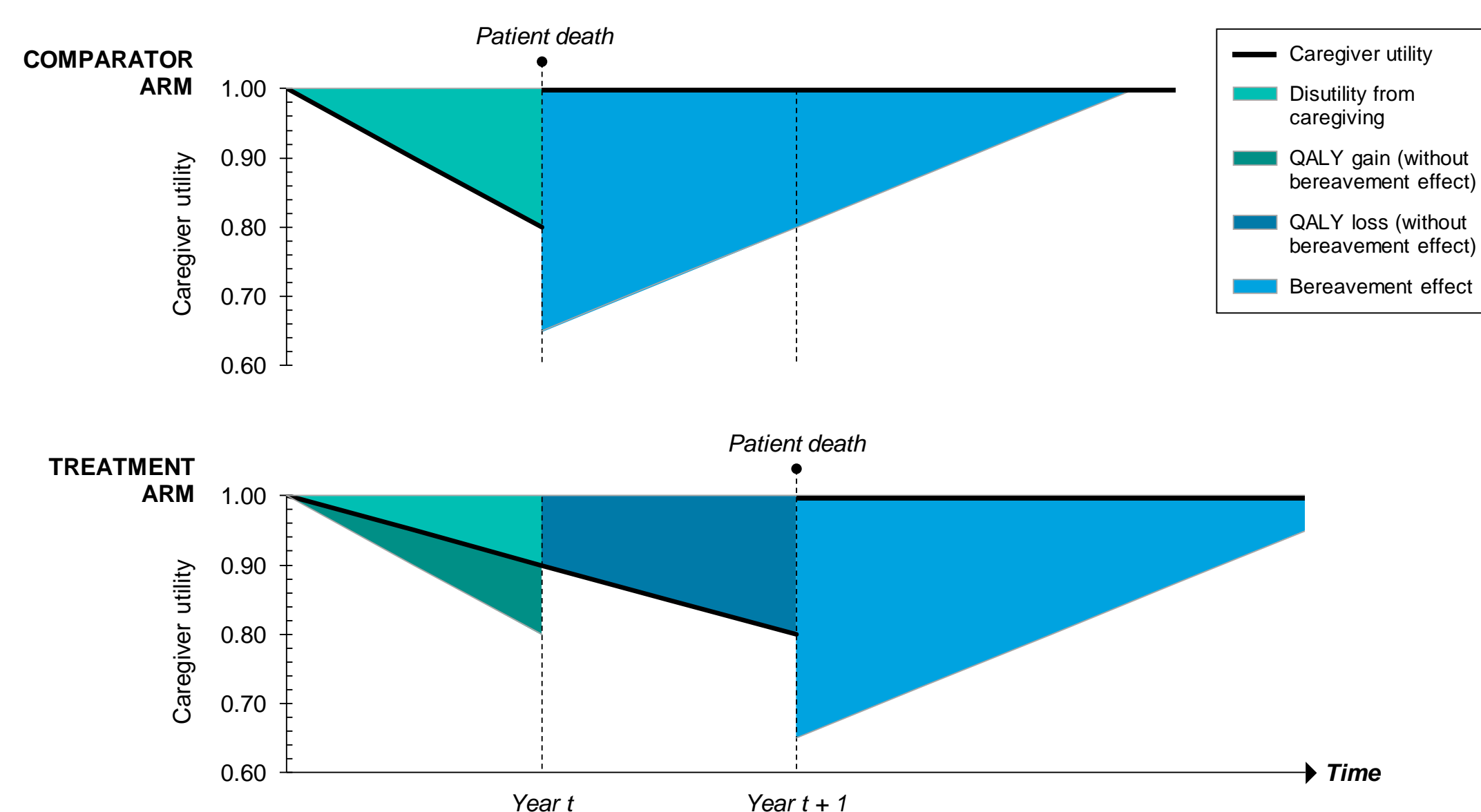


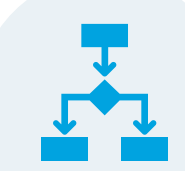
Figure 1: Illustration of the caregiver QALY trap and bereavement effect for a life-extending treatment of DMD

Note: The depicted treatment extends life by 1 year (from  $t$  to  $t+1$ ) in relation to the comparator by delaying disease progression, thereby shifting the caregiver loss in utility. This results in a QALY gain in the absence of a bereavement effect. Upon patient death, caregiver utility is assumed to return to baseline (illustrated at 1.00 for simplicity), resulting in a QALY loss in the absence of a bereavement effect. The total loss from the QALY trap in the absence of a bereavement effect is equal to the QALY loss minus the QALY gain<sup>3</sup>



## Objectives

- The objective of this modelling study was to explore the impact of accounting for health effects associated with bereavement to offset the caregiver QALY trap in Duchenne muscular dystrophy (DMD), a rare, severe debilitating and ultimately fatal neuromuscular disease resulting in loss of ambulation and serious multi-system complications



## Methods

- We developed a partitioned survival model replicating the health states from Landfeldt et al.<sup>4</sup> and standard of care (SOC) efficacy from the DMD model by the Institute for Clinical and Economic Review (ICER)<sup>5</sup> (model cycle length: 3 months) (Figure 2)
- A hypothetical intervention was modelled with a hazard ratio vs SOC of 0.38 for all endpoints, representing the treatment effect; this delayed median loss of ambulation by five years

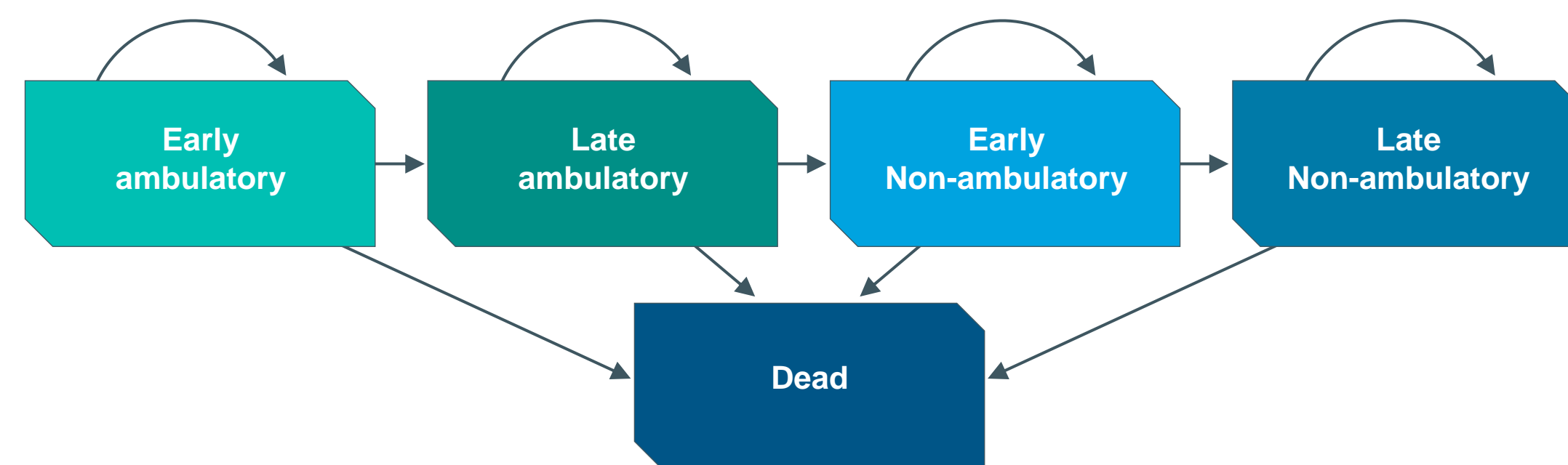


Figure 2: Schematic of the DMD model

- Health states utilities for caregivers were 0.858 for the early ambulatory state, 0.839 for the late ambulatory stage, 0.837 for the early non-ambulatory stage, and 0.774 for the late non-ambulatory state<sup>4</sup>
- The modeled patient start age was 5 years<sup>5</sup>; and one caregiver was modeled per patient<sup>6</sup> (caregiver start age: 33 years<sup>6</sup>; 51% female<sup>7</sup>)
- Discount rate for outcomes was 3.5%<sup>8</sup>
- Different methods of incorporating a bereavement effect to offset the QALY trap in the presence of discounting were explored:
  - Time-dependent bereavement effect:** Upon patient death, the caregiver experiences an initial disutility for a period, followed by a gradual return to general population baseline utility. The return to general population baseline utility can be modelled with various trajectories such as linearly or at a diminishing rate over their lifetime. Permanent disutility can be incorporated by caregivers remaining below the general population baseline utility (Figure 3, panel B)
  - One-off QALY loss:** Upon patient death, the caregiver accrues a one-off QALY loss. Previous methodology to estimate the size of the QALY loss have included using a percentage of the discounted QALYs for the number of years earlier the patient died than the life expectancy for a healthy control. This method of estimating the one-off QALY loss generates a lower loss for treatments delaying disease progression (Figure 4, panel A)
  - Caregiver treatment-specific utilities:** Caregiver utility would also be treatment dependent for the alive patient health states (early/Late ambulatory and early/late non-ambulatory). This would represent differences in subsequent expected bereavement from the treatment's effect on delaying disease progression or improving patient health related quality of life, hence reducing the gap between the total QALYs for the patient and the total QALYs of a healthy control (Figure 4, panel B)

**References:** (1) Adelman RD, et al. Caregiver burden: a clinical review. *JAMA* 2014;311(10):1052-60. (2) Mott DJ, et al. Modelling Spillover Effects on Informal Carers: The Carer QALY Trap. *Pharmacoeconomics* 2023;41(12):1557-1561. (3) Landfeldt E, et al. Economic Evaluations of Treatments for Duchenne Muscular Dystrophy: The Caregiver QALY Trap. *Pharmacoeconomics* 2024;42(5):475-478. (4) Landfeldt E, et al. Economic Evaluation in Duchenne Muscular Dystrophy: Model Frameworks for Cost-Effectiveness Analysis. *Pharmacoeconomics* 2017;35(2):249-258. (5) Institute for Clinical and Economic Review, Deflazacort, Eteplirsen, and Golodirsen for Duchenne Muscular Dystrophy: Effectiveness and Value Final Evidence Report 2019. (6) National Institute for Health and Care Excellence HST22. (7) UK 2021 Census. (8) National Institute for Health and Care Excellence, NICE health technology evaluations: the manual. Process and methods [PMG36]. 2022 Jan 31. (9) Christensen H, et al. Re-evaluating cost effectiveness of universal meningitis vaccination (Bexsero) in England: modelling study. *BMJ* 2014;349:g5725

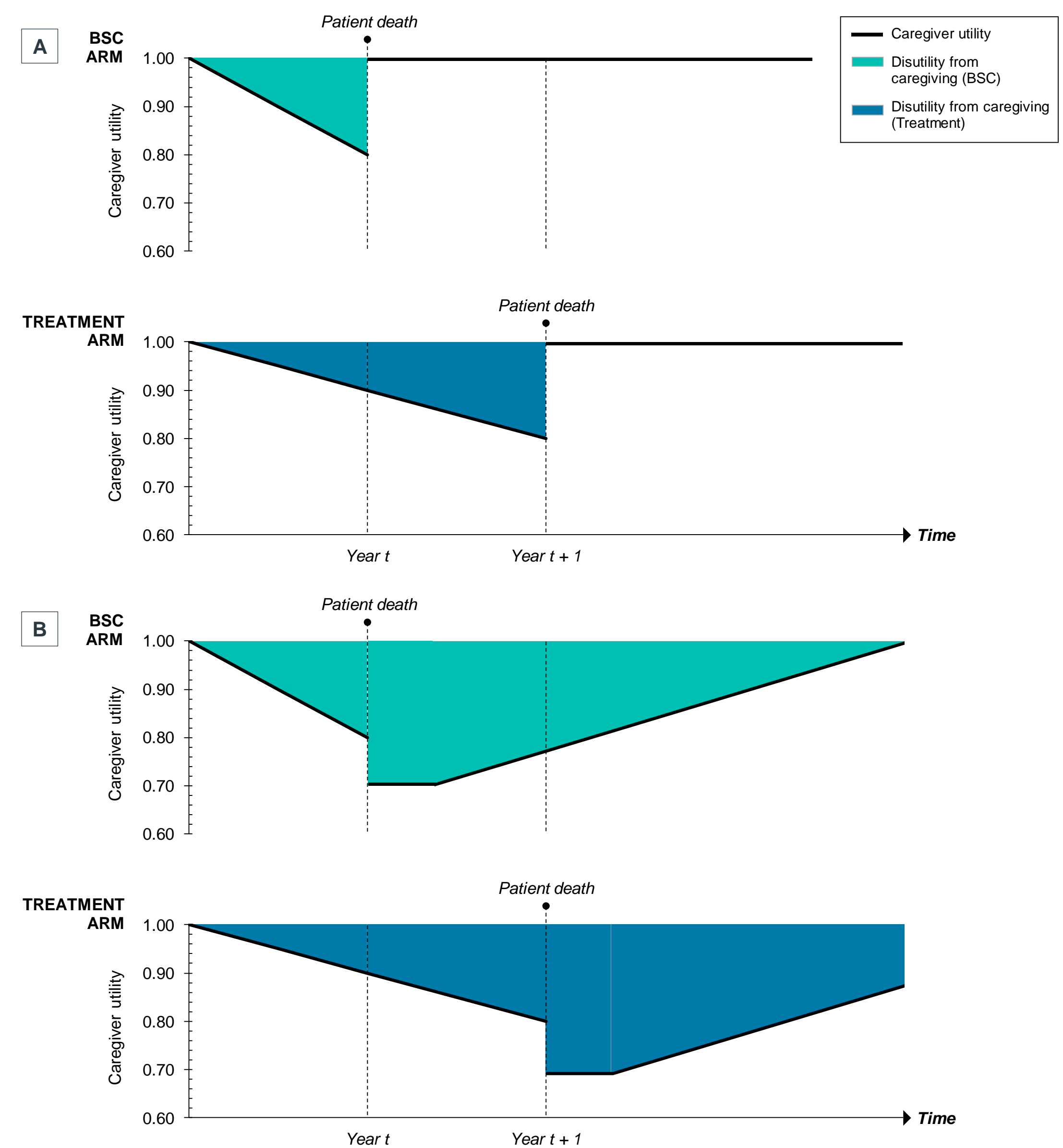


Figure 3: Illustration of the caregiver QALY trap for a life-extending treatment of DMD (A) and time-dependent bereavement effect (B)

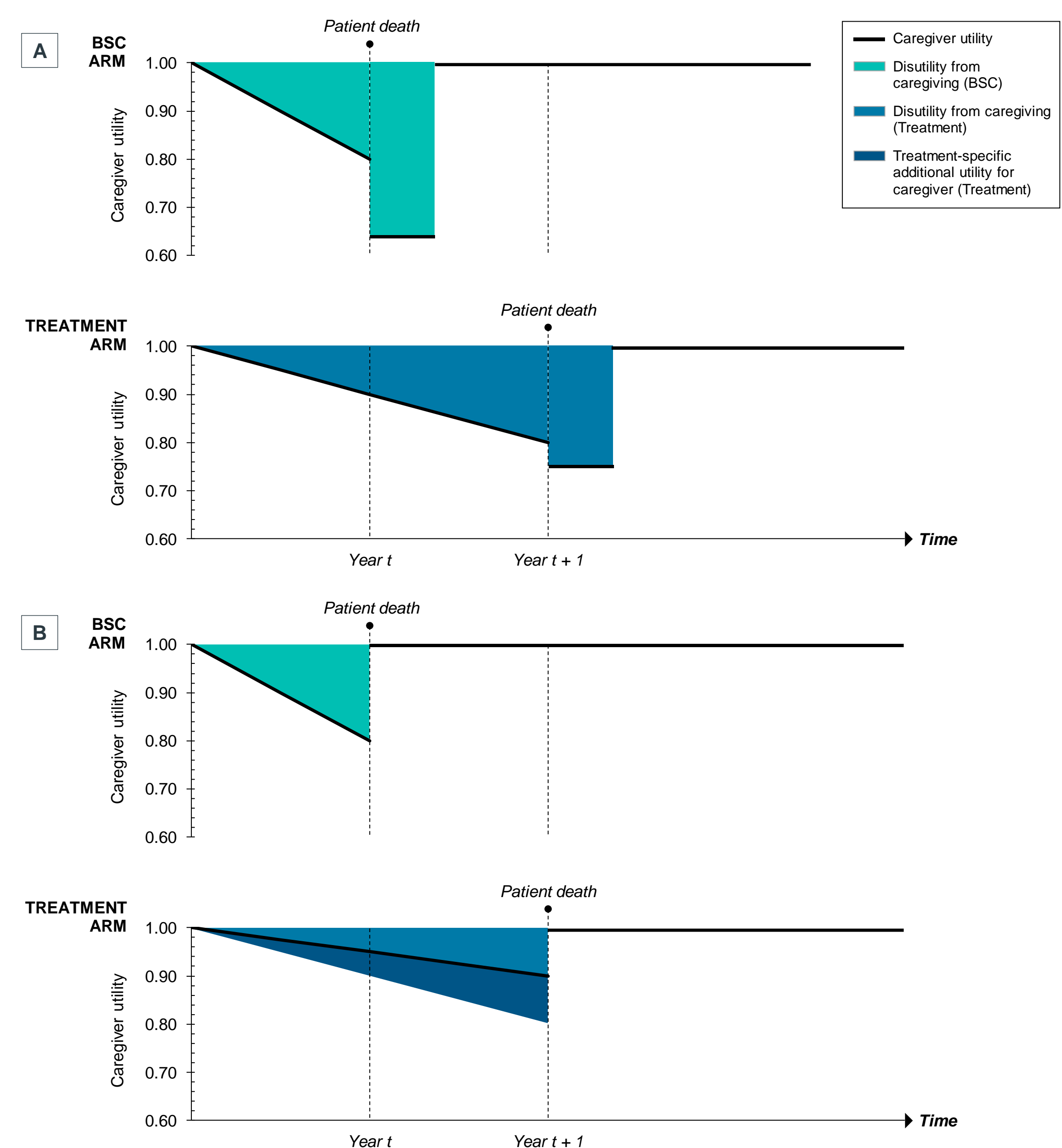


Figure 4: Illustration of the caregiver QALY trap for a life-extending treatment of DMD and a one-off QALY loss bereavement effect (A) and caregiver treatment-specific utilities (B)



## Results

- Without a bereavement effect, the QALY trap resulted in a lifetime caregiver incremental QALY loss of 0.12
- Time-dependent bereavement effect:** A linear return to general population baseline utility over 7 years with no additional initial disutility period was required to offset the caregiver QALY trap. Adding an initial disutility period or a permanent disutility increased the size of the bereavement effect, which increased the caregiver incremental QALYs, and thus required a less gradual return to general population baseline utility to be modelled
- One-off QALY loss:** Using 2.3% of the discounted QALYs for the number of years earlier the patient died than the life expectancy for a healthy control to estimate the size of the one-off QALY loss was required to offset the caregiver QALY trap. Using higher values such as 9% from the National Institute for Health and Care Excellence highly specialised technology appraisal for Strimvelis (based on Christensen et al.<sup>9</sup>) generated a lifetime caregiver incremental QALY of 0.36
- Caregiver treatment-specific utilities:** An increase in utility for caregivers in the treatment arm by 0.01 compared to the BSC arm in each alive patient health state (early/late ambulatory and early/late non-ambulatory) was required to offset the QALY trap



## Conclusions

- We show that the incorporation of a bereavement effect can successfully mitigate the caregiver QALY trap in DMD. All explored methods were able to offset the trap using relatively conservative assumptions. Further research into the health effects of bereavement is warranted