

The impact of family spillover effects in economic evaluation for SMA Type 1 treatments in the United States

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Background

- Global HTA organizations—as well as coverage and reimbursement entities in the US—recognize the importance of including FSEs in economic assessments of health technologies.^{1,2}
- FSEs may include caregiver direct healthcare costs, caregiver indirect costs and caregiver quality of life.^{1,2}
- FSEs are not routinely included in economic evaluations, but a growing body of evidence suggests that their inclusion can lead to notable changes in conclusions regarding drug value in economic evaluations.^{1,3}
- Advances in best practice methods guidance, increases in data availability and new tools to help proxy productivity impacts can be leveraged to enable more routine inclusion of FSEs.^{3,4}

Objective

- To evaluate the impact of including FSEs for unpaid parental caregivers in a CEA of treatments for Type 1 spinal muscular atrophy (SMA) in the US.

Methods

- A US societal perspective CEA, aligned to a published 2019 SMA assessment, was developed to evaluate FSE impacts (date of model: December 2024).⁵
- The model used hybrid Markov and partitioned survival models to capture short-term and projected outcomes for disease modifying therapy (DMT) versus best supportive care across health states aligned to patient motor function milestones: not sitting, sitting, walking, permanent ventilation and death.
- The replicated analysis was based on an economic model with monthly cycles conducted over a caregiver lifetime horizon, with caregiver mortality based on all-cause, age-based mortality rates.
- All inputs for clinical outcomes under best supportive care, patient utilities and health state costs remained consistent with the previous assessment; however, non-treatment direct medical costs were inflated to 2024 USD.
- Key changes to the CEA included (1) creation of a hypothetical treatment arm to reflect the current SMA treatment landscape and longer-term clinical data, and (2) addition of FSEs.
- The new hypothetical comparator reflects the weighted average clinical outcomes and wholesale acquisition costs of three available DMTs for Type 1 SMA (nusinersen, onasemnogene abeparvovec, risdiplam) using efficacy data from a published matching-adjusted indirect treatment comparison and real-world utilization patterns.⁶⁻⁹
- FSE estimates for primary unpaid caregivers were estimated across patient motor function milestones, per published HRQoL data and productivity costs estimated via a published algorithm^{10,11} (**Table 1**).

Table 1. Key caregiver inputs

Health state	Monthly productivity losses	Annual utility
Walking	\$0	0.915
Sitting	\$2,281	0.628
Not sitting	\$3,387	0.484
Permanent ventilation	\$3,387	0.484

- FSE carer utilities and productivity costs representing one unpaid parental caregiver were added to patient outcomes following recent recommendations from the Spillovers in Health Economic Evaluation and Research task force.³
- Drivers of results were explored through univariate sensitivity analysis, with ranges based on reported confidence intervals or an assumed 25% range above and below base-case values.

Results

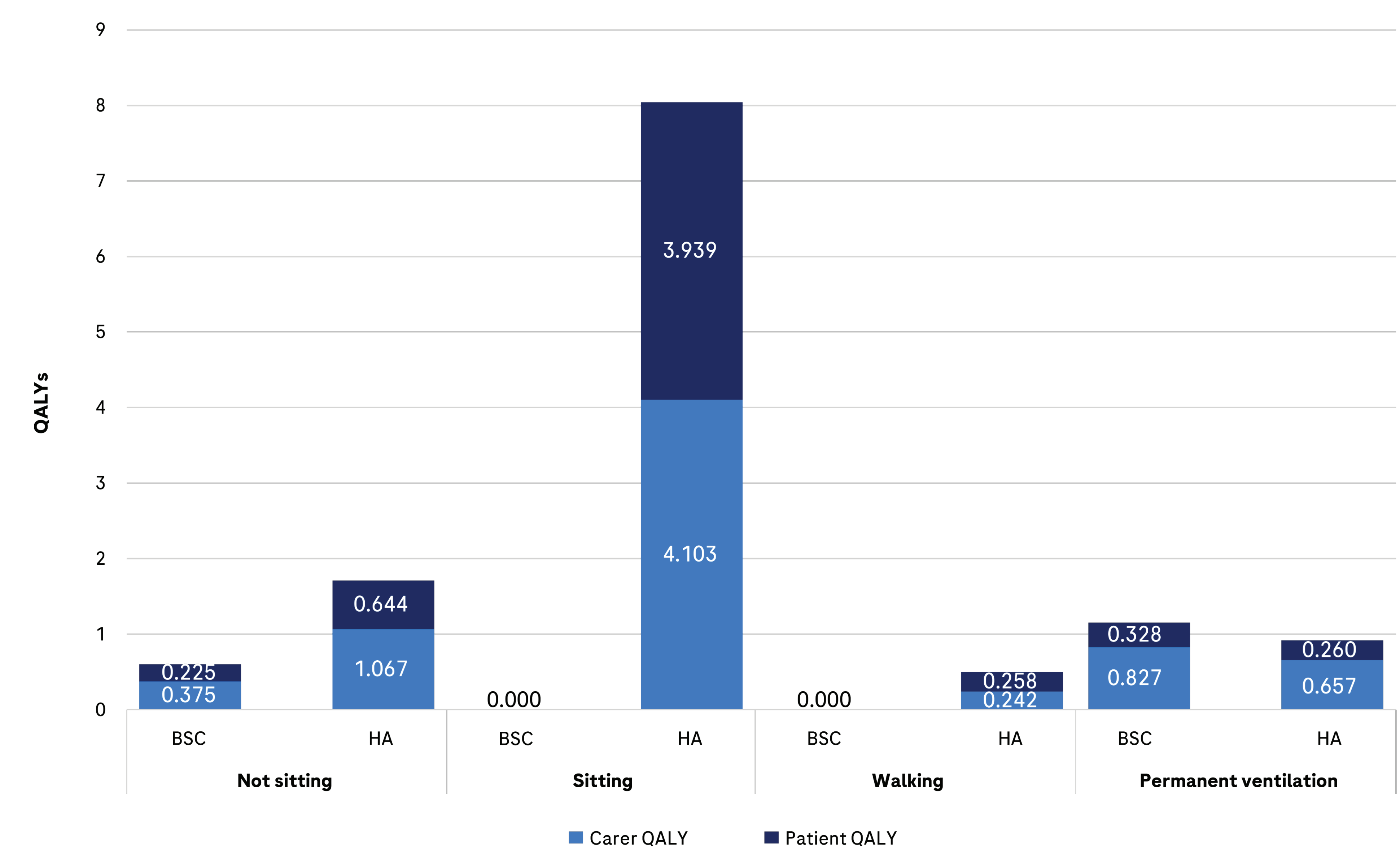
- With FSEs excluded, the lifetime ICER for the hypothetical treatment was \$1,065,627 (incremental \$4,865,582 costs and 4.57 QALYs). This falls within the range of results across DMTs from the initial ICER review but also reflects unique estimates based on the hypothetical comparator with additional clinical data across three DMTs.
- When HRQoL and productivity FSEs were added, the ICER reduced to \$572,443 (incremental \$5,064,328 and 8.85 QALYs), representing a 46% relative reduction (**Table 2**).

Table 2. Model results with and without FSEs

	Without FSEs included (patient only)	With FSEs included (patient + caregiver)	Relative change (with FSEs vs without FSEs)
Cost of hypothetical arm	\$5,898,288	\$6,196,575	5%
Cost of best supportive care	\$1,032,706	\$1,132,247	10%
Cost difference	\$4,865,582	\$5,064,328	4%
QALY for hypothetical arm	5.04	10.50	108%
QALY for best supportive care	0.47	1.67	255%
QALY difference	4.57	8.85	94%
ICER	\$1,065,627	\$572,443	−46%

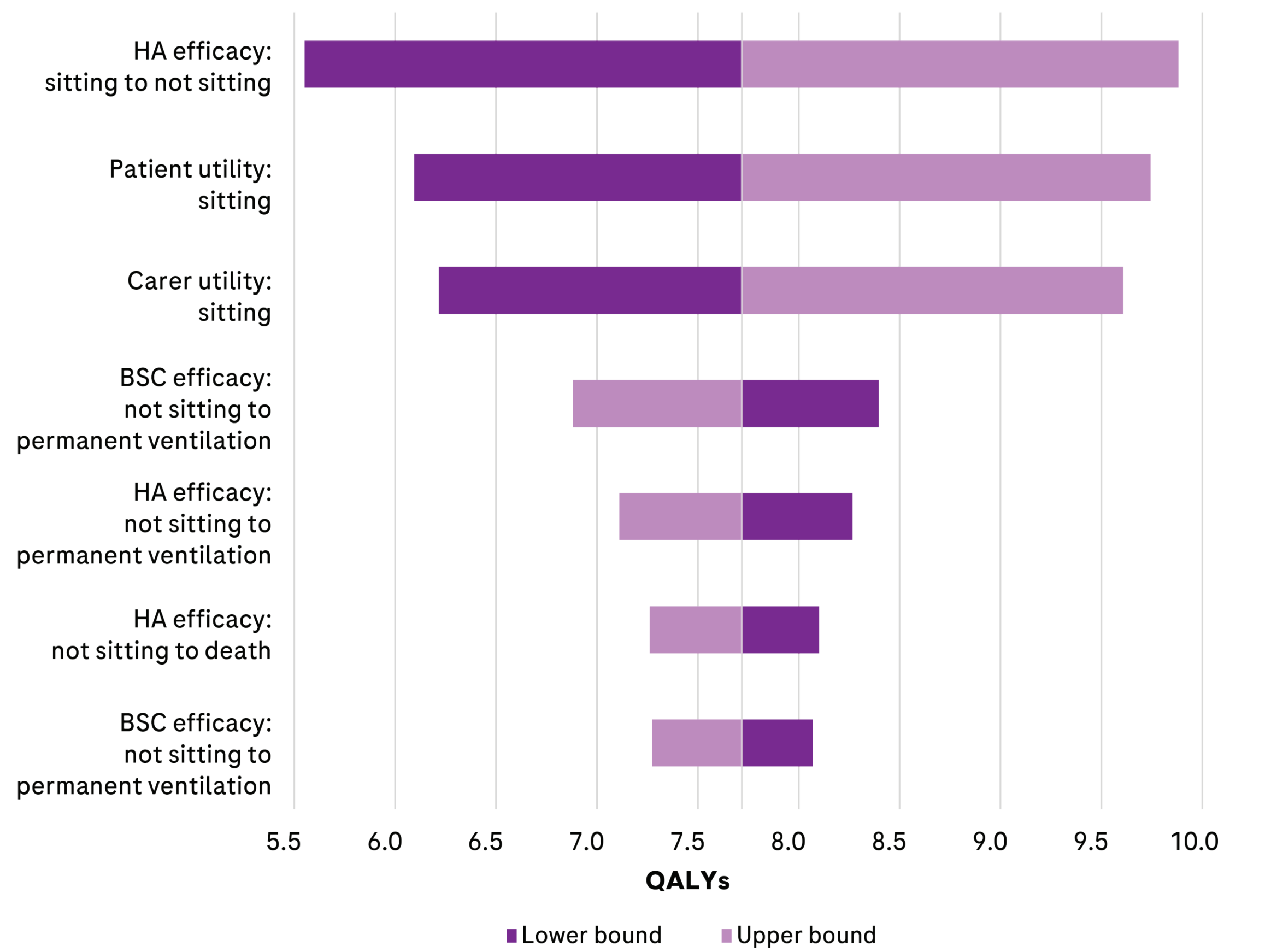
- ICER changes were primarily driven by caregiver HRQoL improvements, given the low caregiver utility associated with caring for not sitting (0.484) or sitting (0.628) patients, as these represent the health states in which patients on the hypothetical treatment spend most of their time (**Figure 1**).

Figure 1. Total family QALYs by health state and family contribution (lifetime time horizon)



- All scenarios including FSEs led to reductions in the ICER and were most sensitive to caregiver and patient utility values in the sitting state and treatment efficacy (**Figure 2**).

Figure 2. Incremental family QALYs with FSEs (HA vs BSC)



Limitations

- To calculate base-case findings without FSEs, we derived a hypothetical intervention arm using a previously published indirect treatment comparison that estimated efficacy outcomes at up to 1 year, but uncertainty remains about the long-term effectiveness of the included DMTs and best supportive care.
- This single case example is not generalizable across HTA applications where caregivers or family members are an integral part of care for patients.
- While the study explored trends for FSEs for utilities and productivity, data gaps prevented inclusion of the full range of potential impacts to caregivers, such as impacts on non-market productivity or changes in direct healthcare costs for carers' health needs.

Conclusions

- The addition of FSEs for primary unpaid caregivers of children with Type 1 SMA notably changed conclusions on treatment value as the ICER was reduced by about half, driven predominantly by addition of carer utilities.
- Future CEAs should explore FSEs using available caregiver data and productivity algorithms to estimate treatment impacts and value for the family.

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Disclosures

SK and SS are employees of Genentech, Inc and shareholders of Roche stock. BC is an employee of Stage Analytics.

Abbreviations

BSC, best supportive care; CEA, cost-effectiveness analysis; DMT, disease modifying therapy; FSE, family spillover effect; HA, hypothetical (treatment) arm; HRQoL, health-related quality of life; HTA, health technology assessment; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-years; SMA, spinal muscular atrophy; US, United States.

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