

Ethical Implications of Quality-adjusted Life Year Assessments for Patients With Disabilities: A Duchenne Muscular Dystrophy Case Study

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Objective

To assess the impact of a quality-adjusted life year (QALY) assessment for early non-ambulatory patients with Duchenne muscular dystrophy (DMD) by calculating the maximum treatment cost of a hypothetical treatment in a cost-effectiveness analysis (CEA)

Key Findings

This study uses a real-world example (early non-ambulatory patients with DMD) to show that a QALY-based assessment may result in a beneficial treatment never being cost-effective, even if the treatment were free



BACKGROUND

- CEAs are growing in importance for resource allocation and may influence insurance coverage policies.¹⁻³ It is critical to understand potential biases in a CEA that may result in unfair/inequitable access for certain patient populations
- QALYs are the most common health metric used in CEAs; however, their ability to capture health-related quality of life accurately for individuals with disabilities has been questioned, particularly for those who are unable to achieve higher utility compared with healthier individuals, even with treatment^{4,5}
 - Alternative metrics include equal value of life years gained (evLYG) that count any gains in length of life equally, regardless of the patient's health state⁶
- Treatments for patients in low utility/high-cost health states may never be cost-effective, even at zero cost⁷
 - Scenario analyses, excluding health-state costs that are not related to the intervention per se, may be informative; thus, it has been proposed that disease-related direct medical costs be removed from the analysis in this situation^{7,8}
- DMD is a progressive, genetic, neuromuscular disease, resulting in loss of ambulation (LOA) by early teenage years and premature mortality from the late teens into the third decade of life⁹⁻¹¹
 - Despite LOA, individuals retain a high degree of independence and participate in daily activities in the early non-ambulatory health state^{12,13}
- The Institute for Clinical and Economic Review (ICER) performed an assessment for 3 DMD treatments (deflazacort, eteplirsen, and golodirsen) in 2019¹⁴
 - Although the assessment focused on treating a 5-year-old Stage 2 early ambulatory patient, both treatments that were approved at the time of the assessment (deflazacort and eteplirsen) are indicated for patients regardless of ambulatory status^{15,16}



CONCLUSIONS

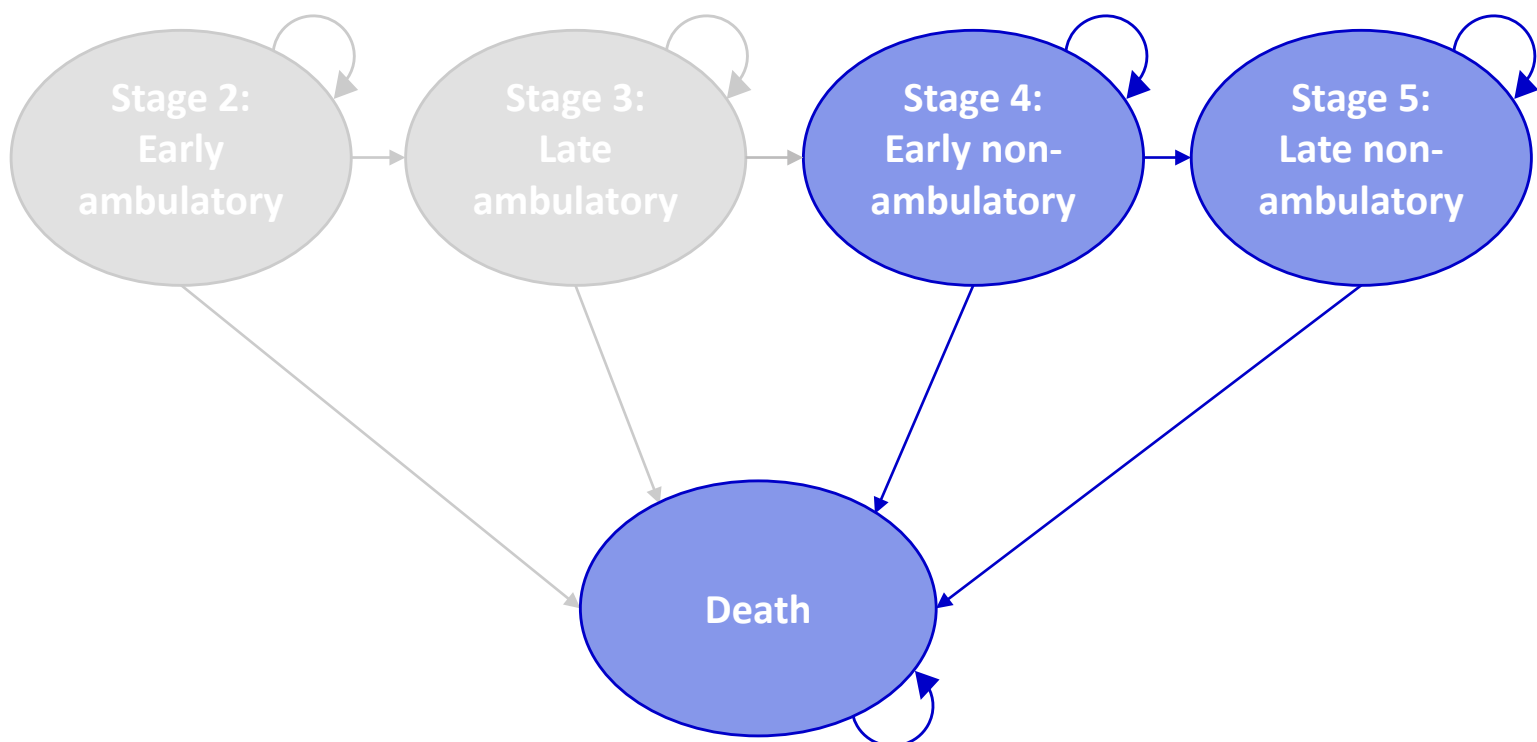
- These results support previously described concerns regarding QALY-based assessments for individuals with disabilities^{4,5}
- Low baseline health-state utility values for patients considered to be in the Stage 4 early non-ambulatory phase (but who still maintain upper body function and independence) have a substantial and concerning impact on the QALY-based value assessments of DMD treatments
- Use of QALYs to measure benefits in diseases with low utility values may result in treatments not being cost-effective, even when their cost is zero
- This study highlights the potential implications of using QALYs to value health technologies in severe conditions



METHODS

- The ICER 5 health state DMD model¹⁴ was replicated and adapted for patients with DMD starting in different health states and ages (Figure 1, Table 1)

Figure 1. 5 Health State DMD Model



DMD=Duchenne muscular dystrophy.

Table 1. Health-State Descriptions From ICER Report¹⁴

Stage	Description
Stage 1: Presymptomatic	Shows no physical signs of disease Diagnosis may be suspected at this stage based on family history or elevated creatine kinase, and confirmed by genetic testing
Stage 2: Early ambulatory	Displays Gowers' sign, waddling gait, toe walking Can climb stairs No respiratory or cardiac compromise Rare orthopedic complications Diagnosis most commonly made in this stage
Stage 3: Late ambulatory	Increasingly labored gait Losing ability to climb stairs and rise from floor May need orthopedic intervention for contractures Some risk of respiratory or cardiac compromise
Stage 4: Early non-ambulatory	May be able to self-propel Able to maintain posture May develop scoliosis and require surgical intervention Increasing risk for respiratory or cardiac compromise
Stage 5: Late non-ambulatory	Limited function of upper extremities Difficulty maintaining posture High likelihood of respiratory or cardiac compromise

ICER=Institute for Clinical and Economic Review.

- The base case assessed a 13-year-old Stage 4 early non-ambulatory patient with DMD
- Assumptions regarding utilities, health-state transitions, costs, and treatment benefits (10-, 20-, and 40-year pause in disease progression) were replicated per the published ICER report (Table 2)¹⁴

Table 2. Model Parameters

State	Patient Utility	Annual Direct Medical Costs
Stage 4: Early non-ambulatory	0.21	\$33,096
Stage 5: Late non-ambulatory	0.18	\$44,326

- Analyses included maximum treatment costs at willingness-to-pay (WTP) thresholds of \$50,000/QALY, \$100,000/QALY, and \$150,000/QALY. Results were rounded to the nearest \$100
- A scenario analysis assessed the impact of removing disease-related direct medical costs if treatment is deemed not cost-effective at zero costs despite QALY gains



RESULTS

Base case

- At \$100,000/QALY or less, incremental non-treatment costs exceeded the value of treatment benefits (QALYs gained), implying no cost-effectiveness of any treatment, irrespective of the amount of benefit, even at a zero-dollar treatment cost
- At \$150,000/QALY, annual maximum treatment costs ranged from \$260 to \$430, which is less than the annual maximum treatment cost of generic prednisone (\$550) (Table 3)

Table 3. Base Case: 13-Year-Old Stage 4 Early Non-ambulatory Patient

	Incremental Direct Medical Costs	QALYs Gained	Maximum Annual Treatment Cost		
			\$50,000/cQALY	\$100,000/QALY	\$150,000/QALY
10-year pause	\$193,300	1.32	Never CE	Never CE	\$260
20-year pause	\$337,100	2.30	Never CE	Never CE	\$360
40-year pause	\$523,600	3.57	Never CE	Never CE	\$430

CE=cost-effective; QALY=quality-adjusted life year.

Scenario analysis: Removing disease-related direct medical costs

- Direct medical costs were removed when the WTP was \$50,000/QALY and \$100,000/QALY, as those scenarios resulted in the hypothetical treatment being deemed not cost-effective even at zero cost despite QALYs gained
- A positive maximum annual treatment cost was achieved across all scenarios (Table 4)

Table 4. Scenario Analysis: Removing Disease-Related Direct Medical Costs

	Incremental Direct Medical Costs	QALYs Gained	Maximum Annual Treatment Cost	
			\$50,000/QALY	\$100,000/QALY
10-year pause	\$0	1.32	\$4000	\$8000
20-year pause	\$0	2.30	\$5400	\$10,900
40-year pause	\$0	3.57	\$6600	\$13,200

QALY=quality-adjusted life year.

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