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Determining the "Severity Premium" for Duchenne Muscular Dystrophy: A Societal Consideration for Cost-effectiveness Analysis

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Objective

To quantify the severity of Duchenne muscular dystrophy (DMD) based on quality-adjusted life years (QALYs) lost using absolute shortfalls (AS) and proportional shortfalls (PS)

Key Findings

Objective assessment of DMD demonstrates the extreme severity of the disease

BACKGROUND

- Evidence shows health gains for patients with severe diseases are valued more by society than equivalent health gains for patients with less severe diseases[1-4]
- Disease severity can be determined objectively using QALY shortfalls that quantify decreased quality of life and premature death due to a particular disease[5-7]
- Some European health technology assessment (HTA) bodies have applied a "severity premium" in QALY-based cost-effectiveness analyses (CEAs) by increasing the willingness-to-pay (WTP) threshold based on QALY shortfalls[5,8-10]
- DMD is a severe, progressive neuromuscular disease characterized by irreversible muscle degeneration leading to loss of ambulation, respiratory insufficiency, and early mortality

CONCLUSIONS

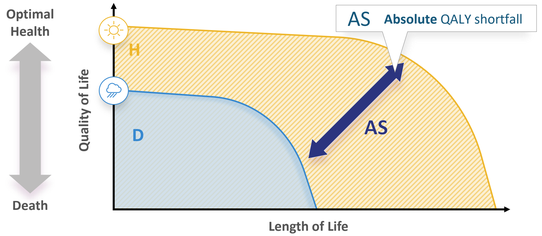
- This first-time quantification of DMD severity using QALY shortfalls highlights the magnitude of DMD disease severity
- Understanding the severity of disease is important for aligning treatment value assessments with societal preferences
- These data emphasize the need to consider the severity of DMD in treatment value assessments, including applying a "severity premium" in a CEA
- Disease severity is therefore an important consideration for value assessments of DMD treatments, as it aligns with society's preference of health gains for patients with more severe health states

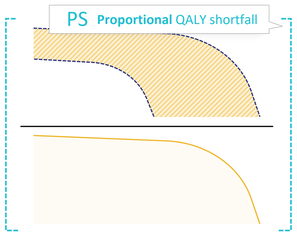
METHODS

Measure of Disease Severity: QALY Shortfall

H — D = AS

H: QALYs without disease; D: QALYs with disease and current SoC; AS: Disease-related QALY loss





Disease-related QALY loss / QALYs without disease = PS: Proportion of QALYs lost relative to remaining QALYs

AS=absolute shortfall; PS=proportional shortfall; QALY=quality-adjusted life year; SoC=standard of care.

- **AS is the difference in remaining QALYs that would be expected of the general population vs patients with a given disease**
- **PS is a ratio between 0 and 1 of the AS to the expected remaining QALYs of the general population, allowing a fair assessment of severity regardless of age of disease onset**

Severity of DMD: Study population and analysis

- 2 cohorts of patients were analyzed:
  - Cohort 1: 5-year-old early ambulatory boys (EA boys)
  - Cohort 2: 13-year-old early non-ambulatory boys (ENA boys)
- Remaining lifetime QALYs of the 2 cohorts of patients with DMD were assessed using a recreation of the 2019 Institute for Clinical and Economic Review (ICER) DMD CEA model
- AS and PS of the 2 cohorts relative to the US general population were derived from the iMTA Disease Burden Calculator severity adjustment online tool
  - Results were contextualized relative to 8 diseases quantified in a prior ICER assessment[11]

RESULTS

Severity of Duchenne based on QALYs lost using AS and PS

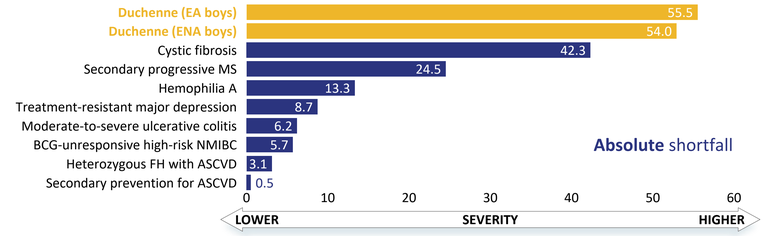
- The remaining undiscounted QALYs for EA and ENA boys were 8.74 and 2.63, respectively
- AS was higher for EA boys compared with ENA boys (55.47 vs 53.98), reflecting the higher AS for younger patients with the same disease
- PS was lower in EA boys (0.86 vs 0.95), highlighting the higher PS for more severe disease trajectory regardless of age
  - Both EA and ENA boys ranked highest in AS compared with the other 8 previously assessed diseases (range, 0.5 for secondary prevention of atherosclerotic cardiovascular disease to 42.3 for cystic fibrosis)
  - The PS of ENA boys was the most severe compared with those of the other diseases, while that of EA boys was less severe than only secondary progressive multiple sclerosis
- Both EA and ENA boys with DMD would classify into the highest severity category for several European HTAs, which adjust WTP based on disease severity:
  - England and Wales: at least 18 AS or 0.95 PS (whichever implies greater severity); Netherlands: greater than 0.7 PS; Norway: at least 20 AS

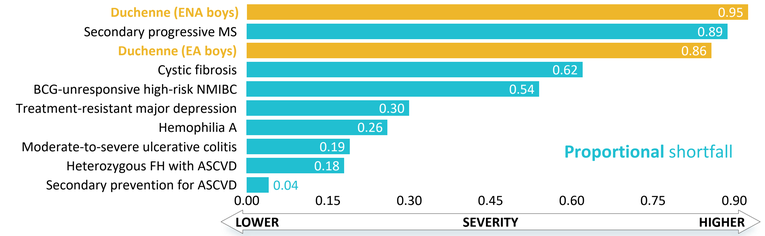
Cohort Characteristics and QALY Shortfall

	Cohort 1 (EA)	Cohort 2 (ENA)
Stage	Early ambulatory	Early non-ambulatory
Baseline age, years	5	13
% Male	100%	100%
Country	US	US
Remaining QALYs for general population	64.21	56.61
Undiscounted remaining QALYs for patients with DMD[a]	8.74	2.63
Absolute QALY shortfall[b]	55.47	53.98
Proportional QALY shortfall[b]	0.86	0.95

[a]This value reflects both the remaining survival (substantially reduced relative to the general population) and the reduction of quality of life due to Duchenne; [b]Calculated using the iDBC Tool[2,1] (US setting).
AS=absolute shortfall; ASCVD=atherosclerotic cardiovascular disease; BCG=Bacille Calmette-Guérin; DMD=Duchenne muscular dystrophy; EA=early ambulatory; ENA=early non-ambulatory; FH=familial hypercholesterolemia; iDBC=iMTA Disease Burden Calculator; MS=multiple sclerosis; NMIBC=non-muscle invasive bladder cancer; PS=proportional shortfall; QALY=quality-adjusted life year; SoC=standard of care.

QALY Shortfall for Duchenne Based on Current SoC (Cohorts 1 and 2)





Objective assessment of Duchenne demonstrates the extreme severity of the disease

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