EE523

Assessing the Economic and Quality of Life Impact of Treatment in Duchenne Muscular Dystrophy

Deo Mujwara, PhD,[1] Rajeev Ayyagari, PhD,[1] Matthew Hayes, FSA, MAAA,[2] John Ford, MA,[3] Randy McGonigal, MS[3]

[1] Analysis Group, Boston, MA, United States; [2] Milliman, Tampa, FL, United States; [3] NS Pharma, Paramus, NJ, United States

Introduction

- Duchenne muscular dystrophy (DMD) is the most common type of muscular dystrophy with a prevalence of 1.51 per 10,000 boys, ages 5 to 9 years, in the US[1]
- DMD causes progressive muscle weakness and loss of ambulation (LOA), which leads to substantial increases in costs and reduction in quality of life for patients and caregivers. However, the impact of treatments that delay LOA remains understudied
- We developed a cost and quality of life calculator for direct and indirect costs and quality-adjusted life-years (QALYs) in DMD patients from ages 5 to <18 years (13-year time-horizon) in the US
- Costs were estimated from a societal perspective and inflation adjusted to 2020 US dollars

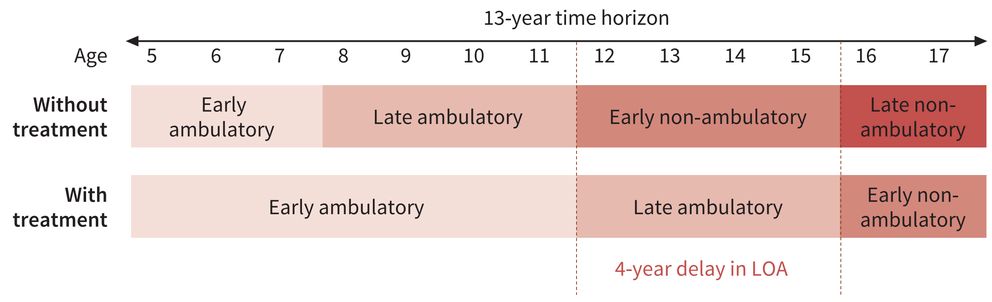
Objectives

- To measure total direct and indirect costs and QALYs associated with DMD in a period of 13 years
- To estimate the impact of delaying LOA on direct and indirect costs and QALYs:
  - Compare annual costs and QALYs between ambulatory and non-ambulatory patients
  - Estimate cost savings and QALYs gained from a treatment that delays LOA by 4 years

Methods

- The natural progression of DMD was divided into four disease stages based on ambulatory status and years spent in each stage: early ambulatory (3 years), late ambulatory (4 years), early non-ambulatory (4 years), late non-ambulatory (2 years)[2]
- Each disease stage was assigned a cost and quality of life utility value, with costs and quality of life for each stage obtained from data analyses or a literature review[3,4]
- Annual patient costs and QALYs were compared between ambulatory and non-ambulatory stages
- To estimate the impact of delaying LOA on direct and indirect costs and QALYs over the course of the disease (13 years), two scenarios were compared (**Figure 1**): with and without a hypothetical treatment that delayed LOA by 4 years as the patient progresses through early and late ambulatory and non-ambulatory disease stages
  - The scenario without treatment reflected the stages of the natural progression of DMD without any interventions that impact time to LOA

Figure 1. Natural disease progression of DMD and impact of treatment on LOA



Abbreviations: LOA = Loss of Ambulation; DMD = Duchenne Muscular Dystrophy

Data

- Direct costs were estimated from DMD patients receiving Exon drugs and/or Emflaza in the Milliman Consolidated Health Cost Guidelines Sources Database (CHSD)[5] in a previously conducted analysis **(see Prior analysis box)**
- Indirect costs and QALY utilities were estimated from published literature[3]
- We applied cost ratios from the literature to estimate disease stage costs for cost-components where data were unavailable. The ratios used for direct and indirect costs were based on average annual patient costs[3] and caregiver income loss[4], by disease stage, respectively
- QALY utilities were applied to each disease stage to estimate the health benefits of the hypothetical treatment, measured as QALYs gained

Prior analysis (Milliman)

- Average patient allowed costs for 12 months pre- and post- non-ambulatory from CHSD were used to represent annual direct costs for the late ambulatory and early non-ambulatory stages, respectively
- DMD patients were identified as those patients who met all of the following criteria:
  - At least a full year of medical and drug coverage in the database at some point between 2016 and 2020
  - One claim for Exondys 51, Vyondys 53, or Emflaza
  - Non-ambulatory patients were identified as those who had an instance of ICD Z99.3
  - Must not have any wheelchair K-codes in the claims database prior to the non-ambulatory transition point

Analysis

- Indirect costs and hours of work lost reflected the economic burden of DMD on both the patients and caregivers
- Since indirect costs were only available as an annual estimate, we developed an equation to estimate costs by disease stage based on the proportion of patients in each disease stage, annual cost per patient for a particular indirect cost component and the cost ratio by disease stage derived from the literature

$$cost_{ij} = \frac{annual\ cost\ per\ patient_i}{\sum proportion\ of\ DMD\ patients_j * cost\ ratio_j} * cost\ ratio_j$$

where i=type of indirect cost, j=DMD disease stage

- Total annual patient costs were calculated as the sum of annual direct and indirect cost components per disease stage
- Over a period of 13 years, total costs and QALYs were calculated as the sum of the product of the number of years spent in each disease stage and annual costs and QALY utilities, respectively

$$Total\ costs/QALYs = \sum costs_{ij}/QALYs_j * number\ of\ years_j$$

where i=type of indirect cost, j=DMD disease stage

- Differences in total costs and QALYs between the scenario with and without treatment were calculated to estimate economic and health benefits of the hypothetical treatment that delayed LOA by 4 years
- Two sensitivity analyses were performed:
  - Added the cost of the hypothetical treatment in the direct costs
  - Assessed cost-savings and QALYs gained at a 2-year delay in LOA

Results

- The majority of DMD patients were in the late ambulatory stage (39%) followed by late non-ambulatory (27%), early ambulatory (17%) and early non-ambulatory (17%)[3]
- Average direct costs from the Milliman analysis were available for 12 months pre- and post-loss of ambulation at $74,744 of allowed cost for pre-non-ambulatory and $106,460 of allowed cost for post non-ambulatory
  - The 10th and 90th percentiles for pre and post non-ambulatory ranged from ($21,000 to $110,000) and ($29,000 and $160,000)
- Indirect costs were only available annually (except for the caregiver income loss) without further breakdown by disease stage
- A review of the literature found direct cost ratios of 1:1 for early ambulatory to late ambulatory and 1:1.35 for early non-ambulatory to late non-ambulatory[3], and indirect cost the ratio of 1:1:337:585 for early ambulatory: late ambulatory: early non-ambulatory: late non-ambulatory, respectively[4]
- The quality of life in each disease stage, measured by QALY utilities, tended to decline with disease progression, particularly, after LOA: early ambulatory (0.72), late ambulatory (0.63), early non-ambulatory (0.21) and late non-ambulatory (0.18)[3]

Outcomes over a period of 1 year

- Direct and indirect costs for a year post-LOA were $63,043 and $163,738 higher, respectively, compared to a year pre-LOA
- Annual total costs increased as the disease progressed with $18,178 for early or late ambulatory, $244,959 for early non-ambulatory and $356,619 for late non-ambulatory disease stages
- The larger proportion of total costs was attributed to direct costs in the early or late ambulatory stages (97%) and to indirect costs in the early (67%) and late (69%) non-ambulatory disease stages

Outcomes over a period of 13 years

- Without treatment, total direct and indirect costs amounted to more than $1.82 million in 13years and were distributed by disease stage as follows: early ambulatory (3%), late ambulatory (4%), early non-ambulatory (54%) and late non-ambulatory (39%)
- The hypothetical treatment that delayed LOA by 4 years resulted in savings of $308,589 and $821,856 direct and indirect costs, respectively, which amounted to 62% of the total costs (**Table)**
- Costs attributed to the patient's and caregiver's reduced quality of life had the largest impact on savings (**Figure 2**)
- Patients that delayed LOA by 4 years gained 2.1 QALYs in a period of 13 years compared to those that did not have any delay in LOA
- In the scenario without treatment, caregivers lost 3,465 work hours compared to 935 work hours under the scenario with treatment, indicating a 73% reduction in work hours lost over 13 years

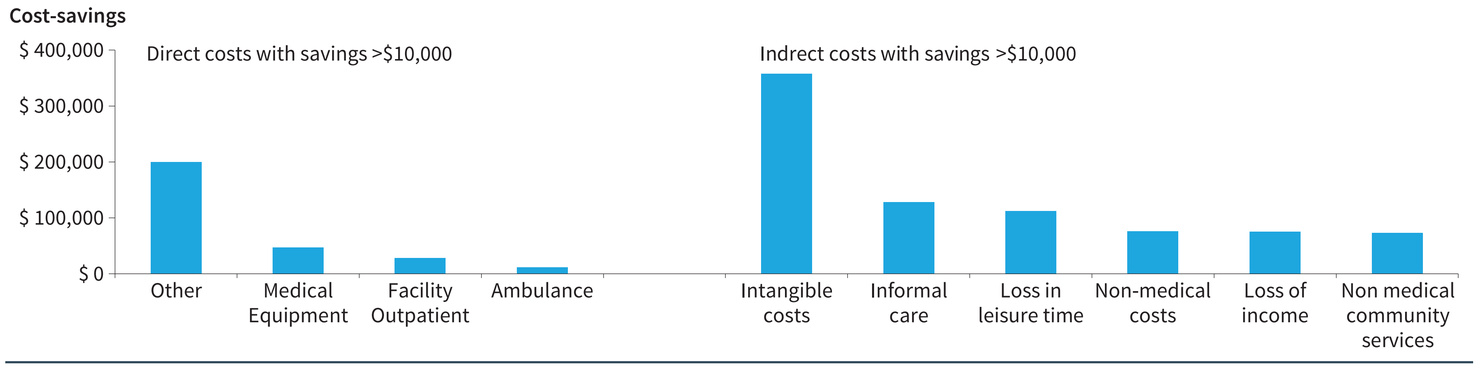
Sensitivity analysis

- With the cost of the hypothetical treatment included in direct costs, the scenario with 4 years delay in LOA remained cost-saving with more 46% lower costs compared to the scenario without treatment
- The delay in LOA by 2 years resulted in savings of $98,244 and $327,477 in direct and indirect costs, respectively, over 13 years, which is approximately 60% lower compared to savings in the 4-year delay in LOA

Table. Average total costs and QALYs, cost savings and QALYs gained over a 13-year period

	Without treatment	With treatment	
	Costs	Costs	Savings
Direct costs			
Facility Inpatient	$ 23,199	$ 13,261	$ 9,938
Facility Outpatient	$ 146,833	$ 118,445	$ 28,388
Professional	$ 49,653	$ 44,995	$ 4,658
Other	$ 284,136	$ 84,832	$ 199,304
Other Prescription Drugs	$ 8,663	$ 8,230	$ 433
Outpatient Pharmacy	$ 22,869	$ 16,745	$ 6,125
Office Administered Drugs	$ 2,368	$ 939	$ 1,429
Ambulance	$ 17,482	$ 6,103	$ 11,380
Durable Medical Equipment	$ 109,457	$ 62,521	$ 46,936
Sub-total	**$ 664,660**	**$ 356,072**	**$ 308,589**
Indirect impact and costs			
Workloss (hours)	3,465	935	2,530
Loss of income	$ 103,589	$ 28,107	$ 75,482
Intangible costs (reduced QoL)	$ 518,128	$ 160,823	$ 357,304
Loss in leisure time	$ 153,833	$ 41,740	$ 112,093
Non-medical costs (e.g., aids, investments)	$ 104,265	$ 28,290	$ 75,974
Non-medical community services	$ 100,057	$ 27,149	$ 72,909
Informal care	$ 175,791	$ 47,698	$ 128,093
Sub-total	**$ 1,155,662**	**$ 333,807**	**$ 821,856**
Total	**$ 1,820,323**	**$ 689,878**	**$ 1,130,444**
	QALYs	**QALYs**	**QALYs gained**
Total	5.88	7.98	2.10

Figure 2. Key drivers of cost-savings over a period of 13 years



Conclusions

- DMD treatments that delay LOA could substantially reduce disease management costs and costs to caregivers and improve patient quality of life
- Indirect costs account for the largest proportion of the economic burden of DMD

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Acknowledgments

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Disclosures

John Ford and Randy McGonigal are employees of NS Pharma

Rajeev Ayyagari and Deo Mujwara are employees of Analysis Group, which conducted the analyses in this study and received funding from NS Pharma for the conduct of these analyses

Matthew Hayes is an employee of Milliman Inc., which conducted a previous analysis (see Box) and received funding from NS Pharma for the conduct of that analysis

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