CHARACTERIZING THE NATURAL HISTORY OF DUCHENNE MUSCULAR DYSTROPHY IN THE UNITED STATES IN REAL-WORLD COMMERCIAL AND MEDICAID DATA

Christina Qian,[1] Alexa C. Klimchak,[2] Shelagh M. Szabo,[1] Evan Popoff,[1] Susan Iannaccone,[3] Katherine L. Gooch[2]

[1]Broadstreet HEOR, Vancouver, BC, Canada; [2]Sarepta Therapeutics, Inc., Cambridge, MA, USA; [3]University of Texas Southwestern Medical Center, Dallas, TX, USA

BACKGROUND

- Duchenne muscular dystrophy (DMD) is a rare, severe, progressive X-linked neuromuscular disease
- Several clinical studies document the progression of DMD with loss of ambulation in late childhood; followed by cardiomyopathy and respiratory insufficiency in the mid to late teens; leading to mortality in the third or fourth decade of life[1-5]
- While estimates of the timing of key clinical milestones exist from clinical cohorts, real-world estimates are scarce
  - There is minimal information at present as to whether the timing of disease progression differs among patients with different types of insurance coverage
  - Given that Medicaid plans provide coverage to more vulnerable populations (low-income adults, children, or people with disabilities) it is worth exploring if patient characteristics, and outcomes, may differ among those covered under Medicaid vs. commercial plans

OBJECTIVE

- To estimate the age at key clinical milestones among commercially- or Medicaid-insured DMD patients in the US using real-world data

METHODS

Data Source

- IBM MarketScan Commercial and anonymized Multi-State Medicaid claims data (2013 – 2018)

Inclusion Criteria

- Males ≤30 years old with ≥1 inpatient diagnosis, or ≥2 outpatient diagnoses separated by ≥30 days, for muscular dystrophy (ICD-9: 359.1) or DMD/Becker's MD (ICD-10:G71.0)
- Index date is defined as the date the patient first met these inclusion criteria

Exclusion Criteria

- ≤12 months of continuous follow-up after index
- Patients with other likely congenital dystrophies, identified by ventilator use before age 6 years; orthopedic procedure of the foot before age 3 years; wheelchair use before age 5 years
- Nusinersen treatment at any point during the study period

Key Clinical Milestones

- Defined in **Table 1:** As records of clinical events were not always available in the databases, proxy events were used where necessary

Statistical Analysis

- The demographic characteristics of the cohorts were summarized
- Comorbidity burden over the period was summarized by median (interquartile range [IQR]) Elixhauser Index score[6]
- The median (IQR) age at the first of each observed key clinical milestone were estimated for each of the commercial and Medicaid cohorts
  - For loss of ambulation and scoliosis, these were estimated among the subset who entered the cohort at <16 years of age, to avoid misclassifying the first event observed in the database with the first event in a patient's life
- The frequency of other comorbidities of interest over the period, identified based on literature review, was summarized

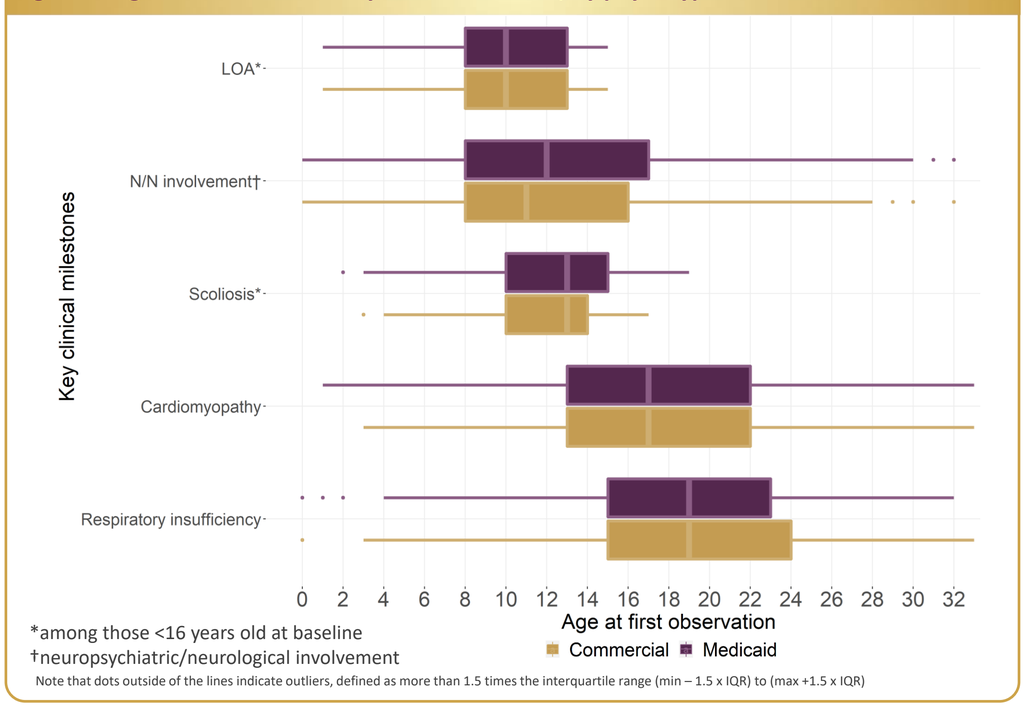
Table 1. Measures of key clinical milestones

Milestone	Outcome measure
Loss of ambulation	▪ Diagnosis codes for difficulty walking ▪ Procedural codes for wheelchair use
Scoliosis	▪ Diagnosis codes for scoliosis ▪ Procedural codes for spinal surgery
Cardiomyopathy	▪ Diagnosis codes for cardiomyopathy and heart failure ▪ Dispensations for ACE inhibitors, ARBs, beta-blockers, diuretics (spironolactone or epleronone)
Respiratory insufficiency	▪ Diagnosis codes for respiratory failure ▪ Procedural codes for tracheostomy, assisted ventilation, and selected codes for pulmonary management
Neurologic / neuropsychiatric involvement	▪ Diagnosis codes for learning disabilities, pervasive development and behavioural disorders, hyperkinetic syndrome of childhood ▪ Procedural codes for neuropsychological testing

RESULTS

- The median (IQR) baseline ages of the commercial (n=1,964) and Medicaid (n=2,007) cohorts were similar (commercial, 15 [9-21] years; Medicaid, 14 [9-20] years)
  - The median (IQR) baseline ages of the subset <16 years at cohort entry was 9 (6 to 13; n=1,024) in the commercial DMD cohort and 9 (6 to 12; n=1,105) in the Medicaid DMD cohort
- Most patients had >1 year of follow-up (75% [commercial] and 89% [Medicaid]), with a median of 2.8 (commercial) and 3.8 (Medicaid) years
- The Medicaid DMD cohort had a significantly higher median (IQR) comorbidity burden over the period (Elixhauser Index score 2 [1-4]), vs the commercial DMD cohort (1 [0-3])

Figure 1. Age at first observed key clinical outcome, by payer type



*among those <16 years old at baseline
†neuropsychiatric/neurological involvement
Note that dots outside of the lines indicate outliers, defined as more than 1.5 times the interquartile range (min – 1.5 x IQR) to (max +1.5 x IQR)

Table 2. Occurrence of other comorbidities of interest, by insurance type

	Commercial (n=1,964)	Medicaid (n=2,007)
Other comorbidities, n(%)		
Respiratory infectious disease	958 (48.8%)	1,176 (58.6%)
Anxiety, dissociative, somatoform disorders	302 (15.4%)	329 (16.4%)
Asthma	285 (14.5%)	424 (21.1%)
Depressive disorder	185 (9.4%)	301 (15.0%)
Fracture and osteoporosis	148 (7.5%)	118 (5.9%)
Epilepsy	89 (4.5%)	136 (6.8%)
Cataract	74 (3.8%)	37 (1.8%)
Diabetes mellitus	56 (2.9%)	78 (3.9%)
Cystic fibrosis	39 (2.0%)	69 (3.4%)

RESULTS

- Age at key clinical outcomes were consistent between the commercial and Medicaid cohorts (**Figure 1**)
- DMD patients in the Medicaid cohort had a higher prevalence of other comorbidities, vs the commercial cohort, with the exception of fracture/osteoporosis and cataract (**Table 2**)
  - The most common comorbidity observed among both commercial (48.8%) and Medicaid (58.6%) cohort was respiratory infectious disease

DISCUSSION

- Ages at key milestones in DMD were similar between commercially- and Medicaid-insured patients and were consistent with published estimates from clinical studies[1-5]
- Limitations:
  - MarketScan claims data are collected for billing not research purposes
  - There is a lack of specific codes to identify only DMD patients
  - For some outcomes (e.g. LOA), proxy endpoints were used as direct endpoints were unavailable
    - The reliability of these proxy data to assess outcomes is presently unclear
  - While the occurrence of some key clinical could be detected (e.g. diagnosis of cardiomyopathy, or scoliosis), the severity of these outcomes cannot be assessed using claims data
  - Key milestones occurring outside of the follow-up window or outside of coverage would not be captured
  - Coding requirements and processes may differ between the commercial and Medicaid payer segments
- Nonetheless, these real-world estimates contribute to the characterization of the natural history among DMD patients in real-world environments

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Contact: cqian@broadstreetheor.com

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