Costs and health resource use in patients with X-linked myotubular myopathy: insights from US commercial claims

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What is already known about this subject

- Most children with X-linked myotubular myopathy (XLMTM) depend on permanent use of mechanical ventilation, feeding tubes, and wheelchairs.
- The current costs of care for this rare disease have not been quantified.

What this study adds

- This is the first study that has attempted to quantify the economic burden of XLMTM in the United States and has found that annualized all-cause medical costs per patient totaled \$897,978 in the first year of life and nearly \$1.5 million total for patients who survived the first 4 years of life.
- This study supports the value of potential future treatment options for XLMTM and could inform the collection of economic impact evidence for other rare genetic diseases.

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ABSTRACT

BACKGROUND: In X-linked myotubular myopathy (XLMTM), mutations in the *MTM1* gene result in absence or dysfunction of myotubularin, a protein required for normal development, maintenance, and function of skeletal muscle. Extreme muscle weakness results in severe respiratory failure that is fatal for approximately half of XLMTM-affected children by age 18 months. Most surviving patients require invasive

mechanical ventilation, feeding tubes, and wheelchairs for mobility, due to profoundly impaired motor function. Little is known about the costs of care for this rare disease. Currently, there are no approved therapies for XLMTM.

OBJECTIVE: To quantify the direct medical costs and health care resource utilization (HRU) incurred by XLMTM patients and paid by commercial insurers.

METHODS: A retrospective, longitudinal study was conducted using the IQVIA

PharMetrics Plus commercial database of adjudicated claims for more than 140 million individuals with commercial insurance coverage in the United States. An algorithm based on demographic information, diagnosis and procedure codes, and medications was used to identify XLMTM patients younger than aged 2 years during the study period from January 1, 2006, through September 30, 2018. All-cause direct medical costs and HRU during each month were calculated. Costs were grouped as inpatient hospital

admissions (including the intensive care unit or neonatal intensive care unit [NICU]); emergency department visits; outpatient services (outpatient hospital visits, office visits, physician/provider office visits, ambulatory surgeries and procedures, laboratory tests, and imaging tests); and prescription medications. Monthly costs and HRU over time were stratified by age and use of mechanical ventilation.

RESULTS: 49 patients met the study criteria. All had at least 1 inpatient hospital admission, and 36 (73%) had at least 1 NICU stay. All patients received ventilation at some time during the study period, including 40 (82%) treated with invasive ventilation. Mean monthly per patient direct medical costs were highest in the first year of life (\$74,831), including costs for inpatient admissions (\$69,025), outpatient services (\$5,266), and prescription medication (\$540). Mean monthly costs were lower in the second, third, and fourth years of life (\$23,207, \$13,044, and \$9,440, respectively). When annualized, these all-cause monthly medical costs totaled \$897,978 per patient in the first year of life and nearly \$1.5 million total for patients who survived the first 4 years of life. Costs were consistently highest when patients were receiving invasive ventilation and lowest when they were not receiving ventilation (i.e., before they started on ventilator support).

CONCLUSIONS: This direct health care cost and HRU analysis demonstrates the substantial economic burden associated with XLMTM. Costs are highest in the first year of life and are particularly significant for patients receiving invasive ventilation.

X-linked myotubular myopathy (XLMTM) is a rare, severe congenital myopathy caused by pathogenic mutations of a single gene, *MTM1*, which codes for myotubularin.¹ These mutations lead to absence or dysfunction of myotubularin, a protein required for the normal development, maintenance, and function of skeletal muscle.² As an X-linked genetic disorder, XLMTM primarily affects males and has an estimated incidence of approximately 1 in 40,000–50,000 live male births.^{3,4}

Approximately 80% of affected patients experience extreme muscle weakness leading to severe respiratory distress,⁵ and approximately half die before age 18 months.^{5,6} Estimate median survival is 1.8 years to 22.8 years, depending on whether patients undergo tracheostomy.⁷ Most surviving patients require permanent (>16 hours per day) invasive mechanical ventilation^{5–7} and feeding assistance with gastrostomy tubes.⁸ XLMTM results in profoundly impaired motor function; most patients are nonambulatory, unable to sit unsupported, and have absent, transient, or delayed achievement of motor milestones.^{8,9}

There are currently no approved therapies for XLMTM and no harmonized guidelines for care of XLMTM patients, in part due to the wide variation in disease manifestations. Current management consists of long-term interdisciplinary

supportive care to maximize functional abilities and minimize medical complications, but does not address the underlying pathology of the disease.³

Given the rarity of XLMTM, little is known about the direct medical and other costs associated with this disease. The financial impact is assumed to be substantial, with costs incurred by families and payers related to providing ventilatory care at home, as well as frequent elective and nonelective hospitalizations.⁵ The costs borne by insurers, as well as health care resource utilization (HRU) associated with XLMTM, are not well understood. Should a treatment become available, it would be critical that costs and HRU associated with XLMTM are understood and quantified.

Using commercial claims data, we sought to study the economic burden of XLMTM in the United States by quantifying the direct medical costs and HRU incurred by XLMTM patients and paid by commercial insurers. We studied costs and HRU stratified by age because XLMTM symptom onset and diagnosis typically occurs in the first year of life, and research indicates that care is intensive at the start of disease,⁵ when patients are youngest. We also studied the direct medical costs and HRU for XLMTM patients stratified by use of mechanical ventilation, as respiratory failure is almost universal in these patients, resulting in the use of noninvasive or invasive ventilatory support and adding to the cost burden.

Methods

STUDY DESIGN AND TIME FRAME

We conducted a retrospective, longitudinal study to evaluate costs and HRU among patients with XLMTM. Our data source was the IQVIA PharMetrics Plus commercial database, which contains fully adjudicated, deidentified medical and prescription drug claims, as well as demographic and enrollment information for more than 140 million individuals with commercial insurance coverage in the United States. The claims data include date of service, provider type, service type and setting, diagnosis and procedure codes, and amounts paid by the insurer to the provider. Demographic information includes gender, geographic region, and year of birth; however, mortality data are not available. Enrollment data were used to identify the months that patients were observable, as patients who died or switched to other commercial insurance coverage would subsequently not be enrolled in their plan. The study time frame was January 1, 2006, through September 30, 2018. This study was exempt from institutional review board approval, as it did not involve any interventional biomedical research with identifiable human subjects.

FIGURE 1 Identification of Study Patients

^aICD-9-CM 359.0 or ICD-10-CM G71.2.

^bOne or more inpatient or 2 or more outpatient SMA diagnoses or evidence of nusinersen (Spinraza) use.

^cEvidence of exondys51 or deflazacort (Emflaza) use.

DMD=Duchenne muscular dystrophy; ICD-9-CM/ICD-10-CM=International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification; SMA=spinal muscular atrophy; XLMTM=X-linked myotubular myopathy.

STUDY PATIENTS

At the time of our analysis, there was no clear diagnosis code for XLMTM (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM] diagnosis code G71.220 was later assigned to XLMTM on October 1, 2020), and

claims data do not include results of tests that would provide a definitive diagnosis of XLMTM. Therefore, we developed an algorithm via diagnosis and procedure codes, medication use, and demographic information to identify our study patients.

We limited patients to males who had 1 or more claims with *International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification* (ICD-9-CM) diagnosis code 359.0 (Congenital hereditary muscular dystrophy) or ICD-10-CM code G71.2 (Congenital myopathies), which are both used for XLMTM patients. Patients were also required to have either a muscle biopsy or genetic test that is used to diagnose XLMTM during the study period. Because a diagnosis could be recorded on a claim on suspicion of XLMTM, the diagnostic test claim was allowed to occur before or after the claim with the first observed diagnosis.

Given that onset of disease symptoms in XLMTM begins in the first year of life, with diagnosis following, we assumed that patients would have an initial diagnosis at a young age, so we required patients to have a first diagnosis of XLMTM before the second birthday. Additionally, patients were required to meet criteria identified through a review of the RECENSUS retrospective, multicenter medical chart review of patients with XLMTM (NCT02231697, Audentes Therapeutics, San Francisco, CA).⁷ These criteria included evidence of mechanical ventilation (invasive or noninvasive) at any point during the study period and an inpatient admission at any time after diagnosis. Patients were not required to be treated with ventilation for the full study period.

Because patients with spinal muscular atrophy (SMA) or Duchenne muscular dystrophy (DMD) may show symptoms similar to those of XLMTM, we excluded patients who had an inpatient and/or 2 or more outpatient claims for SMA and DMD and/or were treated with eteplirsen (Exondys 51, Sarepta Therapeutics, Inc) or deflazacort (Emflaza, PTC Therapeutics, Inc), or

TABLE 1 Characteristics of XLMTM Patients Over the Study Period

Characteristic	XLMTM Patients (n = 49)
Age, mean (SD), months	4.44 (5.88)
Months enrolled before diagnosis, mean (SD)	3.16 (4.18)
Months enrolled following diagnosis, mean (SD)	30.94 (31.38)
Inpatient admissions per patient, mean (SD)	7.29 (7.07)
Length of stay per inpatient admission, mean (SD), days	123.35 (159.15)
1 or more NICU stay, %	73
NICU admissions per patient, mean (SD)	1.29 (1.21)
Length of stay per NICU stay, mean (SD), days	47.39 (65.92)
Patients who ever received invasive ventilation, %	82
Patients who ever received noninvasive ventilation, %	27

Note: 44 of 49 patients diagnosed at age 1 year or younger contributed 473 patient observation months to the study. These patients were observable for an average of 10.75 months per patient ([Supplementary Table 2](#), available in online article).

NICU = neonatal intensive care unit; XLMTM = X-linked myotubular myopathy.

deflazacort (Emflaza PTC Therapeutics, Inc), which are indicated for the treatment of DMD, or nusinersen (Spinraza, Biogen), which is indicated for the treatment of SMA.

We observed study patients for as long as they were enrolled in their health plans (Figure 1). Given the young age of XLMTM patients and the potential of rapid progression to death, there was no minimum observable follow-up period. See [Supplementary Table 1](#) (available in online article) for clinical and drug codes used for inclusion and exclusion criteria.

STUDY OUTCOMES

We identified all months in which each patient was observable. We calculated all-cause direct medical costs and HRU for inpatient and outpatient services and prescription medications during each month, noting patient age in that month. All-cause direct medical costs were the amounts paid by commercial insurers to providers. Costs were adjusted to 2018 U.S. dollars using the medical care component of the Consumer Price Index.

Inpatient services included hospital admissions with intensive care unit or neonatal intensive care unit (NICU) stays during the hospitalization. Hospitalizations longer than 1 month were referenced to the month in which the patient was admitted to the hospital. Outpatient services included emergency department (ED) visits, outpatient hospital visits, office visits, laboratory tests, imaging tests, ambulatory surgeries and procedures, home health care and durable medical equipment. ED visits were those where a patient was discharged because ED visits that result in a hospital admission are billed and paid with the hospitalization and are not distinguished from the admission.

We grouped outpatient services together, as we were interested in direct medical cost drivers for XLMTM patients, and most outpatient services are less costly, compared with hospital admissions. We reported ED visits separately, as these visits can be reflective of disease severity and can also be costly.

Patient-months were assigned to 1 of the following ventilatory support

groups: (1) no ventilatory support, (2) noninvasive ventilation, and (3) invasive ventilation (i.e., transtracheal support). We observed patients over time and tracked them as they initiated ventilation or transitioned to more invasive ventilation. We assumed that patients did not return to a less-intensive ventilation state, based upon disease natural history and clinician input. For example, once a patient received any ventilation (invasive or noninvasive), they were considered to be subsequently on ventilator support. Similarly, once patients received invasive ventilation, they were considered to be on invasive ventilation support in every subsequent month. This assumption was supported by the RECENSUS chart review data, which is stratified by type of ventilation over time. An internal review of these data indicates that patients rarely returned to less-intensive ventilation.

We estimated annual costs of XLMTM patients by year of age because XLMTM costs could vary by age, with highest HRU and costs early in life.⁵ We also stratified annual costs by ventilation type within age, because invasive ventilation would be expected to be more costly than noninvasive or no ventilation regardless of patient age. We used monthly costs to estimate annual costs per patient, because patients were observable for different lengths of time, and limiting annual costs to those patients observable for a full year could exclude the sickest patients. To estimate the total cost burden of XLMTM over time, we summed annual costs per patient for each year of age. Due to small sample size and severity of illness in early life, our primary results focus on costs and HRU in the first 4 years of life only. Older ages are reported in the [Supplementary Table 3](#) (available in online article).

TABLE 2 Total Health Care Cost of XLMTM Patients by Age

Patient Age, Years	Patient Count	Patients New to Study in That Year of Age	Patients Lost to Follow-Up Relative to Previous Year	Mean Monthly Cost per Patient \$	Mean Annual Cost per Patient \$ ^a
0	46	46	—	74,831	897,978
1	44	3	5	23,207	278,485
2	36	—	8	13,044	156,530
3	29	—	7	9,440	113,285

^aAnnual estimates based on monthly costs per patient for 12 months.

XLMTM = X-linked myotubular myopathy.

SENSITIVITY ANALYSIS

As patients with XLMTM could potentially be misdiagnosed with myotonic dystrophy and vice versa, we conducted sensitivity analyses to assess the impact of patients with at least 1 diagnosis for myotonic dystrophy (ICD-9-CM: 359.21; ICD-10-CM: G71.11) on our estimates of health care costs. To do so, we identified patients with at least 1 claim with a diagnosis of myotonic dystrophy, excluded these patients, and regenerated cost and HRU estimates for the remaining cohort.

STATISTICAL ANALYSIS

We conducted descriptive health care cost and HRU analyses, reporting means and SD for continuous variables, and frequency and proportions for categorical variables for all patient-months, stratified by patient age and use of ventilation.

Results

We identified 49 patients who met the study criteria (Table 1). Mean (SD) age at time of diagnosis was 4.44 (5.88) months. Nearly all study patients were initially observed in their first year of life (46/49), but the numbers of study patients decreased as patients grew older, with 44 patients observable at

age 1 year to younger than 2 years, 36 at age 2 years, and 29 at age 3 years (Table 2). All patients had at least 1 inpatient hospital admission, and 36 (73%) had at least 1 NICU stay. NICU stays averaged 47.39 (65.92) days. Hospitalizations outside of the NICU were even lengthier, averaging 123.35 (159.15) days each (Table 1).

All patients received ventilation at some time during the study period, which was a study inclusion criterion. Nearly all (n=40; 82%) received invasive ventilation, whereas fewer (n=13; 27%) received noninvasive ventilation at any time. A total of 21 patients were not receiving ventilation when they were first observed, but all subsequently required some form of respiratory support. Of these 21 patients, 9 transitioned directly from no ventilation to invasive ventilation, and 12 moved from no ventilation to noninvasive ventilation. Of these 12, four eventually moved from noninvasive to invasive ventilation (Figure 2).

HEALTH CARE COSTS BY AGE

Mean (SD) observable monthly per patient direct medical costs over time were highest in the first year of life (\$74,831 [\$75,822]), including costs for inpatient admissions (\$69,025), outpatient services (\$5,266), and prescription medication (\$540). Mean monthly costs were \$23,207, \$13,044,

and \$9,440 in the second, third, and fourth years of life, respectively. When annualized, all-cause medical costs per patient totaled \$897,978 in the first year of life, but were lower in the second, third, and fourth years of life (\$278,485, \$156,530, and \$113,285, respectively). For patients who survived the first 4 years of life (birth to < age 4 years), costs paid by commercial payers totaled nearly \$1.5 million (Table 2 and [Supplementary Table 3](#), available in online article).

HEALTH CARE COSTS BY AGE AND USE OF VENTILATION

At each age, costs were consistently highest among patients receiving invasive ventilation, and lowest among those who were not receiving any ventilation (Table 3). Among patients treated with each type of ventilation, all-cause direct medical costs decreased as patients approached age 5 years. As examples, mean (SD) monthly per patient costs for patients receiving no ventilation support were highest in the first year of life (\$34,367 [\$31,832]), were lower in the second (\$16,967 [\$28,605]), and lower still in the third (\$5,519 [\$718]) and fourth (\$3,828 [\$353]) years of life. Among those treated with invasive ventilation, mean (SD) monthly per patient costs were also highest in the first year of life (\$89,496 [\$88,514]), with lower costs in subsequent years. Overall, direct medical costs for patients treated with invasive ventilation were very high; when annualized, costs for patients on invasive ventilation were highest in the first year of life (\$1,073,947; Table 3).

SENSITIVITY ANALYSIS: HEALTH CARE COSTS AMONG XLMTM PATIENTS, EXCLUDING THOSE WITH MYOTONIC DYSTROPHY DIAGNOSIS

Among 49 XLMTM study patients, 7 (14.3%) also had at least a transitory

FIGURE 2 Ventilation and Ventilation State Changes from Month of Enrollment Until Patient not Observable

	Before Ventilation	Noninvasive Ventilation	Invasive Ventilation
Patient with 1 ventilation state (n=28)	– –	1	27
Patient with 2 ventilation states (n=17)	8 9	→ 8	→ 9
Patient with 3 ventilation states (n=4)	4	→ 4	→ 4
Total=49	21	13	40

diagnosis of myotonic dystrophy. Although this could have been a misdiagnosis in some or all of these patients, we conducted sensitivity analyses that excluded these patients from our analysis and found that mean monthly health care costs were \$75,489 in the first year of life and \$21,875, \$9,957, and \$8,676 in the second, third, and fourth years of life, respectively (Supplementary Table 4, available in online article). These costs were 1.01, 0.94, 0.76, and 0.92 times, respectively, the costs observed in all XLMTM patients (i.e., inclusive of myotonic dystrophy patients).

Discussion

To the best of our knowledge, this is the first study quantifying the economic burden of XLMTM in the United States. Using a commercial claims database, we identified 49 patients with a diagnosis used for XLMTM and characteristics consistent with this disease. On average, annual health care costs for these patients were highest in the first year of life (\$897,978) and decreased by 3-fold, nearly 6-fold, and 8-fold in the second, third, and fourth years of life, respectively, totaling nearly \$1.5 million

per patient in the first 4 years of life. These costs were driven primarily by lengthy inpatient admissions and ventilatory support; all identified patients had at least 1 hospitalization and 73% had a NICU admission. Although some patient did not start on ventilation, all eventually required ventilatory support (per the inclusion criteria), and most (82%) received invasive ventilation, the most expensive respiratory support modality. Costs for inpatient admissions and outpatient services were also highest for patients on invasive ventilation, highlighting their overall medical fragility. Our findings suggest that the management of patients with XLMTM is resource intensive, demanding ongoing support in both the outpatient and inpatient setting and placing a substantial burden on the health care system.

Patients born with XLMTM have severe skeletal muscle weakness, hypotonia, and respiratory distress, resulting in difficulties in sitting, standing, walking, feeding, and breathing.^{5,7} Managing these difficulties requires intensive use of health care resources, which include hospitalizations and respiratory support and may also include nutrition and mobility support, physical therapy, orthopedic treatments, and occupational and

speech therapies. This intensive HRU is associated with a large economic burden—nearly \$900,000 per patient in the first year of life according to our study. Although costs were lower in subsequent years, it is possible that the very high costs in the first year of life reflected costs for diagnosing and stabilizing patients, with stabilized patients less susceptible to other illnesses that ultimately lead to hospitalization.

Additionally, costs paid by commercial insurers likely do not reflect the full set of costs for XLMTM patients. A shift in HRU from inpatient to outpatient services once patients are diagnosed and stabilized may alter costs and reimbursement sources: families incur substantial financial burdens, and dual payment sources, such as Medicaid, cover a large proportion of costs including home nursing.^{10–14} It is also possible that patients who survived required less care than patients who did not. Finally, many study patients were not observable for multiple years, and it is likely that some of them died at very young ages, despite high expenditures in the first year of life. It is also possible that some patients became solely covered through Medicaid and, therefore, were no longer observable within the commercial claims database used for this analysis. Although our focus is on the economic burden of XLMTM our findings are suggestive of the impact of XLMTM on quality of life. Hospitalizations that average 4 months would be expected to adversely affect both patients and their families.

Although data on the economic burden of other congenital myopathies are limited, there are studies on the economic burden of SMA and DMD, which are neuromuscular disorders affecting young children, with symptoms similar to those of XLMTM. In a retrospective cohort analysis of SMA patients, Goble et al. (2018) estimated

TABLE 3 Mean per Patient Health Care Costs Among XLMTM Patients by Age and Use of Ventilation

Age, Years	No Ventilation		Noninvasive Ventilation		Invasive Ventilation	
	Monthly All-Cause Health Care Costs \$	Annual All-Cause Health Care Costs \$ ^a	Monthly All-Cause Health Care Costs \$	Annual All-Cause Health Care Costs \$ ^a	Monthly All-Cause Health Care Costs \$	Annual All-Cause Health Care Costs \$ ^a
0	34,367	412,406	51,352	616,221	89,496	1,073,947
1	16,967	203,604	26,213	314,557	24,837	298,043
2	5,519	66,227	4,358	52,299	16,270	195,235
3	3,828	45,942	7,495	89,935	10,730	128,763

^aAnnual estimates based on average monthly costs per patient for 12 months.

XLMTM = X-linked myotubular myopathy.

that these patients incur mean annual medical costs of \$65,490 in 2017. Costs were highest for SMA patients age <2 years, with mean annual direct medical costs of \$159,227.¹⁵ Landfeldt et al. (2014) reported that the mean annual direct cost of illness in DMD patients was \$54,270 in 2012.¹⁶ Our study indicates that mean annual direct medical costs of XLMTM patients are much higher than SMA and DMD.

This study adds to the limited existing literature on health care resource utilization in patients with XLMTM. A 1-year prospective study of the natural history and disease burden in XLMTM patients by Amburgey et al. (2017) found that 3 in 4 study patients (74%) were ventilator-dependent and required a wheelchair and feeding tube; nearly all patients (96%) required at least 1 of these interventions.⁸ Graham et al. (2015) found similarly high rates of respiratory support (87%, 126/145 patients).⁷ These findings highlight the high degree of technological dependence in XLMTM patients and support our findings on significant ventilation use in this population. In addition, Amburgey et al. also found that each family missed 12.52 workdays per year,⁸ which is significantly higher than the U.S. average of 4 days per year, suggesting that estimates of direct medical burden of XLMTM understate the societal impact of this disease.

LIMITATIONS

Our study has some limitations to consider. First, because of our reliance on claims data, which do not include physiological measures or medical test results, it is possible that some patients identified as XLMTM patients may not actually have the disease. However, the algorithm we developed to identify these patients was consistent with the characteristics of patients with confirmed XLMTM and was reviewed with physicians who work closely with XLMTM patients. Our sensitivity analyses excluding patients with claims diagnoses of myotonic dystrophy suggest the economic burden

may be only slightly higher in the first year of life and only slightly lower in the next 3 years.

Second, our study was conducted using U.S. commercial insurance data, so our findings may not be generalizable to other countries.

Third, our inclusion requirements may have biased our study toward patients with more severe disease, who would be more expensive and may not be generalizable to all patients, including those who never use ventilation. Therefore, our results may overestimate the direct medical costs across all XLMTM patients. However, commercially insured XLMTM patients may also be covered by Medicaid, which would be the primary payer for home health care and durable medical equipment. Consequently, our results may substantially underestimate the total direct medical cost of XLMTM. Additionally, we observed diminishing numbers of patients over time, and our estimates of the long-term costs of XLMTM are, therefore, limited to the first 4 years of life. This study attrition may reflect both mortality and changes in health plan coverage, suggesting that the lifetime costs paid by commercial payers for XLMTM patients may be greater than our estimates. Further, our algorithm filtered out lower cost XLMTM patients with milder clinical presentations who did not require costly mechanical ventilation or inpatient hospitalizations.

Finally, claims data do not include information on mortality, quality of life, direct and indirect family-incurred costs (e.g., noncovered equipment and copays, as well as potential loss of capacity to remain in the workforce while caring for the child), or disease severity, including relevant clinical outcomes. Therefore, our results only represent a partial assessment of the cost of illness based on direct medical costs, excluding indirect costs and other direct nonhealth care costs incurred by patients and their caregivers.

Conclusions

Direct medical costs and HRU are front-loaded in XLMTM, with very high costs and intense HRU at the beginning of life when resource use is highest for acutely ill patients. Annual costs after the first year of life are lower, reflective of ongoing, chronic care once the disease has been stabilized. Reliance on commercial claims as the primary source for this analysis may underestimate the total costs of care. For patients of all ages, annualized health care costs are highest when patients are managed with invasive ventilation. Our findings suggest that treatments with the potential to transform the course of XLMTM, particularly if capable of reducing or eliminating the need for intensive respiratory support, could considerably reduce the clinical and economic burden of disease by shifting the resources used from supportive treatment to treatment of the disease.

DISCLOSURES

This study was funded by Audentes Therapeutics, an Astellas Company, and was conducted by PRECISIONheor with funding from Audentes Therapeutics, an Astellas Company.

Slocumb is an employee of Audentes Therapeutics, an Astellas Company; James was an employee at the time of the study. Sacks, Healey, and Cyr are employees of PRECISIONheor. Graham participated in the medical/scientific advisory board for Audentes as part of a clinical trial design for XLMTM but declares no vested interest or holdings that would represent a conflict of interest. Beggs received consulting fees from Audentes Therapeutics, for work on this study, and has received grants from Alexion Pharmaceuticals, Audentes Therapeutics, Dynacure SAS, Pfizer Pharmaceuticals, along with personal fees from Asklepios Biopharmaceutical, Inc., Ballard Biologics, Biogen, F. Hoffmann-La Roche AG, GLG, Guidepoint Global, and Kate Therapeutics, unrelated to this

study. In addition, Beggs has a patent (Patent number: 10736945) for systemic gene replacement therapy for treatment of X-linked myotubular myopathy (XLMTM) licensed to Audentes Therapeutics.

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