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Direct costs of adhering to selected Duchenne muscular dystrophy Care Considerations: Estimates from a midwestern state

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Abstract

Introduction/Aims: The multidisciplinary Duchenne muscular dystrophy (DMD) Care Considerations were developed to standardize care and improve outcomes. We provide cumulative cost estimates for selected key preventive (ie, excluding new molecular therapies and acute care) elements of the care considerations in eight domains (neuromuscular, rehabilitation, respiratory, cardiac, orthopedic, gastrointestinal, endocrine, psychosocial management) independent of completeness of uptake or provision of nonpreventive care.

Methods: We used de-identified insurance claims data from a large midwestern commercial health insurer during 2018. We used Current Procedural Terminology and national drug codes to extract unit costs for clinical encounters representing key preventive elements of the DMD Care Considerations. We projected per-patient cumulative costs from ages 5 to 25 years for these elements by multiplying a schedule of recommended frequencies of preventive services by unit costs in 2018 US dollars.

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ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

DATA AVAILABILITY STATEMENT

Due to privacy concerns (detailed personal information was obtained from a small number of individuals living in a defined surveillance area), data from MD STARnet are not publicly available. Data used for this analysis are maintained at the Centers for Disease Control and Prevention. Researchers interested in MD STARnet should contact MD STARnet at MDSTARnet@CDC.gov.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

Results: Assuming a diagnosis at age 5 years, independent ambulation until age 11, and survival until age 25, we estimated 670 billable clinical events. The 20-year per-patient cumulative cost was $174 701 with prednisone ($2.3 million with deflazacort) and an expected total of $12 643 ($29 194) for out-of-pocket expenses associated with those events and medications.

Discussion: Standardized monitoring of disease progression and treatments may reduce overall costs of illness. Costs associated with these services would be needed to quantify potential savings. Our approach demonstrates a method to estimate costs associated with implementation of preventive care schedules.

Keywords

clinical; cost of care; DMD care considerations; Duchenne muscular dystrophy; guidelines; muscular dystrophy

1 | INTRODUCTION

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder characterized by progressive muscle weakness affecting multiple systems. To standardize patient care and promote optimal disease management, the US Centers for Disease Control and Prevention sponsored the development of recommendations for the management of patients with DMD in 2010 and updated them in 2018 (herein referred to as the DMD Care Considerations).[1–5] The DMD Care Considerations provide a consensus-based clinical pathway of multidisciplinary care for patients with DMD. Costs of recommended services may be a potential barrier to comprehensive uptake, especially for those elements lacking rigorous empirical evidence.[6]

Published reports estimating costs associated with DMD care in the United States have analyzed administrative claims data for an insured cohort.[7–9] Although such cost-of-illness studies demonstrate high medical costs, those cost estimates include routinely recommended services specific to DMD, nonspecific preventive services, and therapeutic costs for unexpected clinical complications. Overall health-care costs for patients with DMD are not informative of the health-care costs attributable to preventive care outlined by specific elements of the DMD Care Considerations, because of incomplete adherence and the inclusion of costs unrelated to preventive care.[6,10–16] In this study, we estimate per-patient cumulative direct costs of selected elements of the DMD Care Considerations by assigning a relative dollar value to specific services with a schedule of recommended frequency.

2 | METHODS

2.1 | Materials

The DMD Care Considerations are comprehensive in their identification of clinical care elements. As such, we focused on key considerations across eight domains identified for the management of disease progression, as described in the 2018 publications.[3–5] A de-identified fully insured private health insurance claims database from a large midwestern commercial health insurer served as our data source for unit cost estimates. We extracted allowable amounts and expected out-of-pocket expenses for all patients from claims data for

each selected element using the 2017 American Medical Association's Current Procedural Terminology (CPT) manual. The allowable charges following adjudication of claims by payers reflect the amounts providers are reimbursed plus amounts owed to providers by patients, not the amounts charged by the providers. The analysis was restricted to records from preferred provider organizations, the predominant provider type in the data set.

To determine unit costs for medications, we used the allowable generic prices from the insurance claims database for prednisone and lisinopril to estimate costs per milligram for these medications and the cost per milligram reported in the final report of the Institute for Clinical and Economic Review to estimate costs for deflazacort[17] due to the lack of available price data in the claims database.

The estimated cost of the DMD Care Considerations was assessed using both a limited health-care sector perspective based on costs projected to be incurred by private payers inclusive of families,[18,19] and a family perspective, that is, expected out-of-pocket payments for families with private health insurance.

2.2 | Statistical analysis

The DMD Care Considerations provide an overall summary of recommended preventive care and early identification and management of morbidities across five stages of disease progression: at diagnosis, early ambulatory, late ambulatory, early nonambulatory, and late nonambulatory. As most elements evaluated in this study are typically constant within ambulatory (early/late) and nonambulatory (early/late) stages, we assigned most frequencies by ambulation status (ambulatory, nonambulatory). For cardiac management, we used chronological age to determine type of assessment (<7 years for echocardiogram, ≥7 years for cardiac magnetic resonance imaging [cMRI]) and cardiac stage (onset of left ventricular dysfunction at age 15 years) to determine initiation of Holter monitoring. For respiratory interventions, we assumed a decline of pulmonary functioning requiring mechanical insufflation-exsufflation and noninvasive positive pressure ventilation at 15 years of age.[20] We assumed the minimum number of required spinal studies up to the age of corrective spinal surgery at 14 years of age. For those recommendations that are "as needed," we assigned a frequency of at least one because the expected frequency is unknown.

2.2.1 | Calculation of costs—We estimated cumulative frequencies using published averages for ages at diagnosis (5 years),[21–23] loss of independent ambulation (11 years),[22,23] onset of left ventricular dysfunction (15 years),[24] and death (25 years).[23,25] In addition, glucocorticoids (0.75 mg mg/kg per day of prednisone or 0.90 mg/kg/day of deflazacort) and prophylactic cardiac medication (lisinopril: 2.5 mg/day for those up to 40 kg, 5 mg/day for those ≥40 kg)[26] were assumed to be initiated at 8 years of age. We used published average weight data for patients with DMD treated with glucocorticoids[27] to estimate medication costs in combination with the recommended dose per body weight and unit price per dose.

We created a formula to calculate cumulative expected total direct costs and expected out-of-pocket payments for each key element and management domain using a 20-year follow up

period starting at 5 years of age. The list of selected key elements and corresponding data used to estimate costs of care are presented in Tables S1 through S5.

Total cumulative key element cost = $[((\text{Unit cost} \times [\text{Annual frequency}]) \times \text{Years}_{A})]_{n+1}$ + $[((\text{Unit cost} \times [\text{Annual frequency}]) \times \text{Years}_{LOA})]_{n+1}$ + As needed_{n+1}, where A = 6 ambulatory years, LOA = 14 nonambulatory years, and n + 1 = the number of elements within a domain (see Box S1 for examples).

1. For each key element, we multiplied the 2018 allowable charge by the recommended frequency within the relevant stage (ambulation or cardiac).
2. For each management domain, we summed the total cost for each key element within that domain.
3. For total cumulative cost, we summed the total amounts for each domain.

Dollar amounts are reported in 2018 US dollars; current dollar amounts will be higher due to inflation. We also used the formula to estimate costs, where applicable, by ambulation or clinical (cardiac, respiratory) stages.

This project was determined to not be human subjects research by the institutional review board at the University of Iowa.

3 | RESULTS

For our 20-year follow-up period, we estimated 670 total individual health-care encounters across the selected elements (see Table S1). Of these, 290 were specialty outpatient visits with an average of 15 visits per year. The estimated cumulative direct cost estimates in 2018 US dollars were $101 146 for preventive monitoring (office visits and testing), $72 600 for respiratory and skeletal interventions, and either $955 or $2.1 million for corticosteroid and cardiac medications (lisinopril and either prednisone or deflazacort) (Table 1).

Of the total cumulative preventive monitoring costs ($101 146), 31% were attributed to cardiac outpatient visits and testing and 27% to respiratory management, followed by neuromuscular (15%), orthopedic (12%), and other (rehabilitation, gastrointestinal/ nutritional) specialties (5%–10%) (Table 1). The total average annual costs for outpatient visits and testing increased from $3864 during the ambulatory stage to $5551 in the nonambulatory stage, with increased testing costs in the nonambulatory stage accounting for most of the difference (Table 1). The highest percentage of average annual testing costs during the ambulatory stage was due to cardiac testing (52%), followed by pulmonary (20%), neuromuscular (16%), and orthopedic/ bone health (12%). The percentages for average annual testing costs during the nonambulatory stage remained highest for cardiac (45%), followed by respiratory (39%) testing.

Assuming initiation of glucocorticoids and cardiac medication at age 8 years, the total annual medication costs during the ambulatory stage were $39 for prednisone and lisinopril and $85 779 for deflazacort and lisinopril (Table 1). This increased to $60 and $132 183 annual costs, respectively, in the nonambulatory stage. The share of total cumulative costs accounted for by glucocorticoids is 0.51% if the patient takes prednisone throughout

and from 92% if the patient instead takes deflazacort. Additional interventions include respiratory support and scoliosis surgery as disease progresses, which typically occurs in the nonambulatory stage. The percentage of total costs due to these interventions range from 42% with prednisone and 3% with deflazacort.

Total expected out-of-pocket payments for preventive monitoring and medications over the 20-year follow-up period was $12 643 with prednisone and $29 194 with deflazacort. Expected out-of-pocket payments for families were a small fraction of direct costs (7% with prednisone; 1%–5% with deflazacort).

4 | DISCUSSION

Over a 20-year period, we estimated a total cumulative cost per patient for selected components of the recommended management of DMD of $174 701 if treated with prednisone and over $2.0 million if treated with deflazacort. These cost estimates assume that the current prices of the included drugs remain unchanged for the indefinite future. Prednisone is an inexpensive generic drug, whereas deflazacort remains under patent protection. If the price of deflazacort is reduced after there is generic competition, the difference in costs could be substantially reduced. Additionally, our cost estimate for deflazacort was based on the recommended dosage of 0.90 mg/kg per day, which is 17% to 33% higher than commonly reported dosages of 0.60 to 0.75 mg/kg per day.[28–30] The estimate does not take into account either negotiated discounts and rebates that reduce the cost to health plans or pharmacy cost-sharing programs that could reduce out-of-pocket expenses.

Studies on health-care costs and implementation of health-care guidelines have been published for diseases such as cancer,[31] chronic kidney disease,[32] diabetes,[33] heart disease,[34–39] osteoporosis,[40] and tuberculosis.[41] These studies, however, evaluated guidelines that differ from DMD in terms of the complexity, intensity, and duration of implementation. Further, most studies were cost effectiveness studies that did not directly estimate the direct costs of the guidelines. Although we cannot directly compare our findings, these studies establish a precedent for evaluating the cost of preventive care in DMD.

Previous US DMD cost-of-illness studies have estimated health-care costs inclusive of short- and long-term care, from administrative claims data for a patient cohort.[7–9] Typically, an algorithm derived from a combination of patient characteristics (age), *International Classification of Disease*, Ninth Revision, Clinical Modification (ICD-9-CM) muscular dystrophy codes (359.0 or 359.1), or CPT codes was used to identify a patient cohort. For example, Ouyang et al[9] estimated cost and health-care utilization of MD patients under the age of 30 years who were identified by ICD-9-CM codes 359.0 or 359.1. On average, patients had 32 annual outpatient visits (median = 15) and an average expenditure of $20 467 at 2004 prices; annual average prescription costs across all ages were estimated at $1286. The incremental difference between those with and without MD was $18 930, with outpatient visits accounting for 61% of the incremental expenditures for those with MD. The annual number of encounters and average expenditures were shown to vary with the

highest at 0 to 4 and at 15 to 29 years of age. Among older patients, hospitalization costs related to respiratory and cardiac complications were highest. In a study by Larkindale et al,[8] patients were identified using ICD-9-CM code 359.1. The total annual per-patient medical cost, including insurance payments and out-of-pocket expenses, was estimated from commercial claims to be $24 122. This total cost included annual prescription costs of $2154 for DMD; outpatient visits accounted for up to half of the estimate. Thayer et al[7] selected a cohort of patients with DMD under the age of 30 years using an algorithm that augmented ICD9-CM codes 359.0 and 359.1 with clinically relevant procedural and pharmacy codes to exclude individuals with likely diagnoses other than DMD. An average of 11.92 annualized office visits was reported with a total annualized medical cost of $24 017 at 2010 prices; nearly half of this cost was due to inpatient admissions and one fourth was classified as other expenses (eg, durable equipment, ambulances). Annual prescription costs were estimated at $1487 for an average of 2.95 unique medications. Consistent with previous studies, total health-care costs were highest among older patients (14–29 years of age).

The use of different cost analysis methodologies and data sources can result in varying cost estimates.[42–44] In addition, different case-finding algorithms used with claims data to identify patients with chronic conditions can yield cost estimates of varying magnitude and accuracy. Two validation studies that assessed the accuracy of ICD9/10-CM diagnosis codes for identifying MD in administrative claims data found that an algorithm with the presence of two claims with a diagnosis code of hereditary progressive MD had a positive predictive value of 95% for MD overall and 85% for DMD in one study and of 86% and 66% in the other study.[45,46] The successful application of case-finding algorithms to private and public claims data will further advance assigning costs to preventive care and inform economic evaluation studies on adherence to care considerations within clinically relevant populations.

Our focus on selected health-care events and use of allowable amounts from statewide claims data in combination with published deflazacort prices to estimate cost of prescribed care introduces additional methodological differences that limit comparability of our findings to the existing DMD cost estimates. Specifically, our approach focused on monitoring of disease progression and management of selected morbidities over a specified time frame. This approach excludes costs associated with acute health events and hospitalizations and indirect costs reported by other studies. Our approach also includes encounters that may not occur annually and may not be comprehensively captured by cross-sectional cost estimates. These differences in methodologies preclude direct comparisons between our reported costs and those reported in previous studies. However, broad comparisons can be made for categories of costs. For example, studies that reported health-care utilization showed a high percentage of services were due to outpatient visits, with estimates ranging from an average of 12 to 32 visits per year.[7,9] We estimated an average of 15 visits per year, which falls at the low end of this range. Our 20-year averages were based on the median of extracted charges due to high variability in the underlying distributions. Most of the studies just summarized reported mean costs, which, depending on the distribution, may further reduce comparability of our findings. For example, Ouyang et al[9] reported the mean average expenditures among males with muscular dystrophy as $19 819. The median expenditures were much lower ($4049) and in line with our average annual cost for outpatient visits and testing ($5057). Our estimated annual prescription medication

cost was below those of the above studies, excluding the current pricing for deflazacort, but our estimate was based on only two medications and did not include those for acute health events or treatment of chronic health conditions.[7–9] Finally, the reported higher costs among older patients and greater percentages of costs for treatment of cardiac or respiratory complications are consistent with the increased frequency of recommended care and the intensity of managing these primary complications as DMD progresses.[23]

Part of the challenge of evaluating uptake of the DMD Care Considerations has been the absence of standardized clinical criteria from which adherence, and ultimately cost, could be measured.[15] In response to the 2018 DMD Care Considerations, Ong et al[15] discussed this limitation and outlined key criteria that could be considered when evaluating uptake of the 2018 DMD Care Considerations. Although important, the translation of even well-defined clinical criteria into meaningful units for cost analyses will remain a challenge, particularly for those considerations that are dependent on indicators of disease severity (eg, respiratory capacity, spinal curvature, growth impairment), which makes estimating unit frequencies difficult. To be able to calculate costs for clinical criteria, such as average age at which a clinical threshold is surpassed or the percentage of patients expected to surpass a threshold, algorithms may need to be developed for these conditional elements.[23] Alternatively, a mixed-model method that combines approaches that vary in accuracy of assigning unit costs may be necessary to more effectively capture the cost of a complex management plan, such as the DMD Care Considerations.[42,47] The establishment of a nationally representative cost database comprised of service-level, standardized health-care costs for measurable elements of the DMD Care Considerations would promote such an approach.[44] The database could collate cost data from multiple payer sources (private, public) and provider types (hospital and physician billing) that would allow more comprehensive exploration of the range of expected costs. Standardized procedures, such as clinical criteria or disease algorithms, for determining component costs could also be incorporated into the database infrastructure. These data could then be used to estimate expected costs using hypothetical modeling or provide standardized cost data for combining with independently collected health services (eg, registries or surveillance databases) or survey data that may not have associated cost information to estimate costs of services received.

Our proposed approach has limitations. We used private health plan payments as a proxy of costs, and therefore our cost estimates do not apply to public payers.[43] Furthermore, the price of deflazacort may not necessarily represent either true costs or actual net payments.[48–52] An additional limitation is that modeling the cost of adhering to the DMD Care Considerations is dependent on meaningful operationalization of recommended encounters for which dollar values and unit frequencies can be determined.[53] As a result, our study was limited to those considerations for which a reasonable frequency could be defined and a unit cost assigned. Our study was designed to describe the direct costs of health care associated with preventive management of DMD to all payers, which includes both health plans and families. It was not intended to provide estimates of nonmedical costs (eg, home and motor vehicle modifications) nor productivity costs (eg, loss of family income) associated with the management of DMD. We also did not include in our estimate the cost of new disease-modifying therapies, such as eteplirsen, golodirsen, viltolarsen, and casimersen, which may add significant costs to the preventive care of selected DMD

patients. Economic evaluations of these approved treatments will require consideration of the totality of expenditures that is beyond the scope of our investigation, including the potential to modify recommended preventive care and interventions due to changes in disease course.[23,54–56]

In conclusion, the DMD Care Considerations were developed to promote standardized care and preventive management of patients with DMD. Standardized monitoring of disease progression and treatments may reduce overall costs of illness. To quantify these savings, costs associated with the implementation of preventive care would be needed. We have presented a method that could be used to estimate costs associated with selected components of such care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

cMRI	cardiac magnetic resonance imaging
CPT	Current Procedural Terminology
DMD	Duchenne muscular dystrophy
ECG	electrocardiogram
ECHO	echocardiogram
ICD-9-CM	*International Classification of Diseases*, Ninth Revision-Clinical Modification
MD STARnet	Muscular Dystrophy Surveillance, Tracking, and Research Network

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TABLE 1

Selected costs for 2018 DMD care considerations management domains by ambulation status and total in 2018 US dollars[a]

	Allowed amount					
	Ambulatory (5–10 years)		Nonambulatory (11–24 years)			
Management domains	**Average annual cost[b]**	**Total**	**Average annual cost**	**Total**	**Total direct cost**	**Total expected out-of-pocket payment[c]**
Neuromuscular						
Monitoring	426	2556	426	5964	8520	1000
Testing	318	1908	318	4452	6360	2000
Intervention (prednisone)[d]	36	109	56	785	894	789
Intervention (deflazacort)[d]	85 776	257 329	132 179	1.9 million	2.1 million	17,340
Rehabilitation	252	1514	244	3666	5180	70
Respiratory						
Monitoring	213	1278	426	5964	7242	850
Testing	398	2390	1293	18 102	20 492	543
Interventions	NA	NA	NC	15 600	15 600	NC
Cardiac						
Monitoring	213	1278	213	2982	4260	400
Testing	1060	6358	1471	20 588	26 946	4752
Intervention (lisinopril)[b]	3	9	4	52	61	41
Orthopedic and bone heath						
Monitoring	213	1278	426	5964	7242	748
Testing	249	1494	212	2970	4464	650
Intervention	NA	NA	NC	57 000	57 000	NC
Gastrointestinal and nutritional	522	3132	522	7308	10 440	800

Abbreviations: DMD, Duchenne muscular dystrophy; NA, not applicable; NC, not calculated due to less than annual frequencies.

[a]Median charges using a de-identified fully insured insurance claims data from a large midwestern commercial health insurer.

[b]Average annual cost estimated = total cost / number of follow-up years, where nonambulatory stage = 6 years and ambulatory stage = 14 years.

[c]Prednisone (0.75 mg/kg per day) = 88% of direct cost; lisinopril (2.5 mg/day if <40 kg and 2 mg/day if ≥40 kg) = 68% of direct cost. Deflazacort (0.90 mg/kg per day) = $85 per 30-day supply.

[d] Prednisone and lisinopril prices estimated from generic price from insurance claims data. Deflazacort prices estimated by the Institute for Clinical and Economic Review cost-effectiveness analysis of corticosteroids and DMD (https://icer.org/wp-content/uploads/2020/10/ICER_DMD_Evidence-Report_071619.pdf; date accessed: November 24, 2021).