Cost of Illness for Neuromuscular Diseases in the U.S.

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Keywords: Amyotrophic lateral sclerosis, Duchenne Muscular Dystrophy, Myotonic Dystrophy, Cost of Illness, Neuromuscular diseases.

Acronyms:
ALS – Amyotrophic Lateral Sclerosis
CDC – Center for Disease Control
CMD – Congenital Muscular Dystrophy
DMD – Duchenne Muscular Dystrophy
DM – Myotonic Dystrophy
HPMD – Hereditary Progressive Muscular Dystrophy
ICD-9 - International Classification of Diseases, 9th Revision
OLS – Ordinary Least Squares
MDA – Muscular Dystrophy Association
MEPS – Medical Expenditure Panel Survey
SAF – Standard Analytic File
U.S. – United States of America.
VA – Veteran's Affairs benefits

ABSTRACT

Introduction: We conducted a comprehensive study of the costs associated with amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy (DMD). and myotonic dystrophy (DM) in the U.S.

Methods: We determined the total impact on the U.S. economy, including direct medical costs, non-medical costs, and loss of income. Medical costs were calculated using a commercial insurance database and Medicare claims data. Non-medical and indirect costs were determined through a survey of families registered with the Muscular Dystrophy Association.

Results: Medical costs were driven by outpatient care. Non-medical costs were driven by the necessity to move or adapt housing for the patient and paid caregiving. Loss of income correlated significantly with the amount of care needed by the patient.

Discussion: We calculated the annual per-patient costs to be $63,693 for ALS, $50,952 for DMD, and $32,236 for DM. Population-wide national costs were $1,023 million (ALS), $787 million (DMD) and $448 million (DM).

Keywords: Duchenne Muscular Dystrophy; Myotonic Dystrophy; Amyotrophic Lateral Sclerosis; cost of illness; burden of disease

INTRODUCTION

Neuromuscular diseases are a broad group of disorders, many of which cause progressive muscle weakness and premature death. They incur significant costs to society, despite being rare diseases. We conducted a comprehensive study of the costs to patients and their families associated with 3 neuromuscular diseases in the U.S. We calculate not only direct medical costs, but also the costs of caregiving for patients who, in severe cases, will use a wheelchair or other assistive devices and may need a ventilator and/or gastronomy tube[1, 2]. Depending on the severity of the disease, families may need to adapt their homes and cars to accommodate the needs of the patient, lose income due to caregiving time, lose opportunities for education, or select less well-paid jobs. We set out to determine the national cost burden for these conditions in the U.S. and to determine the factors that drive those costs.

This study investigated the costs associated with amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy (DMD), and myotonic dystrophy (DM). These diseases were selected because they represent 3 of the most common neuromuscular diseases and because there are therapies that are either in clinical trials or in late stage preclinical development[3, 4, 5]. Determining the specific costs of a condition can inform disease management and drug discovery programs to ensure that the most cost-effective solutions are prioritized. If these therapies for neuromuscular diseases prove effective, understanding the potential cost savings will be useful to support policy decisions about treatments and access.

Cost of illness studies for neuromuscular diseases have been performed previously[6-10], but only in limited populations and mostly outside the U.S. U.S. costs would be expected to be quite different than in other countries due to differences in the health care system, differences in average incomes, costs for services etc. Most previous studies have investigated only medical costs, not accounting for other significant costs to families and to society as a whole. Thus, we sought to comprehensively analyze the costs associated with ALS, DMD and DM in the U.S.

MATERIALS AND METHODS

We used commercial and Medicare claims data to estimate direct medical costs associated with ALS, DMD, and DM. Data collected from a cost-of-illness survey were used to estimate non-medical costs and indirect family income loss. Total economic cost was calculated from the prevalence of the disease and total annual cost per-patient (including medical, non-medical, and indirect cost). Ethical approval for this study was granted by the New England Institutional Review Board and its affiliated privacy board.

Estimating Direct Medical Costs

We calculated the medical costs per patient using data from a proprietary claims database for members of a large national private insurance plan; this contains medical and pharmacy claims and enrollment information during the year 2009 as well as data from the Medicare Standard Analytical File (SAF) 5% sample claims data from Part A and

Part B beneficiaries covered in 2008 (Supplemental Table 1). It should be noted that data was obtained by ICD-9 code, so we used 359.1, hereditary progressive muscular dystrophy (HPMD, which includes diagnosis of DMD and other forms of muscular dystrophy) as a proxy. For comparison, we also calculated the costs of Congenital Muscular Dystrophy (CMD, ICD-9 code 359.0), which is another severe progressive muscular dystrophy. The distribution of insurance types carried by patients was assessed through our survey (Supplemental Table 2). We also conducted a multivariate analysis where we pooled the 2008-2010 Medical Expenditure Panel Survey (MEPS) data and calculated per-patient annual total cost by types of insurance. We then ran a Generalized Linear Model to calculate the cost ratios of Medicaid, "other insurance," and uninsured as compared with the commercially insured controlling for age, gender, race/ethnicity, and income. The MEPS dataset contained very few patients with ALS, DMD, or DM specifically, as the publically available data contain only up to 4 variables (primary and second diagnoses) of 3-digit ICD-9 diagnosis codes. This meant that we could not define the diseases specifically. Thus, in the MEPS data we conducted this analysis for patients with ICD-9 diagnosis codes 330-337 (Hereditary and degenerative diseases of the central nervous system) or 350-359 (Disorders of the peripheral nervous system). Based on this analysis, average per-patient total medical cost under Medicaid was found to be at 88% of the cost for commercially insured, "other insurance" at 94% of the commercial cost, and uninsured patients at 66% of the commercial cost. Since the Medicare 5% data do not contain pharmacy records, the pharmacy cost of the Medicare sample was imputed based on the observed pharmacy cost to total cost relationship from the private claims analysis.

Subjects were required to have received at least 1 diagnosis (primary or secondary) of 1 of the conditions at any time during the study year. Subjects from the private claims database were required to be younger than 65 years of age and to have complete medical and pharmacy coverage for the study year to ensure complete coverage of medical costs. This requirement was to ensure that we did not include patients in both Medicare and private insurance data sets, and so that the total cost was included for those patients studied. We used ICD-9 codes 335.20, 335.21, and 335.22 for ALS and 359.21 for DM. DMD has no unique ICD-9 code, so we used 359.1 as a proxy in calculation of medical costs (hereditary progressive muscular dystrophy, HPMD, which includes diagnosis of DMD and other forms of muscular dystrophy).

All cost variables were inflated to the 2010 dollar value using the medical and pharmacy components of the Consumer Price Index in order to calculate the total cost in 2010.

The Cost of Illness Survey

Non-medical costs and family income losses were calculated based on data from a cost-of-illness survey developed as a part of this study (supplemental data). The survey was a paper, mail-based, de-identified, household questionnaire with 55 questions (with a password protected web-based option). Respondents were informed that by filling out the survey they were providing consent to participate in the study.

We convened a technical advisory group (academic physicians, nurses, genetic counselors, patient advocacy groups) and conducted expert interviews and family member focus groups to collect feedback on the draft survey instrument. The sampling frame consisted of households registered with the Muscular Dystrophy Association (MDA) with 1 or more household members diagnosed with 1 of the conditions. This represents a broad profile of families across demographic and socio-economic groups. Based on a power analysis and to obtain a representative study sample, we developed a balanced stratified random sampling approach (per age group, gender, and disease), where 600 sample households were targeted for each disease, anticipating a response rate of 20% or above. Strata with small cell sizes were oversampled to ensure that the final sample size met the minimum requirement for strata level analysis. In order to account for our sampling approach, a non-response adjusted weight was derived for each survey respondent.

Estimating Non-Medical Costs and Indirect Costs Using a Cost of Illness Survey

Per-patient non-medical costs were calculated as the weighted mean cost (and 95% confidence interval) for each disease and by type of expense from the survey data. Indirect cost was calculated by assessing the earnings lost from illness or injury as measured by income forgone due to morbidity or mortality and the earnings lost by household members as they care for affected family members. Total household income loss was used to calculate the value of indirect costs in the U.S. in 2010. The effects of disease on earnings were estimated using ordinary least squares (OLS) regression analysis, where total family income (a sum of individual income of adult family members

in the past 12 months) was estimated as a function of the primary earner's demographic factors, including age (a proxy for work experience), gender, race/ethnicity, and education; disease characteristics (e.g. level of care needed) of the most affected person; and other family characteristics such as number of adults and whether the most affected person was receiving Social Security Disability Income or paid daily care at home. The final model produced an adjusted R square value of 0.24.

Expected family income was predicted by the known determinants of income when no care due to disease was needed. We then calculated the predicted family income loss due to disease-induced intensive care by calculating the difference between actual self-reported family income (with disease-related care) and expected family income (without disease-related care).

Estimating Total National Cost of Disease

The overall cost to society of each of these diseases was calculated as the product of the total per-patient cost (medical, non-medical and indirect) and prevalence estimates for the 3 diseases. Because there is very limited U.S.-specific data on the overall prevalence of the conditions, we used 2 available prevalence estimates for ALS and DMD - the prevalence rate per 100,000 individuals reported by Orphanet[11], which provides a mean prevalence of rare diseases in Europe based on aggregate data and the best U.S. based prevalence study available[12, 13]. No U.S. data were available for DM, so we used only the Orphanet numbers. We then multiplied the prevalence rate for each disease by the total

U.S. population in 2010 to estimate the number of patients affected by the disease nationally, and the total national cost of each disease was calculated.

RESULTS

Calculation of Direct Medical Costs Using Health Insurance Claims Data

Analysis of the insurance distribution from the survey showed that about 83% (ALS), 51% (DMD), and 70% (DM) of patients were either covered by private insurance or by Medicare, respectively. The total annual per-patient medical costs (weighted by proportion of patients covered by different insurance types) were $31,121 for ALS, $22,533 for DMD, and $17,451 for DM, including both insurance paid amount and patient out-of-pocket expenditure.

The per-patient healthcare costs (in 2010 dollars) for each disease were similar for commercial insurance and Medicare (Table 1). For both, outpatient care was the largest cost driver, a category that includes hospital outpatient, physician visits, and physical and occupational therapy. For each disease, this accounted for up to 50% of all medical costs. Acute inpatient care accounted for much of the remaining costs, although this category was a larger contributing factor in ALS and DMD than in DM.

Chronic or long-term inpatient care and durable medical equipment represented a larger proportion of per-patient cost under Medicare than under private insurance. Total per-

capita medical costs to patients on Medicare are similar to those calculated from commercial insurance.

Calculation of Non-Medical and Indirect Costs from the Cost of illness Survey

We assessed the non-medical costs and indirect cost (i.e. family income loss) to patients with ALS, DMD, and DM using a cost-of-illness survey of families registered with MDA (supplemental data). It should be noted that the diagnosis depended on the patient's registered diagnosis with MDA. Particularly for older patients, this diagnosis is unlikely to have been confirmed genetically. A very small proportion of patients registered as "DMD" may actually be affected by Becker Muscular Dystrophy or some other dystrophy, as it is unlikely that a DMD patient reached an age of greater than 65. Similar misdiagnoses may occur at very low rates in the other categories. Similarly, the table would suggest that there is a bias toward white people being affected. Again, this reflects the surveyed population, not necessarily the population of people with the diseases. These non-uniformities in the sampled population are not thought to affect the overall conclusions of the study. The survey achieved a 25% overall response rate (Supplemental Table 3) with a fraction of item-nonresponses imputed based on characteristics of other family members (e.g. patient's race imputed by parents' race). Among those who responded 124, 131, and 123 reported being affected with, or having a relative affected with ALS, DMD, or DM, respectively. This represented 12,324, 7,217, and 9,975 families when weighted with the non-response adjusted weights.

Calculation of Non-Medical Cost

Table 2 shows the average per-household non-medical cost weighted with non-response adjusted weights, along with 95% confidence intervals. These costs include home costs, vehicle costs, paid professional daily care, and "other costs" to the family (such as food supplements, travel costs, and training costs). These costs were assessed per annum and averaged over patients at different stages of disease.

Non-medical costs were highest for ALS. The largest contributing factor was moving homes or modifying the existing home. Patients also spent significant amounts on "other non-medical costs" and in caregiving. Lowest annual costs were for DM, where the largest cost driver was "other costs". In DMD, "other costs" was also the largest contributing factor, closely followed by caregiving and home modifications.

Calculation of Loss of Family Income

We used an OLS regression analysis (Supplemental Table 4) to calculate the loss of total family income associated with having a family member affected by these diseases. To test the impact of disease-associated care on total family income, the main independent variable included in the model was the level of care; 4 categories indicate the number of hours the most affected person requires for daily care. Other predictors of family income that were selected as candidate covariates included variables such as the age, gender, race/ethnicity, level of education of the primary income-earner of the household, and family characteristics such as number of adults in the family, disease duration, and

whether the patient received any Social Security disability income. We first tested a naive model where, in addition to variables indicating disease and level of care, only the primary income-earners' age, gender, level of education, and number of patients and number of adults in the family were included. We compared this parsimonious model with a number of alternative models using a guided selection approach and chose the final model that has the smallest AIC value and an adjusted R^2 value comparable to that of the naïve model (see full model specification in Supplemental Table 4).

Table 3 shows that the level of care was associated directly with family income loss. The families of patients that required 16-24 hours of daily care earned $21,600 less than the income earned by the "care not needed" group (omitted group). Families with the most affected person requiring 8-15 hours and 1-7 hours of daily care earned, on average, $7,325 and $4,172, respectively, less than the "care not needed" group. Based on the same regression model, we predicted the expected total family income and calculated that DMD incurred the greatest weighted annual loss of income of $15,481, followed by ALS ($14,682) and DM ($9,628).

Calculation of the Total National Costs of ALS, DMD and DM in the U.S. in 2010

The overall annual costs to society of each of these diseases were calculated by multiplying the total per-patient cost (medical, non-medical and indirect costs) by the prevalence of each disease. As described in Methods, we estimated the prevalence of these diseases by applying the prevalence rate as reported in the Orphanet report and the

best U.S. studies of disease prevalence to the U.S. population in 2010 (based on census data). The prevalence rates from the Orphanet report were 5.2 patients per 100,000 for ALS, 5.0 per 100,000 for DMD, and 4.5 per 100,000 for DM. By comparison, U.S. numbers may be lower, as a study of ALS prevalence in Texas reported a prevalence of 1.3-2.2 per 100,000, [12] and the CDC (Centers for Disease Control) reports DMD prevalence in 4 U.S. states as 2.3-3.1 per 100,000 (calculated from the population given)[13]. No U.S. prevalence numbers have been reported for DM. Table 4 shows that ALS has the greatest estimated national cost ($256-$433M using the Texas prevalence numbers, $1,023M using Orphanet numbers), followed by DMD ($362-$488M using the CDC prevalence and $787M using the Orphanet numbers), and DM ($448M).

Significant Drivers of Costs

As neuromuscular diseases progress, patients and their caregivers may encounter new challenges (e.g. loss of ambulation resulting in full-time use of a wheelchair, impaired respiration requiring ventilatory support, or difficulty swallowing necessitating insertion of a feeding tube). We further analyzed the survey data to determine factors that significantly affect the costs. Total annual family cost was calculated as the total of out-of-pocket payment for medical care, non-medical cost, and loss of family income. Ventilator and wheelchair use are associated with increased family cost for ALS, while cognitive impairment was a significant cost driver for DM (Table 5).

Discussion

This is a comprehensive attempt to calculate the annual cost of illness for ALS, DMD, and DM in the U.S. We considered all of the costs of disease – medical, non-medical, and loss of income. We estimate an annual per-patient total cost (medical, non-medical, and indirect) in the U.S. of $63,693 for ALS, $50,952 for DMD, and $32,236 for DM, which is an average over the course of the disease. For all conditions, increased costs are associated with increased care requirements. ALS patient costs are significantly associated with use of wheelchairs and ventilators, and DM patient costs are affected by cognitive impairment. These data suggest that interventions that slow disease progression, reduce care requirements, and keep patients walking for longer could significantly reduce the annual cost of these diseases. It should be noted that longer survival due to an intervention may increase the cost of illness overall, as prevalence numbers increase.

Although it is difficult to compare costs directly with studies on neuromuscular diseases outside of the U.S. due to differences in healthcare systems and differences in methodology. Our estimated costs of neuromuscular diseases are similar to those reported previously in other countries (Supplemental Table 5) [6-10]. U.S. per-patient medical costs across all muscular dystrophies for people with commercial insurance in 2008 were estimated at $18,930 [7], which is comparable to our estimated medical cost for DMD ($22,798) and DM ($17,592). Our estimates are also similar to those for other chronic, disabling diseases in the U.S. A study of multiple sclerosis in 2006 estimated that average costs are about $47,215 per-patient per year [14]. Annual direct medical costs per-patient

with Parkinson disease were estimated to be between $10,043 and $12,491, and annual indirect costs, including lost workdays for patients and caregivers, are estimated at $9,135 [15,16]. Thus, our cost estimates for neuromuscular diseases are comparable to or somewhat higher than those associated with other disabling diseases.

The total medical cost for DMD is likely to be an underestimate of the true cost, because there is no specific ICD-9 diagnosis code for DMD. The code 359.01 (HPMD) that is used in the medical cost calculations includes not only DMD, but also Becker muscular dystrophy, limb girdle muscular dystrophy, and other less severe types of MD. Congenital muscular dystrophy, which has its own ICD-9 code (359.0), is another severe childhood onset muscular dystrophy and might be expected to have medical costs similar to DMD. We calculated the per-patient annual medical costs associated with CMD to be $32,341 (data not shown) vs. $24,122 (HPMD) for the commercially insured and $39,365(CMD) vs. $22,852 (HPMD) for patients enrolled in Medicare. Thus, real medical costs for DMD could be 34% to 72% higher than our estimates.

There are a few caveats that should be considered in our cost analysis. The analysis required that patients have insurance coverage for an entire year to be included in the study in order to include all aspects of care within a single type of insurance. This resulted in exclusion of individuals who died in the course of the year. This may have resulted in exclusion of some terminally ill individuals and contributed to an underestimation of true costs.

Furthermore, as noted by a few survey responses, some of the diagnoses listed were inaccurate. We also anticipate a certain degree of sampling error based on those patients who chose to return the survey, as they might be expected to be better educated, more motivated, and perhaps less affected. However the direction and magnitude of potential bias due to such sampling error is unknown due to a lack of data on the non-respondents. For instance, our OLS regression analysis of the survey data showed that education (whether the primary income-earner has a college degree) was a significant predictor of family income. If the survey non-respondents were less educated than the respondents, inclusion of the non-respondents in the study sample would lower both the predicted family income and actual family income. This means that the predicted mean family income loss (the difference between predicted and actual family income) without non-response bias would be different from, but not necessarily smaller than, our current estimates, especially given the joint impact of other factors such as disease severity.

Although our survey collected insurance coverage information for the study sample, we did not collect the amount of medical cost that was paid by the insurance due to concerns about recall bias. Furthermore, while we obtained very rich insurance claims data for the privately insured and Medicare beneficiaries for calculation of their total medical cost (insurance and self-paid), we were not able to collect medical cost data for patients covered by Medicaid, other benefits (e.g. Veterans Administration), and a small proportion of patients who had no insurance coverage. Instead, we imputed the medical cost for those who are under Medicaid and other benefit coverage and those who are uninsured using cost differences (from privately insured) estimated from the MEPS data.

We were surprised that the costs of illness were not affected significantly by markers of disease progression in DMD. Trends were seen in this data that suggested increased costs associated with wheelchair and ventilator use and with time since diagnosis, but they did not reach significance. The major cost driver for DMD was caregiving costs. This may be less modulated by disease course in a pediatric disease, where less affected patients are young children who require full time caregiving regardless of disease. ALS and DM primarily affect adults at ages where caregiving is typically not required.

Finally, in order to calculate the national cost of illness for these diseases, we need to know the number of patients in the U.S. who have each condition. There are very limited prevalence data in the literature for any of these diseases in the U.S. The prevalence rate (per 100,000 population) from the Orphanet report used in this study was calculated through a meta-analysis of multiple studies (many outside of the U.S.)[11]. Recent reports of U.S. prevalence for ALS and DMD suggest that the Orphanet numbers may be higher that the U.S. prevalence for these diseases[12, 13]. There are no reports of DM prevalence in the U.S. We do not believe that the prevalence rates for these diseases are necessarily higher in Europe than in the U.S. as these data suggest. The European studies have been done over a period of time, and the prevalence of these diseases (particularly DMD) has changed because of a combination of longer life-spans due to improved medical management and possibly prenatal diagnosis[13]

Conclusions

This report is a comprehensive study conducted in the U.S. concerning the economic impact of neuromuscular diseases, including ALS, DMD, and DM. Moreover, it is 1 of only a few studies that have attempted to estimate the total cost to the household of a debilitating disease, including non-medical costs and loss of income. The findings help to underscore the importance of research into the causes and treatment of these conditions. In addition, the results suggest a possible role for additional policy initiatives to better help affected individuals and families in terms of treatment and long-term care, disease management, employment, and occupational training to improve quality of life and to alleviate human and economic burden. The total estimated national cost of illness for ALS, DMD, and DM is between $1.07 and $2.26 billion per year, and this is likely to be a conservative estimate.

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Table Legends:

Table 1: Annual Medical Costs (Insurance and Self Paid) for Neuromuscular Disease Patients. Per-patient average annual medical costs for patients covered by Medicare or commercial insurance. Costs were calculated from records for continuous yearly coverage for the indicated number of patients with each type of insurance. Due to the fact that DMD does not have a single ICD-9 code, values for hereditary progressive muscular dystrophy (HPMD) were used as a proxy.

Table 2: Annual Non-medical Costs (Self and Other Paid) by Disease and Type of Expenses. Annual non-medical costs calculated from the responses to the cost-of-illness survey. These are costs directly due to the patient's illness, paid by either the family or by insurance.

Table 3: Annual Predicted Income Loss by Level of Care Required. Predicted income loss to a household due to patient status, depending on hours of care needed by the patient. This was calculated from the cost-of-illness survey based on reported household income in families where the patient required little care compared to those where the patient needed more care. Disease diagnoses were included in the regression as indicator variables, however they were not tested for interaction with hours of care variable due to small sample size.

Table 4: Overall Annual Cost of Illness. Summary of the annual per-patient cost of illness for patients with the 3 conditions, including medical, non-medical, and indirect costs, the prevalence estimates for each disease, and the total cost of illness in the U.S.

Table 5: Aspects of Disease Progression that Affect the Cost of Illness. The annual per-household expenses for each disease were analyzed to determine the factors that most affected the cost. For instance, total family costs were compared between wheelchair or ventilator users vs. non-users. [N.B. – the number of ALS patients diagnosed more than 10 years ago is high. This is due to a combination of some misdiagnoses as noted on page 16, and some slowly progressing patients – due to increased lifespan these patients are somewhat over-represented in the MDA mailing list]~~)~~

Table 1: Annual Medical Costs for Neuromuscular Disease Patients

		Commercial Plan			Medicare		
		ALS	**DMD [d]**	**DM**	**ALS**	**DMD [d]**	**DM**
N		945	1,966	378	583	199	137
Inpatient (Acute)	Mean	$10,290	$9,393	$6,870	$9,411	$7,095	$4,939
	SE[c]	$1,374	$1,179	$1,885	$1,041	$1,582	$1,013
Inpatient (Non-Acute or Long-term)	Mean	$617	$615	$328	$3,913	$1,445	$1,685
	SE	$132	$247	$167	$460	$476	$606
Outpatient	Mean	$17,555	$11,960	$9,450	$10,745	$6,362	$9,512
	SE	$1,710	$881	$759	$527	$866	$1,801
Durable Medical Equipment	Mean	$1,810	$1,108	$588	$5,158	$4,034	$1,079
	SE	$217	$91	$162	$413	$634	$177
Prescription Medication [a]	Mean	$2,473	$2,154	$1,589	$2,539	$2,041	$1,643
	SE	$176	$158	$324	NA	NA	NA
Total Annual Cost [b]	**Mean**	**$30,934**	**$24,122**	**$18,236**	**$31,766**	**$22,852**	**$18,858**
	SE	$2,336	$1,667	$2,224	NA	NA	NA

[a] Percentage of pharmacy cost (over total medical cost) used for Medicare pharmacy cost calculation: 5-9%.

[b] Total cost under Medicare is the sum of the estimated cost of prescription medication and all other medical costs .

[c] SE: Standard error

[d].Cost of patients with ICD-9 diagnosis code of 359.1(HPMD) is used as a proxy for DMD.

Table 2: Annual Non-medical Costs (Self and Other Paid) by Disease and Type of Expenses

Disease	Type of Expenses	N	Mean	Standard Error	95% CL for Mean	
ALS	Moving or modifying home	109	$7,106	$2,096	$2,950	$11,261
	Purchase or modifying motor vehicle	107	$2,064	$385	$1,300	$2,827
	Professional caregiving	111	$4,570	$1,446	$1,704	$7,435
	Other non-medical cost (e.g. food, travel, dietary supplements)	118	$5,908	$975	$3,977	$7,840
	Total non-medical cost	**124**	**$17,889**	**$3,265**	**$11,426**	**$24,351**
DMD	Moving or modifying home	113	$3,050	$615	$1,832	$4,268
	Purchase or modifying motor vehicle	119	$1,680	$216	$1,252	$2,107
	Professional caregiving	113	$3,189	$1,315	$583	$5,794
	Other non-medical cost (e.g. food, travel, dietary supplements)	123	$6,605	$1,837	$2,969	$10,240
	Total non-medical cost	**131**	**$12,939**	**$2,465**	**$8,063**	**$17,816**
DM	Moving or modifying home	113	$990	$687	-$371	$2,350
	Purchase or modifying motor vehicle	116	$435	$356	-$269	$1,139
	Professional caregiving	109	$925	$712	-$487	$2,338
	Other non-medical cost (e.g. food, travel, dietary supplements)	121	$3,067	$900	$1,285	$4,850
	Total non-medical cost	**123**	**$5,157**	**$1,820**	**$1,554**	**$8,761**

*Ns are based on un-weighted raw counts. Means are weighted.

Table 3: Annual Predicted Income Loss by Level of Care Required

	Parameter Estimate	Standard Error	t Value	Pr > |t|
16 to 24 hours of care	-$21,600	$7,710.20	-2.79	0.0054
8 to 15 hours of care	-$7,325	$8,914.50	-0.83	0.4068
1 to 7 hours of care	-$4,172	$8,570.30	-0.5	0.6182
Care not needed (Omitted)	$0.00	$0.00	0	0

*See Supplemental Table 4 for full regression model results

Table 4: Overall Annual Cost of Illness

Disease	Direct Cost		Indirect Cost [b]	Total Per-capita Cost	Prevalence Estimates (Orphanet)	Prevalence Estimates (Best U.S. Estimate)	Total National Cost (in millions) (Orphanet)	Total National Cost (in millions) (best U.S.)
	Medical Cost [a]	Non-Medical Cost [b]						
ALS	$31,121	$17,889	$14,682	$63,693	16,055	4014-6792	$ 1,023	$256-$433
DMD	$22,533	$12,939	$15,481	$50,952	15,437	7101-9571	$ 787	$362-$488
DM	$17,451	$5,157	$9,628	$32,236	13,894		$ 448	$448
Total							$ 2,257	$1065-$1368

a. Analyzed using health plan claims data

b. Analyzed using cost of illness survey data

Table 5: Aspects of Disease Progression that Affect the Cost of Illness

			Total Family Cost			
			N	**Mean**	**Standard Deviation**	***P*-value ****
ALS	Disease duration	Less than 10 years	65	$44,101	$61,747	0.174
		More than 10 years *	21	$23,753	$49,857	
	Ventilator use	On invasive ventilator/respirator	10	$84,789	$66,564	0.008
		On non-invasive ventilator	26	$50,478	$31,986	0.019
		Not on ventilator/respirator *	50	$24,102	$63,784	
	Cognitive Impairment	No	70	$34,842	$58,922	0.163
		Yes *	16	$57,903	$59,898	
	Wheelchair use	No	29	$9,932	$59,425	0.001
		Yes *	57	$53,989	$54,134	
DMD	Disease duration	Less than 10 years	46	$29,530	$46,750	0.522
		More than 10 years *	49	$36,282	$54,941	
	Ventilator use	On invasive ventilator/respirator	12	$51,733	$64,044	0.123
		On non-invasive ventilator	19	$37,624	$61,021	0.459
		Not on ventilator/respirator *	64	$28,133	$44,729	
	Cognitive Impairment	No	67	$30,975	$55,376	0.492
		Yes *	28	$37,887	$38,963	
	Wheelchair use	No	36	$26,439	$47,340	0.329
		Yes *	59	$37,023	$53,074	

			Total Family Cost			
			N	**Mean**	**Standard Deviation**	***P*-value ****
DM	Disease duration	Less than 10 years	11	$21,474	$30,330	0.623
		More than 10 years *	57	$15,659	$54,750	
	Ventilator use	On invasive ventilator/respirator	0	.	.	N/A
		On non-invasive ventilator	10	$24,823	$56,883	0.588
		Not on ventilator/respirator *	58	$15,182	$50,863	
	Cognitive Impairment	No	38	$2,307	$46,955	0.009
		Yes *	30	$34,704	$51,929	
	Wheelchair use	No	47	$9,056	$44,432	0.070
		Yes *	21	$33,484	$62,411	

* The comparison group within each category
***P*-values are based on independent group *t*-test