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# A Population-based Study of Scoliosis among Males Diagnosed with a Dystrophinopathy Identified by the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STAR*net*)

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## Abstract

**INTRODUCTION/AIMS:** Scoliosis is a common comorbidity among individuals diagnosed with a dystrophinopathy. We examined associations between clinical predictors and scoliosis in childhood-onset dystrophinopathy.

**METHODS:** The progression and treatment of scoliosis were obtained from data collected by the US population-based Muscular Dystrophy Surveillance, Tracking, and Research Network. Associations between loss of independent ambulation (LoA) and corticosteroid use and scoliosis outcomes (ages at or exceeding Cobb angle thresholds [10°, 20°, 30°]; surgery) were estimated using Kaplan-Meier curve estimation and extended Cox regression modeling.

**RESULTS:** We analyzed curvature data for 513 of 1054 individuals ascertained. Overall, approximately one-half had at least one radiograph and one-quarter had a curvature of at least 20°. The average maximum curvature was 25.0° (standard deviation [SD]=21.5°) among

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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.

all individuals and 42.8° (SD=18.8°) among those recommended for surgery. Higher adjusted hazards of curvature ($aHR_{(curvature)}$ [95% confidence interval]) were found among individuals with LoA compared to those without LoA ($aHR_{(10)}$=6.2[4.4,8.7], $aHR_{(20)}$=15.3[7.4,31.7], $aHR_{(30)}$=31.6[7.7,128.9]), among individuals who did not use corticosteroids compared to those who did ($aHR_{(10)}$=1.2[0.9,1.7], $aHR_{(20)}$=1.8[1.1,2.7], $aHR_{(30)}$=2.3[1.3,4.0]), and among non-ambulatory individuals who used corticosteroids after LoA compared to those who did not ($aHR_{(10)}$=1.8[1.2,2.8], $aHR_{(20)}$=1.6[1.0,2.6], $aHR_{(30)}$=3.6[1.6,7.9]). Scoliosis surgery among individuals with LoA who did not use corticosteroids was more than double compared to those who used (aHR=2.3[1.3,4.2]).

**DISCUSSION:** Our retrospective observational study suggests corticosteroids may delay spinal curvature progression and need for scoliosis surgery. Continuing corticosteroids after LoA also showed potential benefits of delaying curvature progression, additional studies are needed to confirm this finding or address the magnitude of benefit.

### Keywords

Duchenne muscular dystrophy; scoliosis; corticosteroid; dystrophinopathy

## INTRODUCTION

The dystrophinopathies, Duchenne muscular dystrophy (DMD) and allelic Becker muscular dystrophy (BMD), are X-linked recessive disorders caused by mutations in the *DMD* gene that result in deficient dystrophin production. Although DMD has a relatively stereotyped progression, variability has been observed in age at onset of muscle weakness and rate of progression.[3] BMD includes a wide spectrum of severity and is historically distinguished from DMD by having loss of independent ambulation (LoA) after age 16 years. Advances in the multidisciplinary care, especially regarding respiratory care and use of corticosteroids, have produced considerable improvement in life expectancy.[2, 4-7]

Individuals with DMD are at risk for scoliosis due to diminished postural strength. Progression of scoliosis occurs most rapidly during the adolescent growth spurt and following LoA.[8-10] Interventions aimed at delaying LoA have had variable impact on development of scoliosis. Non-pharmacologic preservation of ambulation status with orthoses has been shown to delay the onset of scoliosis in some,[11, 12] but not all, [13] studies. Oral corticosteroids, administered with daily or intermittent dosing regimens, have wide-ranging benefits, including preserving respiratory function, prolonging ambulation, and delaying the progression of scoliosis.[14-17] As such, corticosteroids are a key component of dystrophinopathy management.[18] Despite these benefits, corticosteroids have several potential adverse effects, including but not limited to constitutional changes, endocrine disruptions, fractures, or behavioral changes; so, some families choose to not use them or to discontinue use due to these adverse effects. We present a population-based analysis of the epidemiology of scoliosis in individuals with childhood-onset dystrophinopathy and describe progression as it relates to timing of LoA and patterns of corticosteroid use.

## METHODS

The Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STAR*net*) is a US, multisite population-based cohort for surveillance and research of muscular dystrophy has previously been described.[19, 20] Briefly, starting in 2004, MD STAR*net* retrospectively identified and longitudinally followed all children born since January 1, 1982 who were diagnosed with childhood-onset (prior to age 21 years) dystrophinopathy and resided in four catchment areas, Arizona, Colorado, Iowa, and the western 12 counties of New York State. In 2005 and 2008, Georgia and Hawaii, respectively, joined the network. Health and vital status information were systematically collected on all eligible individuals through December 31, 2011, or until the time of their death or out migration from the network catchment areas. Individuals identified from September 2011 through December 2011 were followed through December 2012 to ensure a minimum of one-year of follow-up. Public health authority was enacted for medical record abstraction in Colorado, Georgia, Hawaii, Iowa, and western New York. For Arizona, institutional review board approval was obtained at the University of Arizona and at individual healthcare facilities where data were collected.

Trained abstractors identified the medical records of potentially affected individuals and collected key health information associated with diagnosis, clinical tests, and disease progression using well-defined methods.[21] Diagnostic data collected were reviewed by a clinical care review committee, composed of neurologists experienced in treating individuals with dystrophinopathy. The committee reviewed clinical signs and symptoms, diagnostic data, and family history and used defined criteria to assign a case status assessment of definite (confirmation by DNA or muscle biopsy in self or first degree relative), probable (elevated creatine kinase [CK] plus family history), possible (elevated CK without confirmatory DNA, muscle biopsy, or family history), asymptomatic (DNA confirmation without clinical signs and symptoms), or manifesting female (DNA or muscle biopsy confirmation, clinical signs and symptoms, and female sex) (Supplemental eTable 1).[22] In addition to the clinical rating, clinical phenotypes (DMD, BMD, female, elective pregnancy terminations, not classified) were assigned using a post-hoc multivariable analytic algorithm. The distinction between DMD and BMD was based on phenotypic indices derived from molecular findings (Western blot and genetic analysis), age at first symptoms, and age at LoA (with or without corticosteroids) (Supplemental eTable 2).[23] The algorithm also included a confidence rating based on the number of indices available to assign the phenotype (low [one index], medium [two indices], and high [three indices]).

### Analytic Sample

Our analytic sample was selected from the total sample of individuals ascertained with a childhood-onset dystrophinopathy (n=1054). Exclusions included: Hawaii residents (n=28), individuals who were not assigned a definite or probable case status (n=136), individuals who were a younger sibling of any affected male (n=119), or those with documented co-morbid conditions (e.g. cerebral palsy) (n=24). Data for the remaining cases (n=778) were reviewed for adequacy of available follow-up data, and those (n=176) with limited

data due primarily to migration into an MD STAR*net* site or clinical source, or infrequent follow-up were excluded. After these exclusions, our sample comprised 602 individuals.

## Outcomes

Our outcomes were predefined thresholds for spinal curvature (≥10°, ≥20°, ≥30°) to approximate severity of progression of scoliosis and recommended or completed scoliosis surgery. Abstractors reviewed medical records for evidence of thoracolumbar radiographs and entered available Cobb angle data, as well as the month and year it was recorded. Individuals were identified as having scoliosis surgery, either recommended or completed; month and year were entered for each. Assigning the 15$^{th}$ day of the month, we calculated the time from birth to the age at which an individual's recorded presurgical spinal curvature reached or exceeded a threshold. We also calculated the time from age at LoA to the age at meeting or exceeding each curvature threshold and recommendation or completion of surgery.

## Exposures

We created analytic exposure variables from available mobility and corticosteroid data to assign LoA and non-use of corticosteroids using dates recorded for each. The LoA date was defined as the date at which the individual entered a wheelchair full-time. For corticosteroids, complete start and stop dates were recorded from clinical visits in the medical record and used to determine periods of use.

We created monthly status variables, considering partial months as full months, to be entered as time-varying covariates in our time-to-event analyses. LoA status was coded as non-ambulatory (1) or ambulatory (0). Corticosteroid status was coded as non-use (1) or use (0). Similarly, we coded monthly status variables for corticosteroid use (non-use=1, use=0) beginning at the age at LoA. Finally, we created two categorical variables that described corticosteroid use relative to LoA (no use after LoA or corticosteroid use after LoA; no lifetime corticosteroid use, corticosteroid use before or at LoA, or corticosteroid use after LoA).

## Statistical Analysis

We conducted analyses using Statistical Analysis Software (SAS) version 9.4 (SAS® Institute, Cary, NC). Descriptive statistics included counts and percentages for categorical variables and means (*M*), medians (*Md*), standard deviations (*SD*), and minimum and maximum (*min, max*) values for continuous variables. We used Kaplan-Meier (K-M) curve estimation for each spinal curvature threshold and surgery outcome through age 30 years; the generalized Wilcoxon test statistic was used to determine statistical significance ($p < 0.05$) of the difference in survival estimates between strata. To evaluate associations between each scoliosis outcome (curvature threshold, surgery recommendation) and exposure (corticosteroid non-use or LoA), adjusted hazard ratios (HR)s and 95% confidence intervals (CI)s were estimated from extended Cox regression models with time-varying covariates. Individuals with missing ambulation status or timing of LoA were excluded (n=29). The models examining LoA status and time from birth to scoliosis outcomes were adjusted for corticosteroid use as a time-varying covariate and MD STAR*net* site as a fixed covariate.

The models examining corticosteroid non-use and time from birth to scoliosis outcomes were adjusted for LoA status as a time-varying covariate and MD STAR*net* as fixed covariate. Finally, the models examining time from LoA to scoliosis outcomes were only adjusted for MD STAR*net* site due to the sample being restricted to those with LoA. Age at last clinical visit was used for censored individuals who did not experience the outcome. To examine associations between corticosteroid non-use after LoA and our outcomes, we restricted the sample to those individuals who lost the ability to ambulate independently (n=224) and follow-up was limited to 5 years post-LoA given follow-up for the majority (75%) of the sample fell within this period.[24] We compared any corticosteroid use after LoA, as well as corticosteroid use relative to LoA.

We also conducted secondary analyses that restricted the sample to individuals classified as DMD phenotype (all phenotype confidence levels combined), those classified as DMD with a corresponding phenotype confidence level of high or medium, or those without any gaps in corticosteroid use.

## RESULTS

Although we attempted to identify cases with comprehensive follow-up, there were some individuals who had recorded dates of radiographs or scoliosis surgery but no recorded curvatures or first recorded curvatures that exceeded 20° suggesting results from earlier radiographs were not available. Therefore, we examined potential bias by comparing time to surpassing the curvature thresholds among those with at least one missing radiograph curvature or first radiographs with curvatures >20° and those not meeting those criteria. We observed statistically significant differences for K-M curve estimations suggesting incomplete natural histories among those with initial values >20° (Supplemental eFigure 1). Thus, we excluded an additional 105 individuals with a first curvature value >20° (n=74) or a missing curvature value (n=31), leaving 513 individuals for analysis.

Characteristics of the final analytic sample are presented in Table 1. Approximately one-half of individuals experienced LoA at a mean of 11.3 years. Most individuals (80.9%) were classified as having DMD and the number of individuals at each site was consistent with that expected given a site's population size (data not shown). Overall, about one-half of individuals had at least one recorded radiograph value (Table 2). The percentages of individuals exceeding the curvature thresholds decreased with increasing severity. A referral to an orthopedic surgeon was recorded for 112 (86%) individuals who surpassed 20° (data not shown). Surgery was recommended for less than 20% of individuals and the average maximum curve value before surgery exceeded 20°, which is the threshold for consideration of surgical intervention (Table 2). Figure 1 (A-D) shows the K-M curve estimations for each curvature threshold. By age of 17.0 years (95% CI=16.1, 18.9), 50% of individuals had reached or surpassed the 20° threshold, which is the standard threshold at which orthopedic evaluation is recommended.[25-27]

### Ambulation Status and Corticosteroid Use

The extended Cox regression models showed that LoA is a risk for developing scoliosis; using ambulation status as a time-varying covariate there is a higher adjusted hazard

of exceeding each scoliosis threshold during periods of non-ambulation compared to periods of independent ambulation with greater hazards as the threshold cutoff increased (Figure 2A). Approximately one-half of all individuals had documented corticosteroid use (Table 3). On average, corticosteroids were initiated within a couple of years of the first neuromuscular visit. K-M curve estimation stratified by any lifetime corticosteroid use did not show differences in time to exceeding any curvature threshold (Supplemental eFigure 2). However, results from the extended Cox regression models with corticosteroid non-use as a time-varying covariate showed higher adjusted hazards of exceeding thresholds during periods of non-use compared to periods of use (Figure 2B). The magnitude of the hazards increased with higher curvature thresholds.

## Corticosteroid Use after LoA

K-M estimation showed 50% of individuals exceeded the 10° curvature threshold within 2.5 years (95% CI= 1.9, 2.9) following LoA and the 20° threshold within 4.3 years (95% CI=3.9, 4.7) (Supplemental eFigure 3). Fewer than 50% surpassed the 30° threshold, which may be due in part to surgical intervention once curvatures exceeded 20° [28, 29]. Among those who lost independent ambulation, 103 (45%) continued corticosteroid use following LoA. Of these 103 individuals, 65 (63%) were still receiving corticosteroids at last visit, 12 (12%) discontinued use due to fulltime wheelchair, and 26 (25%) discontinued use by parental choice due to adverse effects or no perceived benefit (data not shown). The median duration of use after LoA was almost 2 years. For any corticosteroid use after LoA, K-M analyses showed longer times to each curvature threshold with use compared to non-use (Figures 3a, 3c, 3e). The greatest differences in delays among corticosteroid users were between approximately 1-3.5 years post-LoA for thresholds up to 20° and between 2-4.5 years for 30°. For corticosteroid use after LoA, those who used corticosteroids before or at LoA were more similar to those who did not receive corticosteroids in terms of the delays in surpassing curvature thresholds through 20° (Figure 3b, 3d, 3f). The extended cox regression models with corticosteroid use as a time-varying covariate showed adjusted hazards ranging from 1.79 to 3.59 of exceeding thresholds during periods of non-use after LoA compared to those when corticosteroids were continued (Figure 2C).

## Surgical Intervention

A total of 73 (56%) cases with recorded curvatures at or above 20° had scoliosis surgery; 100% were under the age of 20 years (data not shown). Of those who did not have surgery, but whose curvatures exceeded 20° (n=49; 44%), surgery was declined (n=14; 29%), the highest curve was measured at or near the last recorded visit (n=17; 35%), surgery was recommended at the last recorded visit (n=4; 5%), or the surgical status between the last radiograph and last follow-up was unknown (n=16; 33%). Of the 16 cases with unknown surgical status, 5 (31%) were deceased. Hazards of having scoliosis surgery recommended or completed among individuals who did not continue corticosteroids after LoA were over twice as high compared to those who received corticosteroids (HR=2.3, 95% CI 1.3, 4.2) (data not shown).

### Secondary Analyses

Analyses were replicated on a subset of the total population who were assigned the DMD phenotype (n=415) and those assigned a medium or high confidence DMD phenotype (n=330) using the MD STAR*net* multivariable phenotype algorithm.[23] We also replicated analyses among those who did not have any gaps in corticosteroid use (n=474). Overall, our analyses did not result in substantive differences in interpretation (see Supplemental eTables 3-6). The percentages of individuals exceeding curvatures of 20° (29% DMD, 34% high-medium DMD, 24% no gaps in use; 25.5% analytic sample) and scoliosis surgery that was recommended (22% DMD, 26% high-medium DMD, 17.9% no gaps in use; 20% analytic sample) or completed (18% DMD, 21% high-medium DMD, 14% no gaps in use; 15% analytic sample) were similar (no gaps in use) or higher (DMD subgroups) in the subsamples than those observed for the analytic sample. Corticosteroid use was documented for approximately 60% of the DMD, 62% for the high-medium DMD, and 51% for the no gap in use subsamples compared to 55% for the analytic sample. Higher percentages for ambulation ceased were observed for the phenotype subsamples (53% DMD, 61% high-medium DMD), but were similar for the no gap in use subsample (44%) compared to the 47% analytic sample. Finally, results for the K-M and extended Cox regression models were in the same direction as those reported for the analytic sample (Supplemental eFigures 1-5).

## DISCUSSION

Our study showed that one-quarter of individuals had scoliosis with a Cobb angle measuring at least 20°, which is the threshold at which current care guidelines recommend surgical consultation and consideration of surgical intervention.[25] Non-ambulatory individuals were at higher hazard of surpassing pre-determined curvature thresholds than those still ambulating, as has been seen in previous series.[30, 31] Individuals who did not receive corticosteroids had a higher hazard of developing scoliosis, which increased progressively with greater degrees of spinal curvature. Further, individuals not receiving corticosteroids were more than twice as likely as those receiving corticosteroids to undergo spinal surgery for scoliosis.

The reduced hazard of scoliosis development associated with corticosteroid use observed is consistent with previous analyses. A long-term, retrospective study demonstrated that corticosteroid use was associated not only with a delay in the progression of scoliosis, but also with a reduced occurrence of scoliosis and scoliosis surgery.[32] This effect was suggested to be associated, in part, to prolongation of ambulation status beyond a critical point in skeletal maturation, as this has been shown to reduce the risk of development and severity of scoliosis.[26] Analysis of data from administrative records showed that a decline in scoliosis surgery followed the widespread adoption of corticosteroids;[33] however, not all studies have shown this benefit. The largest cohort reported to date consisted of a single-center, clinic referral population comprised of 174 patients, 55 of whom had scoliosis surgery.[34] The study reported an average age at time of scoliosis surgery of 14.2 years and mean preoperative Cobb angle of 49°, which is consistent with our findings (surgery at 14.4 years, mean pre-operative curve of 43°). Another study did not report a significant

effect of any corticosteroid use on Cobb angle progression, which was in line with our findings.[26] However, modeling corticosteroid use as a time-varying covariate showed reductions in hazard of scoliosis and scoliosis surgery in our study suggesting the benefits of corticosteroids may be underestimated by lifetime classifications due to diminution of benefits after stopping treatment with corticosteroids. Further supporting our interpretation are the greater similarities we observed for time to surpassing curvature thresholds between those who stopped corticosteroids before or at the time of LoA and those who never used compared to those who continued corticosteroids after LoA. Our study did not examine scoliosis progression by corticosteroid type, dosage, nor regimen. Additionally, because we collected corticosteroid treatment from medical records, we were not able to account for compliance. Variability in these factors may contribute to differences in findings across studies.

Prior analyses of the effect of corticosteroid use on the development of scoliosis in DMD consisted primarily of single-center studies with smaller groups of patients.[11, 14, 15, 17, 26, 32, 34-37] Our results, like those of smaller studies reported previously, demonstrated an association of corticosteroid use with reduced hazard of developing significant scoliosis and thus fewer individuals undergoing scoliosis surgery. We also demonstrated that continued corticosteroids after LoA was associated with lower hazard of exceeding curvatures of at least 10° when compared with those who discontinued corticosteroids after LoA. Nonetheless, long-term corticosteroid use is associated with numerous side effects, including weight gain, hirsutism, cushingoid appearance, short stature, delayed puberty, long bone and vertebral fractures, acne, cataracts, and behavioral changes. Recommendations made in the most recently published care guidelines for individuals with DMD emphasize the need for monitoring for adverse effects of corticosteroids.[1, 18, 25] Weighing these risks and benefits of corticosteroids to find the appropriate clinical balance for individual care is a determination that must be made with input from clinicians, caretakers, and the patients themselves.

It is of clinical importance to understand the predictors and variables that contribute to the development and progression of scoliosis. Understanding these factors and the therapies that slow the progression of scoliosis and reduce the need for surgical intervention, are an important healthcare contribution. When scoliosis develops, the currently recommended intervention is for posterior spinal fusion in selected patients when the Cobb angle is >20-30 degrees.[25] Current recommendations also recognize corticosteroid use may modify progression, but additional data are needed to confirm. Expected benefits of scoliosis surgery include comfort and sitting tolerance, cosmesis, ease of nursing care, and overall quality of life.[38] Studies of the effect of scoliosis surgery on mortality have been inconclusive, with some investigations demonstrating a positive effect on survival and others demonstrating no effect.[21, 28, 39-43] It is also recognized that scoliosis surgery is associated with potential risks including post-operative ventilator-associated pneumonia, wound dehiscence or infection, hemorrhage, loosening of surgical fixation devices, pseudarthrosis, deteriorated respiratory function, and increased difficulty with hand-to-head motions, and is not undertaken lightly.[38] Reducing the need for scoliosis surgery would thereby avoid these potential surgical risks.

A potential limitation of our study is the geographical regions represented in MD STAR*net*. Different regional and individual practice styles might affect approaches used to monitor and treat scoliosis in muscular dystrophy. Another limitation of our study is the retrospective study design, requiring a heavy reliance on available clinical and vital records for data collection. It is possible that some radiographs were performed outside of our surveillance sources and were missed. However, the percentage of the sample with available radiographs was consistent with what would be expected given the average age of the sample and percentage still ambulating. Further, missed radiographs would bias the results towards non-significance if curvatures that exceeded our thresholds were missed. Although the retrospective design does have the benefit of immediate case characterization, standardization of monitoring for scoliosis onset and opportunities for treatment was not possible. Specifically, we were unable to consistently identify those individuals for whom radiographs were taken in a seated position; dates of recommended radiographs or surgical correction were not collected; and metrics for standard orthopedic care could not be established. The interpretation of radiographs presented here represents clinical practice, and it is not possible to re-interpret them. Finally, the intervals between radiographs were not standardized, which introduces imprecision in identifying the point in which a threshold was surpassed.

Analysis of a large, population-based sample of individuals with childhood onset dystrophinopathy from selected geographical regions of the United States shows that loss of ambulation precedes clinically significant scoliosis (defined as a Cobb angle of >20 degrees) by approximately 4 years. Corticosteroids have been the standard of care in the management of DMD for over a decade, with growing evidence of their effectiveness following the first report by Drachman et al. over 40 years ago.[44, 45] We provide further evidence that corticosteroid use is associated with reduced probability of developing progressive scoliosis and reduced likelihood of requiring surgery to correct scoliosis. Our data also suggest that continued corticosteroid use after LoA may reduce the frequency of spinal fusion surgeries by lowering risk of surpassing the recommended threshold for surgery. Understanding the predictors and variables associated with scoliosis development in DMD is an important contribution to the care of individuals with dystrophinopathies.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations:

| | |
|---|---|
| **LoA** | loss of independent ambulation |
| **MD STAR*net*** | Muscular Dystrophy Surveillance, Tracking, and Research Network |
| **SD** | standard deviation |
| **aHR** | adjusted hazards ratio |
| **DMD** | Duchenne muscular dystrophy |
| **BMD** | Becker muscular dystrophy |
| **K-M** | Kaplan-Meier curve estimation |
| **M** | mean |
| **Md** | median |
| **min** | minimum |
| **max** | maximum |
| **CI** | confidence interval |

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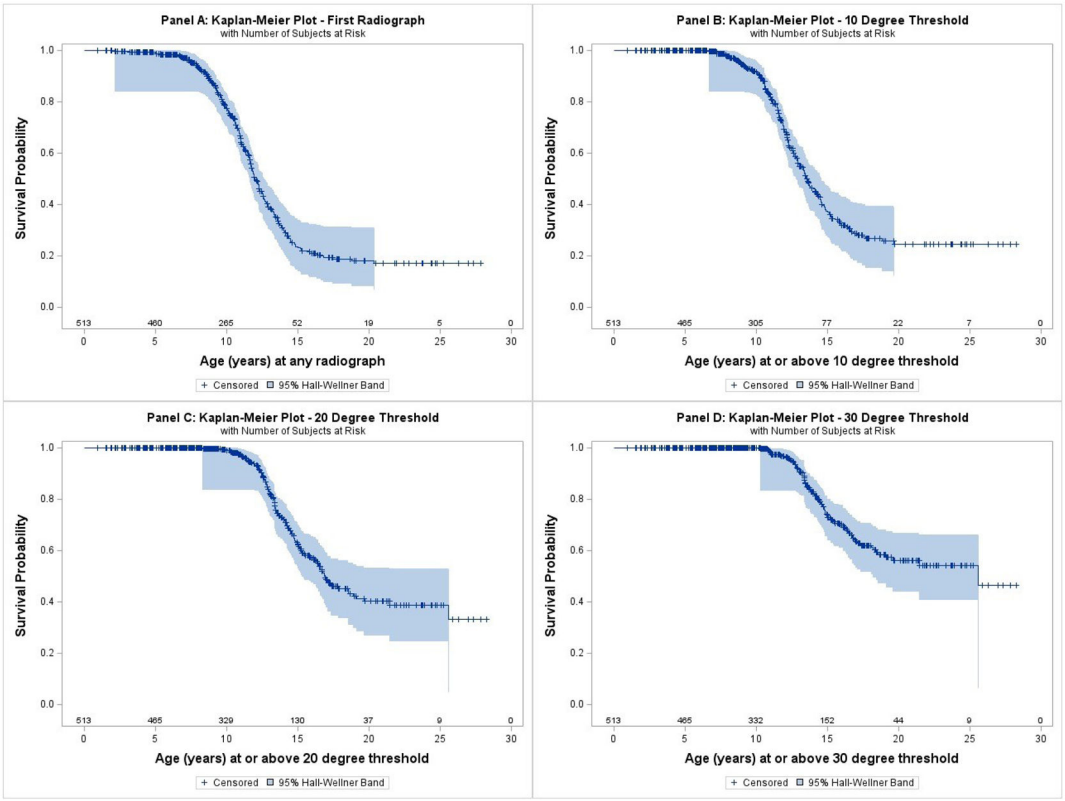
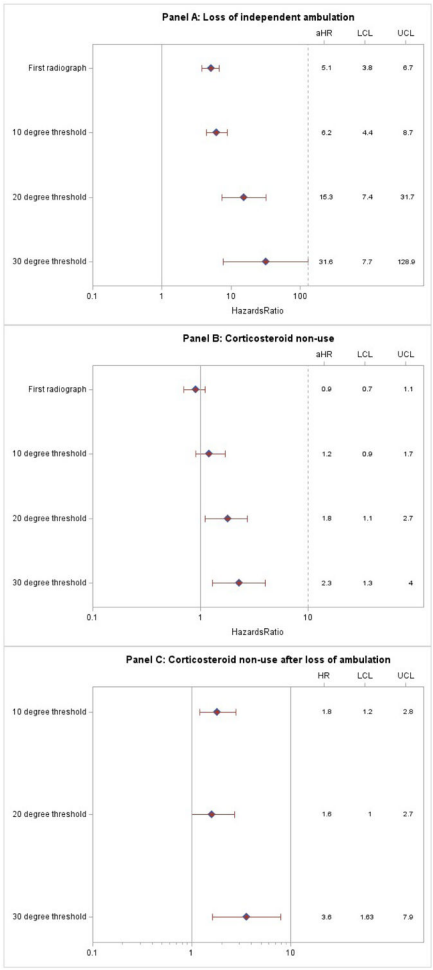


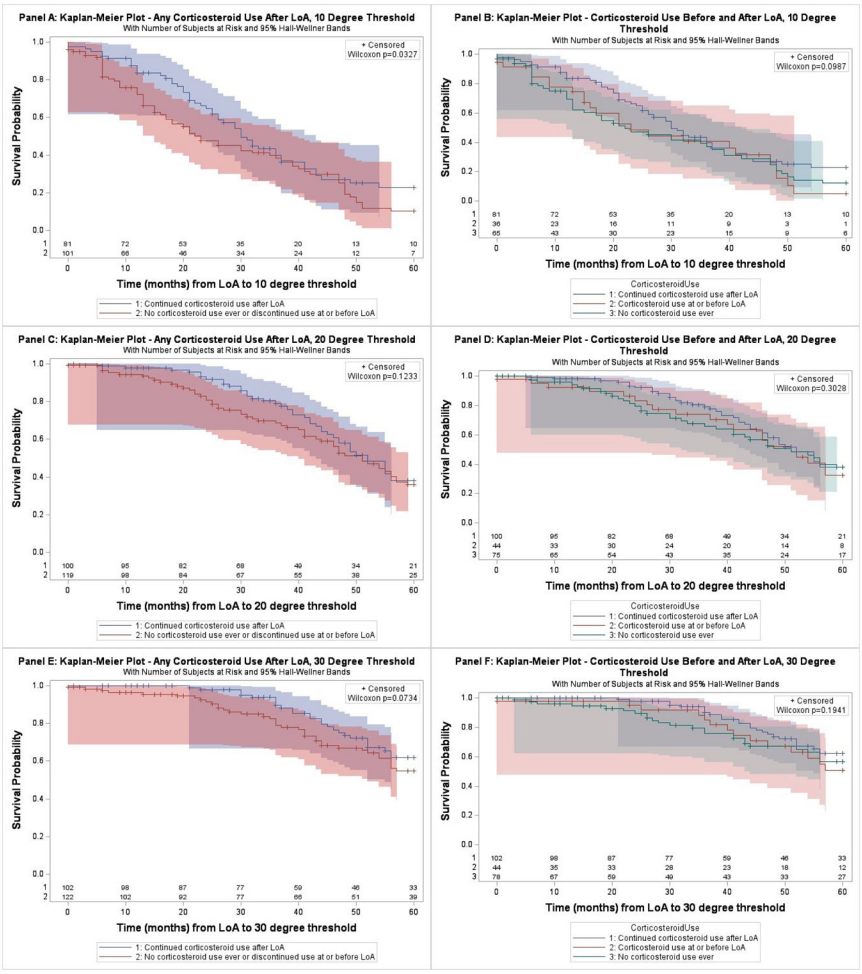

**I.**

Kaplan-Meier curve estimations for time (age in years) to first radiograph (a) and curvature thresholds (b-d) among eligible individuals (n=513).




**II.**

Adjusted hazards ratios and 95% confidence intervals for time (age in years) to first radiograph and curvature thresholds by time-varying ambulation status (Panel A) and time-varying corticosteroid status (Panel B), and for time (months) from LoA to curvature thresholds among those with LoA by time-varying corticosteroid status after LoA. (Extended Cox regression model with time-varying ambulation status [1=LoA; 0=independently walking] adjusting for time-varying corticosteroid status [1=non-use; 0=use], and MD STAR*net* site as a fixed covariate, n=513). Note. Individuals with unknown ambulation status excluded (n=29). aHR=adjusted hazard ratio, LCL=lower confidence limit, UCL=upper confidence limit. LoA=loss of ambulation.




**III.**

Kaplan-Meier curve estimation for time (months) from LoA to curvature thresholds among those with LoA by corticosteroid status after LoA. LoA=loss of independent ambulation. Notes. Individuals with unknown ambulation status (n=29) and those who surpassed thresholds prior to or at the time of LoA were excluded (10° threshold, n=51; 20° threshold, n=8; 30° threshold, n=3). Follow-up limited to 5-year period post-LoA. Corticosteroid use after LoA (a, c, e); Corticosteroid use before and after LoA (b, d, f).

**Table 1.**

Sample characteristics for eligible individuals with a dystrophinopathy (n=513).

| Variables | n | % | *M* | *SD* | *Md* | *Min* | *Max* |
|---|---|---|---|---|---|---|---|
| Age at first neuromuscular visit (years) | 513 | 100.0 | 5.4 | 3.1 | 5.2 | 0.0 | 23.6 |
| Age at last neuromuscular visit (years) | 513 | 100.0 | 13.1 | 6.1 | 12.8 | 0.9 | 28.3 |
| Loss of independent ambulation (years)[1] | 227 | 46.9 | 11.3 | 2.9 | 10.6 | 6.1 | 24.3 |
| Length of visits (years) | 513 | 100.0 | 7.7 | 5.5 | 6.8 | 0.0 | 24.8 |

Dash means not calculated.

*M*=mean (years). *SD*=standard deviation. *Md*=median. *Min*=minimum value. *Max*=maximum value.

[1]Cases with unknown mobility status or timing of loss of independent ambulation (n=29).

**Table 2.**

Lumbar radiograph and surgery outcomes among eligible individuals with a dystrophinopathy (n=513)

| Variables | n | % | *M* | *SD* | *Md* | *Min* | *Max* |
|---|---|---|---|---|---|---|---|
| Any radiograph record | 252 | 49.1 | 11.0 | 2.6 | 11.0 | 2.1 | 20.4 |
| Maximum curve value (degrees) | 252 | 48.3 | 25.0 | 21.5 | 20.0 | 0.0 | 100.0 |
| Age at maximum curve (years) | 252 | 48.3 | 13.8 | 3.3 | 13.5 | 2.7 | 25.6 |
| Scoliosis Threshold | | | | | | | |
| ≥0 degrees (years) | 252 | 49.1 | 11.0 | 2.6 | 11.0 | 2.1 | 20.4 |
| ≥10 degrees (years) | 198 | 38.6 | 12.1 | 2.4 | 12.0 | 6.7 | 19.7 |
| ≥20 degrees (years) | 131 | 25.5 | 14.0 | 2.4 | 13.4 | 8.3 | 25.6 |
| ≥30 degrees (years) | 92 | 17.9 | 14.4 | 2.4 | 14.0 | 10.3 | 25.6 |
| Maximum curve value at surgery recommended or done (degrees) | 98 | 19.1 | 42.8 | 18.1 | 40.0 | 15.0 | 100.0 |
| Scoliosis surgery age at recommended or done (years) | 98 | 19.1 | 14.5 | 2.0 | 14.3 | 10.3 | 20.1 |
| Scoliosis surgery age done (years) | 78 | 15.2 | 14.4 | 1.8 | 14.2 | 10.4 | 18.4 |
| Years between dates of last radiograph and surgery recommended/done | 97 | 17.7 | 0.7 | 1.0 | 0.4 | 0.1 | 5.5 |
| Years between dates of last radiograph and surgery done | 77 | 15.0 | 0.7 | 0.9 | 0.4 | 0.1 | 5.6 |

*M*=mean. *SD*=standard deviation. *Md*=median. *Min*=minimum value. *Max*=maximum value.

**Table 3.**

Corticosteroid use among eligible individuals (n=513).[1]

| Variable | n | % | *M* | *SD* | *Median* | *Min* | *Max* |
|---|---|---|---|---|---|---|---|
| Any Steroid Use | | | | | | | |
| Earliest age of use (years) | 280 | 54.6 | 7.1 | 2.2 | 7.0 | 2.4 | 15.4 |
| Latest age of use (years) | 280 | 54.6 | 12.0 | 4.8 | 11.0 | 3.5 | 27.1 |
| Duration of use (years) | 280 | 54.6 | 5.0 | 4.4 | 3.8 | 0.1 | 19.8 |
| Gap in corticosteroid use[2] | | | | | | | |
| First gap duration (years) | 39 | 13.9 | 1.4 | 1.7 | 0.7 | 0.1 | 6.5 |
| Second gap duration (years) | 5 | 1.8 | 1.2 | 0.7 | 1.1 | 0.5 | 2.2 |
| Corticosteroid use after LOA[2] | 227 | 46.9 | - | - | - | - | - |
| None | 79 | 45.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Use before LOA (years) | 45 | 19.8 | −1.3 | 1.30 | −1.0 | −6.6 | −0.01 |
| Use after LOA (years) | 103 | 34.8 | 3.5 | 3.5 | 2.1 | 0.02 | 15.7 |

Dash means not calculated. LOA=loss of ambulation.

*M*=mean. *SD*=standard deviation. *Md*=median. *Min*=minimum value. *Max*=maximum value.

[1]Note. 11 individuals had the same start/stop date and were coded as not ever using corticosteroids.

[2]Gap of at least one month.

[3]Individuals with unknown mobility status or timing of LOA (n=29).