A composite prognostic score for time to loss of walking ability in Duchenne muscular dystrophy (DMD)

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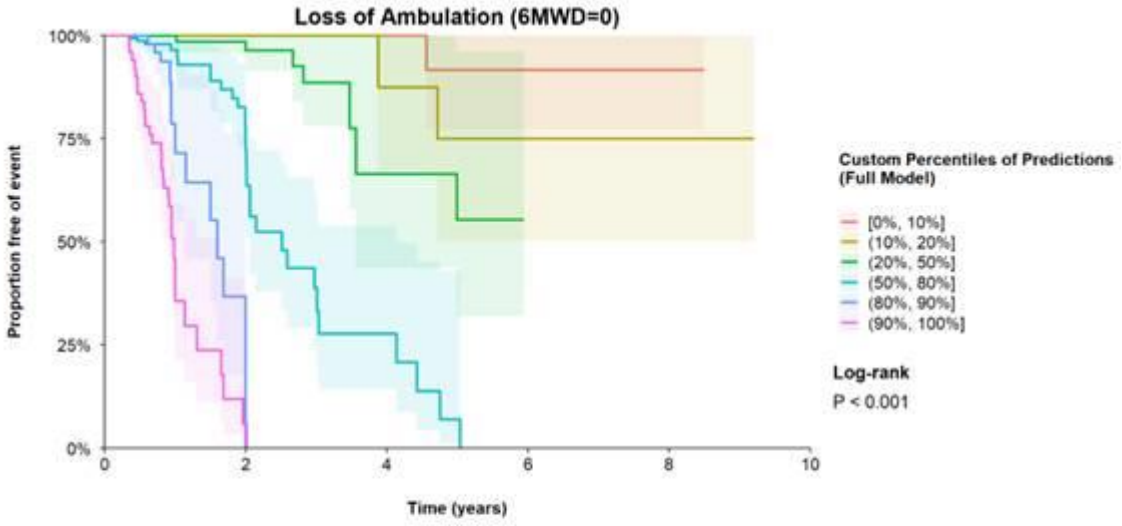
Prediction of loss of ambulation (LoA), a critical milestone in DMD, is important for clinical practice and clinical trials. We assessed the extent to which combinations of patient characteristics help predict time to LoA among 500 ambulatory boys (mean age=9.2) with DMD drawn from two natural history databases (UZ Leuven and PRO-DMD-01 data provided by CureDuchenne) and three trial placebo arms (phase 2b and phase 3 trials of ataluren, phase 3 trial of tadalafil). Time to LoA, approximated as inability to complete the six-minute walk test, was analyzed using Cox proportional hazards models. Eighty-five boys (17%) experienced LoA over 915 patient-years. A model including three timed function tests (rise from supine, 4-stair climb and 10-meter walk/run), 6MWD, age, height, weight, steroid use and data source gave better predictions of time to LoA than a model based only on age > 7 years, walk distance < 350m and data source (pseudo-R^2: 37% vs. 21%). Better TFT performance, deflazacort use (compared to prednisone), greater weight, lower height and lower BMI were significant predictors of longer time to LoA. Data source differences in time to LoA were present when adjusting only for age and baseline 6MWD ($p<0.05$), but were not significant after adjustment for the additional factors ($p=0.18$). Ad-hoc stratification of boys based on risk score percentiles produced good separation, with the highest risk groups having 1-year LoA risks of 64%, 28% and 3% and 2-year risks of 94%, 63% and 28%, corresponding to median times to LoA of approximately 1, 1.6 and 2.5 years, respectively. The median was not reached for lower-risk groups. A composite prognostic score, incorporating multiple measures of ambulatory function, can substantially improve prediction of time to LoA. Once validated, such a score can inform clinical practice and trial designs, and enable adjusted comparisons between patients receiving newer therapies (e.g., in extension trials) and natural history controls.

Characters (incl. spaces): 1,997/2,000



[0%, 10%]	50	28	13	6	4	0
(10%, 20%]	50	32	7	1	1	0
(20%, 50%]	150	39	6	0	0	0
(50%, 80%]	150	25	4	0	0	0
(80%, 90%]	50	0	0	0	0	0
(90%, 100%]	50	1	0	0	0	0

Patients at risk