

Predicting the 95th Centile Stride Velocity (SV95C) at 6-, 12-, 18-, and 24-Months in Steroid-treated boys with Duchenne muscular dystrophy.

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BACKGROUND

- The SV95C is a wearable-derived assessment of ambulation, for use as a primary or secondary outcome in DMD clinical trials.
- Predicting the evolution of a patient in absence of intervention may allow the evaluation of treatment efficacy of at the single patient level.
- Best current models explain 41% of the *change* in NSAA¹.
- The ActiLiège Next (ALN; NCT05982119) and Genethon Natural History (NCT03882827; GNT-014-MDYF) studies are multi-centre observational studies collecting longitudinal clinical and wearables (SYDE device) data.
- We developed models in the ALN cohort that use baseline variables to predict the SV95C at 6, 12, 18, and 24-months follow-up. Model validation was performed in the Genethon cohort

METHOD

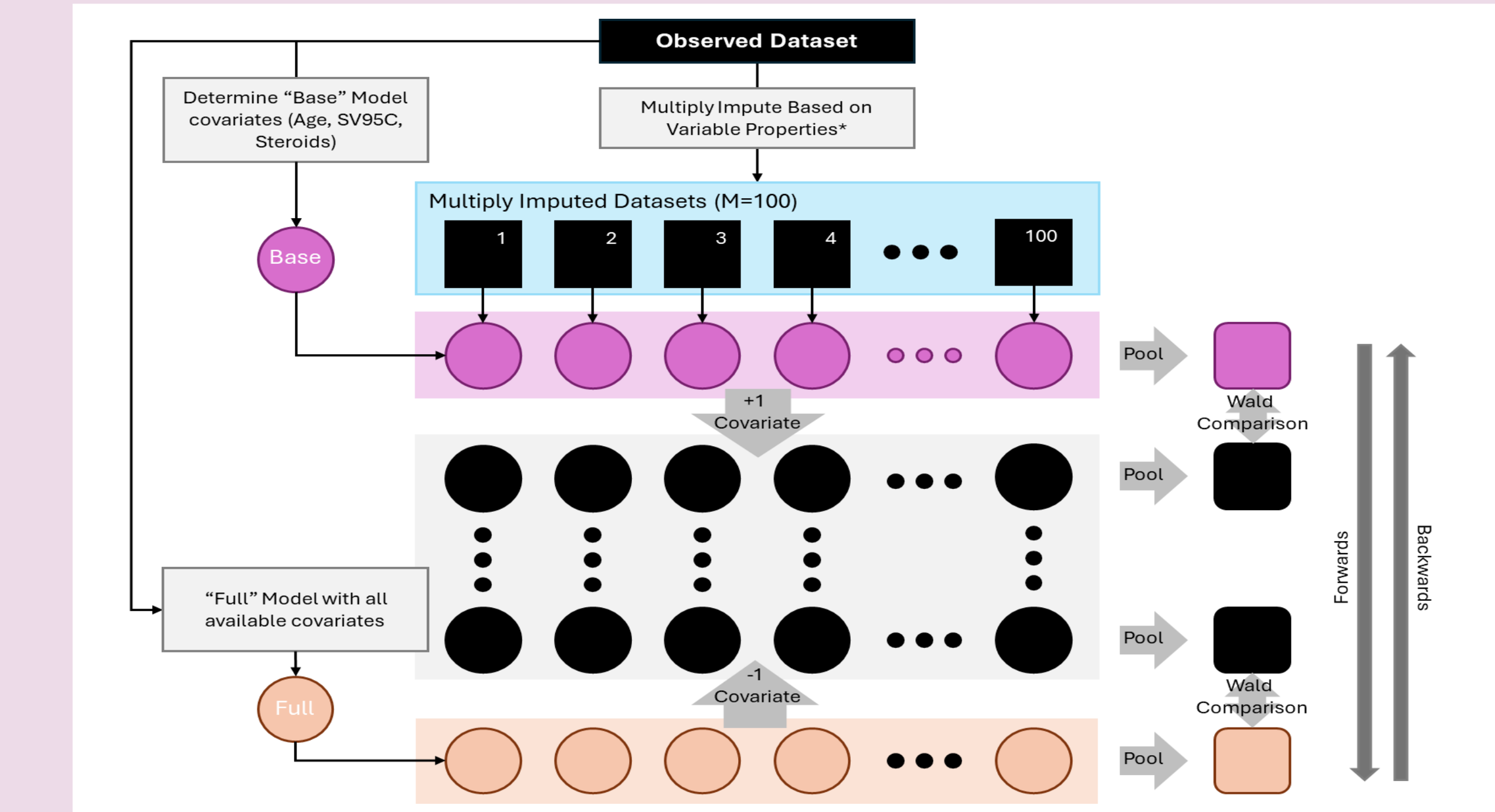
ALN Inclusion Criteria:

- On glucocorticoids
- 4-12 years
- Recording periods with >50 hours of recording

Pairs of visits at 6, 12, 18 and 24 month intervals were considered irrespectively of the initial protocol timeline. Missing data, primarily due to differences in the visiting process for in-person and wearables assessments, were addressed using multiple imputation.

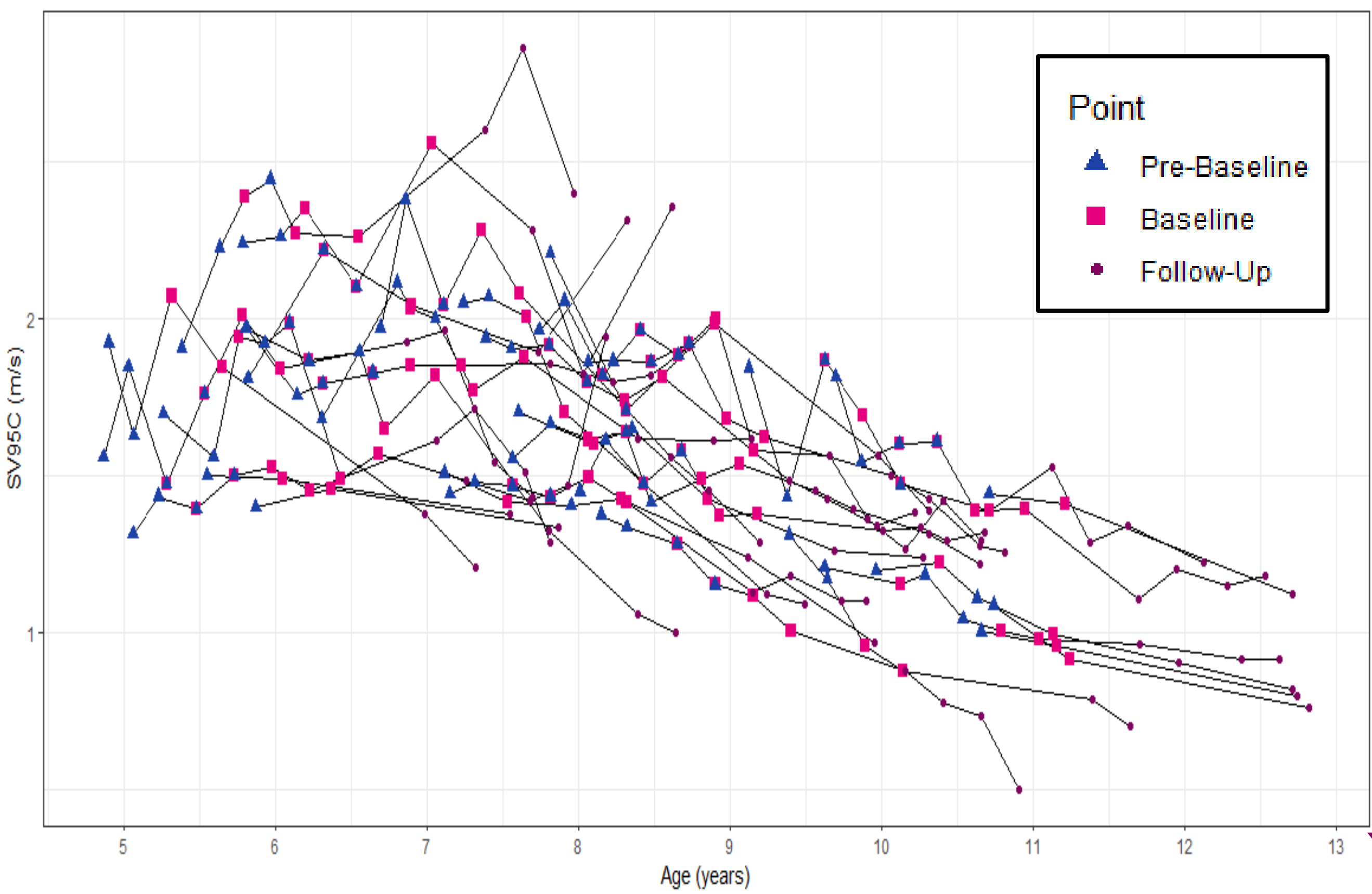
Model Fitting

Four separate generalised (Gamma) linear models for SV95C at 6, 12, 18 and 24 months were developed. From the list of candidate variables, variable selection was performed using both forward and backwards nested Wald model selection as below. The selected “best” model specification was checked using the specification with respect to the random effects model.



INCLUDING PRE-BASELINE INFORMATION

For each baseline and follow-up pair across the four models, any visits 6 months prior to the baseline were considered as “pre-baseline” visits. We considered this modelling to understand if a natural history period could improve trajectory prediction in a clinical trial setting. Including an additional baseline datapoint 6 months prior led to a significantly improved prediction in the 6 (+0.8% variance explained), 12-month (+0.6% variance explained) and 18 month (1.8%) models, but did not improve the model performance at 24 months.



CANDIDATE VARIABLES

The following baseline candidate variables were considered for the 6, 12, 18 and 24 months prediction models:

Wearable-derived:

- Stride Velocity (95th and 50th Centile)
- Number of Strides per Hour
- Stride Length (95th and 50th Centile)
- Walking Duration

Physiotherapist Assessed:

- NSAA Total
- NSAA Items
- 6MWT
- 4SC
- 10MWR Time
- RFF Velocity

Demographic and Growth:

- Age
- Steroid Usage
- Weight ZScore
- Height ZScore
- BMI ZScore

COHORT

The participants in each cohort are described below at their first visit. The Genethon participants are overall slightly younger at baseline than the ALN cohort which reflects the differences in age-based inclusion criteria for the two studies. The Genethon participants are also significantly stronger across all outcomes except the NSAA.

The number of assessments and participants varies by follow-up model. In the ALN study there were 348, 229, 146 and 85 pairs of data across 86, 65, 45 and 34 participants in the 6-, 12-, 18-, and 24-month follow-up cohorts. In the Genethon study there were 204, 141, 97 and 69 pairs of data for 65, 47, 37 and 30 participants in the 6-, 12-, 18-, and 24-month follow-up cohorts.

Mean (SD)	Cohort		Wilcoxon Rank Sum Comparison
	ActiLiege Next	Genethon NHS	
N	86	116	
Age (years)	7.4 (2.2)	6.8 (1.34)	0.169
NSAA	24.2 (5.5)	25.2 (4.4)	0.256
Rise From Supine Time (s)	5.7 (4.2)	4.1 (1.5)	0.005
SV95C (m/s)	1.6 (0.4)	1.9 (0.4)	<0.001
Number of Strides per Hour	202 (87)	251 (112)	0.003
SV50C (m/s)	0.8 (0.1)	0.8 (0.1)	<0.001
SL50C (m)	0.8 (0.1)	0.8 (0.1)	0.057
SL95C (m)	1.1 (0.1)	1.2 (0.2)	<0.001

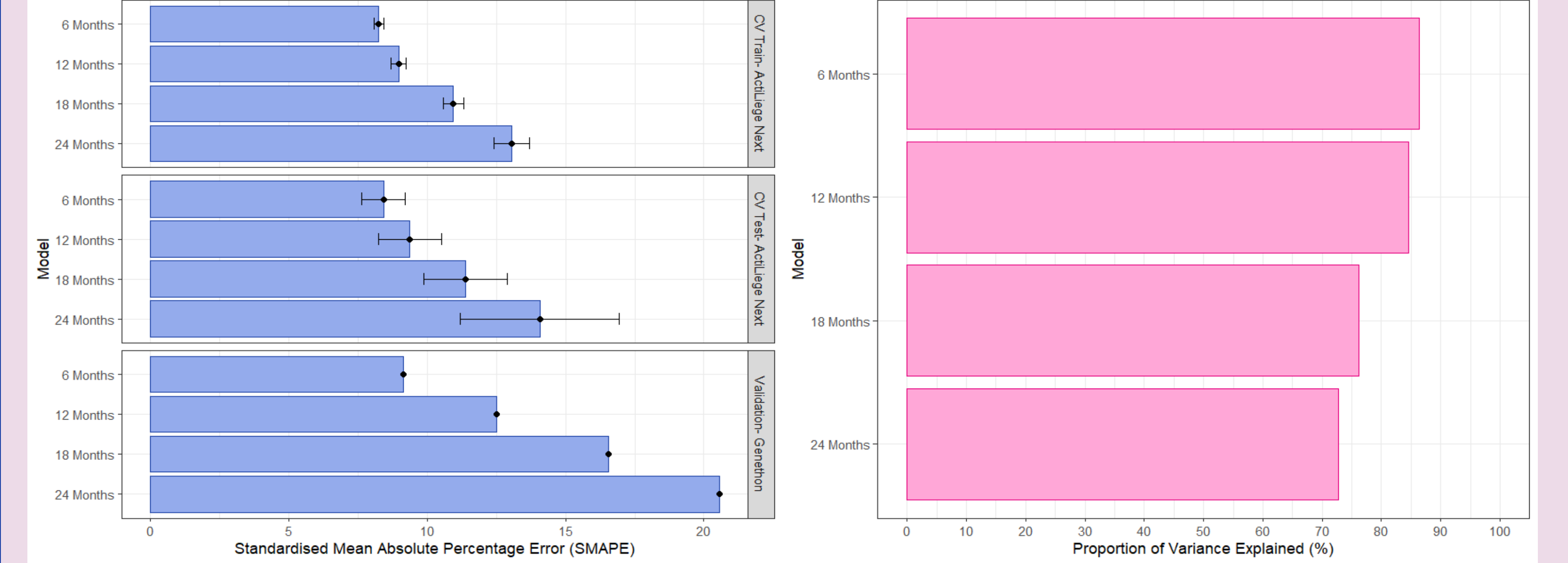
VARIABLES SELECTED

Of the candidate variables, the following were selected during the Wald comparison process as the variables that lead to the best models for SV95C at 6, 12, 18 and 24 months:

- Baseline age, using a natural spline (6-, 12-, 18- and 24-month models)
- Baseline SV95C (6-, 12-, 18- and 24-month models)
- Baseline strides per hour (12-, 18- and 24-month models)
- Baseline SV50C (6-, and 12-month models)
- Baseline stride length (50th and 95th; 12-month model only).

MODEL PERFORMANCE

In the ALN cohort, 86.4%, 84.7%, 76.2% and 72.8% of the variation in the SV95C at 6, 12, 18, and 24-months are explained by the models respectively. In the ALN data, the 6- and 12-month models showed consistent performance across the training and testing datasets, with an average percentage error for predictions of the SV95C at 6- and 12-months follow-up of 9.1% and 12.5% respectively in the Genethon validation cohort.



CONCLUSION

Follow-up SV95C scores can be predicted accurately up to 24 months, using only wearable-derived outcomes, including in the validation cohort. Pre-baseline information marginally improves performance in the shorter-term models. Accurate predictive models can inform clinical trial designs, by providing counterfactual trajectories for treated patients.

References: 1 - Muntoni F, Signorovitch J, Goemans N, et al. Predicting trajectories of the north star ambulatory assessment total score in Duchenne muscular dystrophy. *PLoS One*. 2025;20(6):e0325736. DOI:10.1371/journal.pone.0325736

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