Longitudinal Stride-Level Evaluation of Ambulatory Function with Ankle Wearable Technology in Ambulant DMD Patients Below 4 Years Old

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BACKGROUND

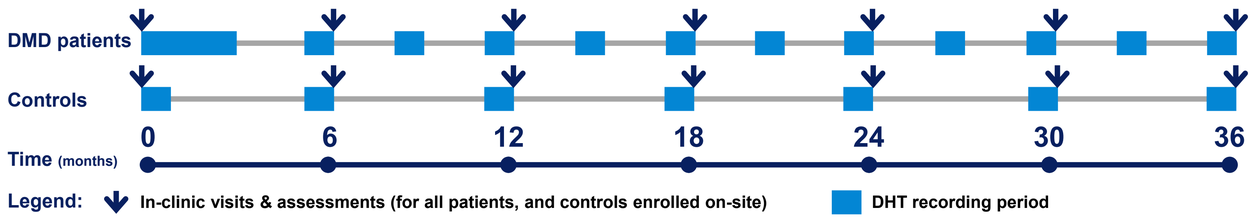
- **Assessment of ambulatory function in DMD below 4 years old (y/o) is currently challenging, yet crucial** to develop disease-modifying treatments
- **Stride velocity 95th centile (SV95C):** the 5% fastest strides measured during daily living with a valid and suitable wearable digital health technology (DHT), qualified as 1ary endpoint in 2023 by the European Medicines Agency in patients with DMD above 4 y/o[1]
- **Study objectives in this population:**
  To investigate feasibility, robustness and sensitivity of using SV95C to assess ambulation in DMD before the age of 4 y/o

METHODS

STUDY DESIGN

- ActiLiège-Next study (NCT05982119): multicenter natural history study, 3 sites enrolled subjects below 4 y/o (Belgium, Hungary and Slovenia)
- First subject enrolled in April 2023
- Most controls (N=23) were enrolled remotely

Figure 1. ActiLiege-Next study schedule of assessments.



WEARABLE DHT (Syde)

- Based on inertial technology
- Wearable sensors worn on both ankles
- Provides accurate stride-level ambulation data
- Daily recording in the real-world setting

Figure 2. Syde DHT.

ASSESSMENTS

- In-clinic assessments include North Star Ambulatory Assessment (NSAA; for patients only), 6-minute walking test (6MWT), 4-stair climbing test (4SC), Time to rise from floor (TRF)
- DHT-derived variables include SV95C and number of strides per hour (Nb strides/h)

RESULTS

DATA AVAILABILITY

- As of Dec. 4th 2024, 26 ambulant DMD patients, and 32 healthy subjects have been enrolled (Table 1). Patients were diagnosed incidentally or because of positive family history.

Table 1. Baseline characteristics of the subjects.

Median [min; max]	DMD (N=26)*		Controls (N=32)	
Age (months)	35.8 [16.0; 47.4]	N=26	31.0 [12.8; 47.7]	N=32
NSAA	17.0 [6.0; 27.0]	N=17	Not applicable	
6MWT (m)	305 [50; 384]	N=11	305 [50; 384]	N=5†
4SC (s)	5.56 [3.07; 13.68]	N=14	3.56 [3.07; 13.68]	N=7†
TRF (s)	5.30 [3.97; 10.22]	N=14	2.93 [1.66; 3.78]	N=7†
SV95C (m/s)	1.31 [0.67; 1.76]	N=24	1.61 [0.60; 2.69]	N=32
Nb strides/h	212.8 [1.0; 352.4]	N=26	294.6 [25.3; 652.9]	N=32

* 3 patients were receiving steroids before inclusion, 2 initiated upon enrolment, and 3 initiated during follow-up.
† As most controls were enrolled remotely, only a few controls performed these in-clinic tests.

Table 2. Adherence with DHT wear.

Visit	Subjects	< 50 h of data	≥ 50 h of data
Baseline (first month)	DMD (N=26)	7.5%	92.5%
	Controls (N=32)	0%	100%
Month 6	DMD (N=24)	0%	100%
	Controls (N=17)	0%	100%
Month 12	DMD (N=8)	0%	100%
	Controls (N=7)	0%	100%

- Only a subset of patients (N=11 to 17/26) were able to understand and/or reasonably comply with the instructions to perform in-clinic assessments (Table 1)
- Most subjects are adherent to wearing the DHT (N=24/26; Table 2), allowing to derive digital variables for most patients

RESULTS (continued)

RELIABILITY

Table 3. Intra-class correlation coefficient between 2 consecutive 2-week recordings.

Variable	Subjects	ICC2k† Baseline	ICC2k† Month 6	ICC2k† Month 12
SV95C	DMD 1-4 yo	0.99 (N=22)	0.97 (N=23)	0.98 (N=8)
	Controls 1-4yo	0.99 (N=30)	0.94 (N=15)	NA‡
	DMD 5-14 yo	0.96 (N=64)	0.99 (N=41)	0.97 (N=33)
Nb strides/h	DMD 1-4 yo	0.84 (N=24)	0.80 (N=23)	0.75 (N=8)
	Controls 1-4yo	0.85 (N=32)	0.56 (N=17)	NA‡
	DMD 5-14 yo	0.87 (N=71)	0.88 (N=62)	0.87 (N=48)

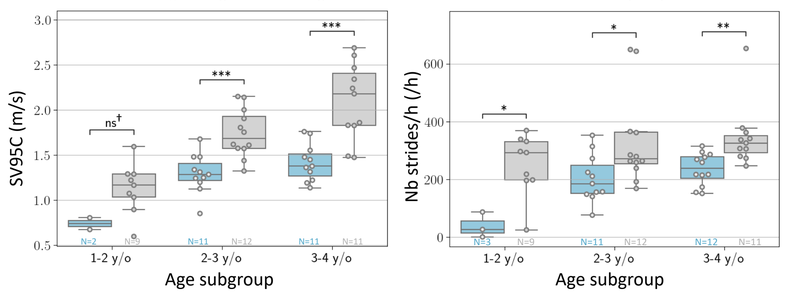
† Intra-class correlation coefficient mean-rating (multiple raters k = 2), absolute-agreement, 2-way random-effects model.
‡ Not applicable: not enough subjects to calculate an ICC for the Month 12 visit.

- SV95C reliability was excellent (ICC>0.9) for patients with DMD and controls below 4 years old (Table 3)
- Nb strides/h reliability was fair for patients with DMD (ICC ≥ 0.75), but poor for controls (ICC ≥ 0.56)

EXTERNAL VALIDITY

Figure 3. Known-group validity analysis at baseline.

Mann Whitney U test: * p<0.05, ** p<0.01, ***p<0.001, ns=not significant.
†Difference in the 1-2 y/o subgroup is not significant due to the low number of patients (N=2).

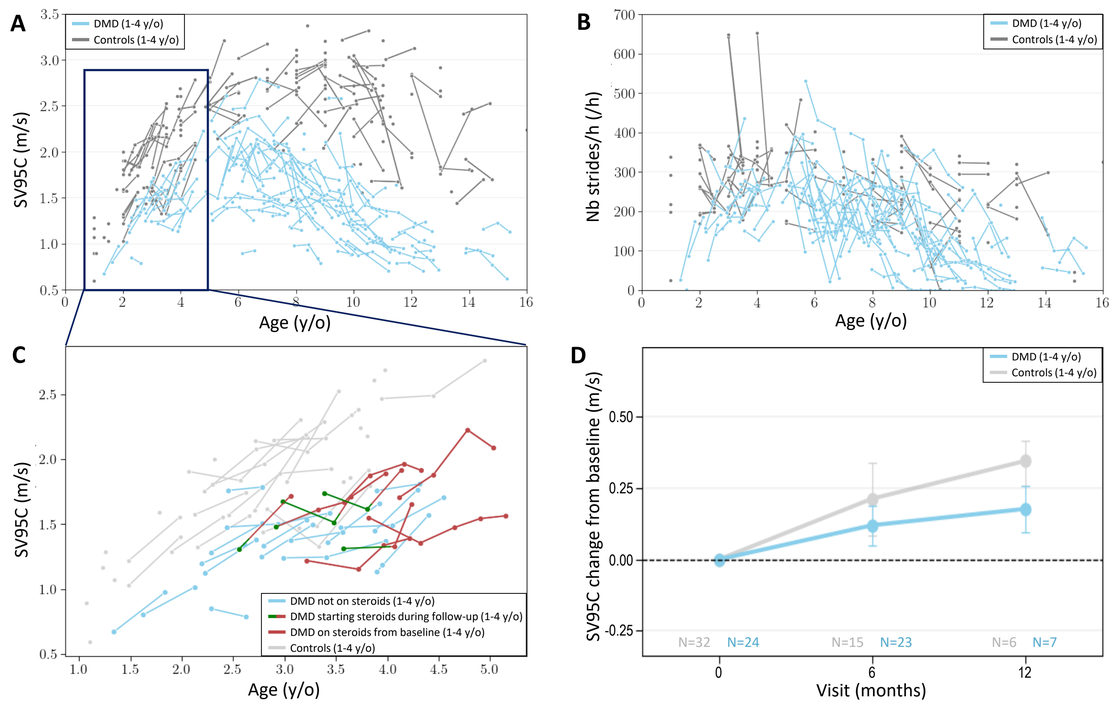


- Baseline SV95C clearly separated patients from controls (Figure 3)
- Nb strides/h showed greater overlap between the two populations (Figure 3)

LONGITUDINAL EVOLUTION (ongoing)

Figure 4. Longitudinal evolution of digital variables in patients and controls.

A and B: Longitudinal evolution of SV95C (A) and Nb strides/h (B) in all controls and patients with DMD enrolled in the ActiLiege-Next study (1-14y/o). **C:** Longitudinal evolution in young controls and patients with DMD (1-4 y/o at inclusion). Steroid treatment status is color-coded: light blue for patients who are not on steroids at any visit, red for patients on steroids before inclusion, and green/red for patients who initiated steroids at some point during the follow-up (change of color corresponding to the steroid start date). **D:** SV95C change from baseline (mean and 95% confidence interval) in young controls and patients with DMD (1-4 y/o at inclusion; all patients with available data, treated or not with steroids).



- SV95C is improving after initiation of steroid treatment, as expected (N=5, green/red lines on Figure 4C)
- SV95C data of the first young subjects who reached 1 year of follow-up suggest differences already at this young age, with a potentially larger progression in controls than in patients (Figure 4D)

CONCLUSIONS

- **Good adherence** with sensor wear, allowing to derive digital variables in an age group where other assessments are challenging to obtain
- **SV95C** exhibited **better metric properties** than Nb strides/h
- SV95C **reliability and ability to discriminate patients from age-matched controls** were good and comparable with data obtained in older patients
- 1-year follow-up data for the full cohort needed to **confirm whether progression rates are different between patients and controls, and effect of steroid treatment**

REFERENCES

1. European Medicines Agency CHMP, Qualification Opinion for Stride Velocity 95th centile as a primary endpoint in studies in ambulatory Duchenne Muscular Dystrophy studies. 28th July 2023. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne_en.pdf

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