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SV95C: a real-world measure of mobility for neuromuscular diseases

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Value of measuring gait in neuromuscular diseases such as DMD

Gait and functional ambulation are important markers of disease in NMDs

Functional ambulation provides an assessment of how gait function and speed impact an individual's mobility during daily living.[1]

Individuals with NMDs frequently present with gait disorders and reduced ambulatory capacity[1,2]

Gait disorders can affect[1]

- Walking ability
- Balance and steadiness
- Risk of trips and falls
- Energy levels during walking
- Participation in social activities

Symptoms that affect mobility and ambulation are reported as among the most bothersome in NMDs[1,3]

In a survey of 1109 individuals with NMDs, the most bothersome symptoms cited were:[3]

- Muscle weakness (78%)
- Muscle fatigue (77%)
- Impaired physical function/activity (74%)

Gait and functional ambulation are relevant measures for assessing disease progression and treatment efficacy in individuals with NMDs[1]

NMD, neuromuscular disease.

1. Kennedy RA, et al. *J Foot Ankle Res.* 2020;13:10; 2. Hadouiri N, *Eur J Phys Rehabil Med.* 2024;60:257-269; 3. Mancuso M, et al. *Orphanet J Rare Dis.* 2025;20:221.

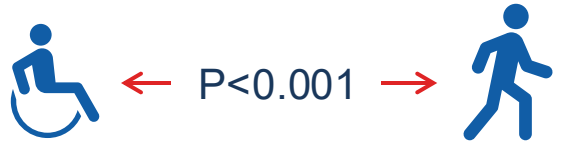
Patients with DMD experience progressive decline in mobility and ambulation

Individuals with DMD exhibit differences in gait compared to unaffected individuals, including reduced walking velocity and step length[1]

Gait quality decreases over time in individuals with DMD, likely due to increasing muscle stiffness and weakness[1,2]

Rate of DMD disease progression is heterogeneous, but loss of ambulation typically occurs around the age of 10–14 years[3,4]

- Mobility restrictions associated with DMD have a **negative emotional impact** for patients and caregivers[5]
- Non-ambulatory patients with DMD have a **significantly poorer HRQoL** than those who are still ambulatory[6]



Mean utility value[6]	-0.05 (SD 0.24)	vs	0.51 (SD 0.28)

- Caregivers of non-ambulant vs ambulant individuals with DMD experience a **significantly greater impact on daily activities** ($p<0.001$)[6]

Maintaining mobility and ambulation is important to both patients with DMD and their caregivers[5,6]

DMD, Duchenne muscular dystrophy; HRQoL, health-related quality of life.

1. Vandekerckhove I, et al. *Front Hum Neurosci*. 2022;16:861136; 2. Rinaldi M, et al. *Clin Biomech (Bristol)*. 2020;78:105101; 3. Zambon AA, et al. *Dev Med Child Neurol*. 2022;64(8):979–88; 4. Nascimento Osorio A, et al. *Neurologia (Engl Ed)*. 2019;34(7):469–81; 5. Brown V, et al. *J Patient Rep Outcomes*. 2023;7(1):129; 6. Andreozzi V, et al. *Health Qual Life Outcomes*. 2022;20(1):36.

Measures of DMD disease progression are needed for optimal patient care and conducting clinical trials

Patient care

Individuals with DMD have different disease trajectories, including ambulatory function[1]

Treatment and support should be tailored to DMD disease stage[2]

Accurate anticipation of prognosis helps in counseling patients and their caregivers[1]

Clinical trials

Reliable biomarkers of DMD disease progression are necessary for assessing risk/benefit of potential new treatments in clinical trials[3,4]

Challenges in identifying DMD biomarkers that can be used as trial endpoints include the heterogeneous nature of the disease and small number of patients[3]

Gait quality is a biomarker of disease severity in pediatric neuromuscular diseases such as DMD[5]

Ambulatory functional assessments in DMD[6–8]

- NSAA
- 6MWT
- SV95C
- Timed function tests:
  - 4SC
  - TTR
  - 10MRW
- Motor Function Measure Scale (MFMS)

Accurately monitoring DMD disease progression using standardized functional assessments is important for tailoring patient care and assessing potential new treatments[3,4]

4SC, 4 stair climb; 6MWT, 6-minute walk test; 10MRW, 10-meter run/walk; DMD, Duchenne muscular dystrophy; EMA, European Medicines Agency; NSAA, North Star Ambulatory Assessment; SV95C, stride velocity 95th centile; TTR, time to rise.

1. Zambon AA, et al. *Dev Med Child Neurol*. 2022;64(8):979–88; 2. Nascimento Osorio A, et al. *Neurologia (Engl Ed)*. 2019;34(7):469–81; 3. Benemei S, et al. *Acta Neurol Belg*. 2025;125(1):1–12; 4. Servais L, et al. *Nat Med*. 2023;29(10):2391–2; 5. Kennedy RA, et al. *J Foot Ankle Res*. 2020;13(1):10; 6. EMA Qualification Opinion. July 2023.Accessed May 1, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 7. EMA. Guideline on the clinical investigation of medicinal products for the treatment of Duchenne and Becker muscular dystrophy. 2016. Accessed May 1, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-medicinal-products-treatment-duchenne-and-becker-muscular-dystrophy_en.pdf; 8. Birnkrant DJ, et al. *Lancet Neurol*. 2018;17(3):251–67 (and appendix).

Strengths and weaknesses of functional assessments historically used in studies of ambulatory individuals with DMD (1 of 2)

	4 stair climb (4SC)	Time to rise (TTR)	10-meter run/walk (10MRW)
Description	• The time taken for an individual to climb four stairs[1]	• The time taken to stand from supine position[2]	• The time taken for an individual to run or walk 10 meters[1]
Prognostic values	• Cut-off for predicting loss of function (inability to complete test ≤45 second) over 1 year: >6.2 seconds (95% CI: 4.5–7.4)*[1]	• Cut-off for predicting functional decline: ≥5 seconds‡[2] • Cut-off for predicting loss of ambulation within 2 years: ≥10 seconds‡[2]	• Cut-off for predicting loss of function (inability to complete test ≤45 second) over 1 year: >7.6 seconds (95% CI: 7.6–9.2)*[1]
MCID (over 1 year)	• 0.035 tasks/second (velocity)[3]	• 0.023 rises/second (velocity)[3]	• 0.212 meters/second (velocity)[3]
Median age at loss of ability to complete assessment	• 13.2 years (SE; 95% CI: 0.4; 12.4–14.1)†[2]	• 11.6 years (SE; 95% CI: 0.3; 11.1–12.3)#[2]	• 12.2 years (95% CI: 11.5, 13.9)¶[4]
Advantages	• Reflect strength and function of lower limb proximal muscles[5] • Feasible to perform in clinic[5]	• Reflects core and proximal limb strength[1,2] • Good predictor of disease progression[2]	• Useful in natural history studies and clinical trials as it may be completed up to a greater age than TTR and 4SC (12 years vs 7–10 years)[1,6]
Disadvantages	• Performance subject to motivation or fatigue[7] • Susceptible to compensatory movement strategies[1]	• Performance subject to motivation or fatigue[7]	• Performance subject to motivation or fatigue[7]

*Longitudinal, multicenter study in 92 individuals with DMD aged 5–12.9 years over 1 year;[1] †Prospective, multicenter study in 440 individuals with DMD aged 2–28 years. Age at loss of ambulation based on 225 individuals with ≥1 year corticosteroid treatment;[2] ‡Longitudinal, multicenter study in 340 individuals with DMD aged 2–28 years;[8] #Prospective, multicenter study in 440 individuals with DMD aged 2–28 years. Age at loss of ambulation based on 207 individuals with ≥1 year corticosteroid treatment.[2] ¶Prospective, multicenter study in 826 individuals with DMD aged 5–16 years.[4]

CI, confidence interval; DMD, Duchenne muscular dystrophy; MCID, minimal clinically important difference; SE, standard error.

1. Arora H, et al. *Muscle Nerve.* 2018;58(5):631–38; 2. McDonald CM, et al. *Lancet.* 2018;391(10119):451–61; 3. Duong T, et al. *J Neuromuscul Dis.* 2021;8:939–48; 4. Stimpson G, et al. *J Neuromuscul Dis.* 2024;11(1):153–66; 5. Schorling DC, et al. *J Musculoskelet Neuronal Interact.* 2023;23:4–25; 6. Bushby K, Connor E. *Clin Investig (Lond).* 2011;1:1217–235;
7. EMA Qualification Opinion. July 2023. Accessed May 02, 2025. https://www.ema.europa.eu/en/documents/scientificguideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 8. McDonald CM, et al. *Neuromusc Disord.* 2013;23:752.

Strengths and weaknesses of functional assessments historically used in studies of ambulatory individuals with DMD (2 of 2)

	6-minute walk test (6MWT)	North Star Ambulatory Assessment (NSAA)
Description	• The distance an individual can walk in 6 minutes[1]	The sum of scores on 17 ordinal tasks, each scored as:[3,4] • 0 = inability to perform task • 1 = modified method of completing task, or • 2 = normal activity with no obvious modification Tasks include rising from the floor, moving from sitting to standing, jumping, running, and ascending or descending steps.[3,4] Younger and older individuals may sometimes have the same NSAA total score but are likely to have a different prognosis, so total score should be interpreted within a trend of decline (e.g., loss of ≥3 points in the last 14 months) or stability/improvement[6]
Prognostic values	• Cut-off associated with loss of ambulation at 48 weeks: <325 meters*[2]	Probability of being ambulant when aged ≥13 years:†[5] • Scoring <22: 13% (95% CI: 5–34%) • Scoring 22–25: 19% (95% CI: 9–38%) • Scoring 26–28: 34% (95% CI: 21–55%) • Scoring 29–31: 34% (95% CI: 21–54%) • Scoring 32–34: 61% (95% CI: 47–79%)
MCID	• ~30 m*[2]	• ~3.5 points/year#[6]
Median age at loss of ability to complete assessment	• Can be completed until loss of ambulation[2]	• 12.6 years (95% CI: 11.8, 14.7)‡[7]
Advantages	• Correlates with TFT and NSAA[8] • Has been used extensively in trials[8]	• Captures broad range of ambulatory motor functions[4] • Used extensively in trials[4]
Disadvantages	• Performance subject to motivation or fatigue[9] • May lack sensitivity[1] • Taxing for the patient[10]	• Performance subject to motivation or fatigue[9] • Ordinal scale limits sensitivity to small change[10]

*Longitudinal multicenter natural history data from 57 individuals with DMD aged 5–15 years over 48 weeks;[2] †Retrospective, multicenter study in 293 individuals with DMD with a mean age at first visit of 5.5 years.[5] ‡Prospective, multicenter study in 826 individuals with DMD aged 5–16 years.[7] #For boys aged >7 years. MCID derived using an anchor-based approach using data from the iMDEX natural history study; an annual decline of 30m in the 6MWT was used as the anchor.[6]
CI, confidence interval; DMD, Duchenne muscular dystrophy.

1. Arora H, et al. *Muscle Nerve.* 2018;58(5):631–38; 2. McDonald CM, et al. *Muscle Nerve.* 2013;48(3):343–56; 3. Stimpson G, et al. *Eur J Paediatr Neurol.* 2024:53:123–30; 4. Muntoni F, et al. *PLoS One.* 2019;14(9):e0221097; 5. Zambon AA, et al. *Dev Med Child Neurol.* 2022;64(8):979–88; 6. Ayyar Gupta V, et al. *PLoS One.* 2023;18:e0283669; 7. Stimpson G, et al. *J Neuromuscul Dis.* 2024;11(1):153–66;
8. McDonald CM, et al. *Muscle Nerve.* 2013;48:357–368; 9. EMA Qualification Opinion. July 2023.Accessed May 1, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 10. EMA Qualification Opinion. April 2019. Accessed May 02, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondary-endpoint-duchennemuscular-dystrophy-measured-valid-and-suitable-wearable-device_en.pdf.

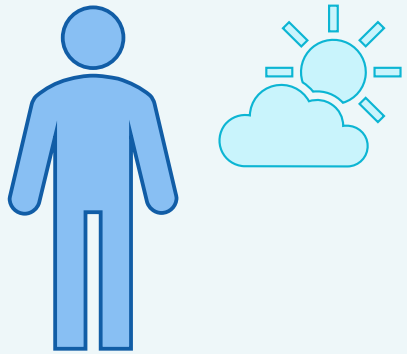
Established functional ambulatory assessments have limitations

6MWT, 4SC and NSAA can be affected by external factors that impact reliability, and only provide an idea of an individual's maximal functional ability at a specific timepoint[1–3]

Factors affecting reliability of clinic-based functional assessments in DMD

Person-specific factors[1–3]

- Mood/motivation
- Fatigue, concentration
- Wellbeing
- Growth
- Intellectual maturation/ability



Environmental/social factors[3]

- Time of day
- Burden of travelling to clinics
- Artificial (clinic) setting

Digital wearable endpoints may provide a more accurate representation of mobility through continuous and non-invasive monitoring of a patient's daily activities[1,4]

Robust digital outcome measures have the potential to transform evaluation of disease progression and help to advance drug development[1,2]

4SC, 4 stair climb; 6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; EMA, European Medicines Agency; NSAA, North Star Ambulatory Assessment; SV95C, stride velocity 95th centile.

1. Servais L, et al. *Nat Med.* 2023;29(10):2391–92; 2. Servais L, et al. *Sci Rep.* 2024;14(1):29681; 3. EMA Qualification Opinion. July 2023. Accessed May 1, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf;
4. Benemei S, et al. *Acta Neurol Belg*. 2025;125(1):1–12.

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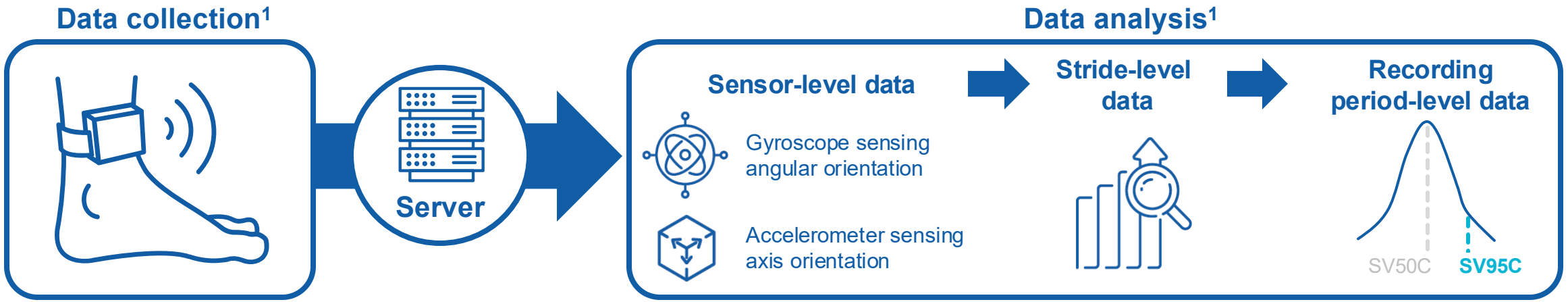
Stride velocity 95th centile (SV95C) in clinical trials for DMD

SV95C is a digital ambulation measure derived from a wearable device that allows the passive collection of continuous data in RW settings



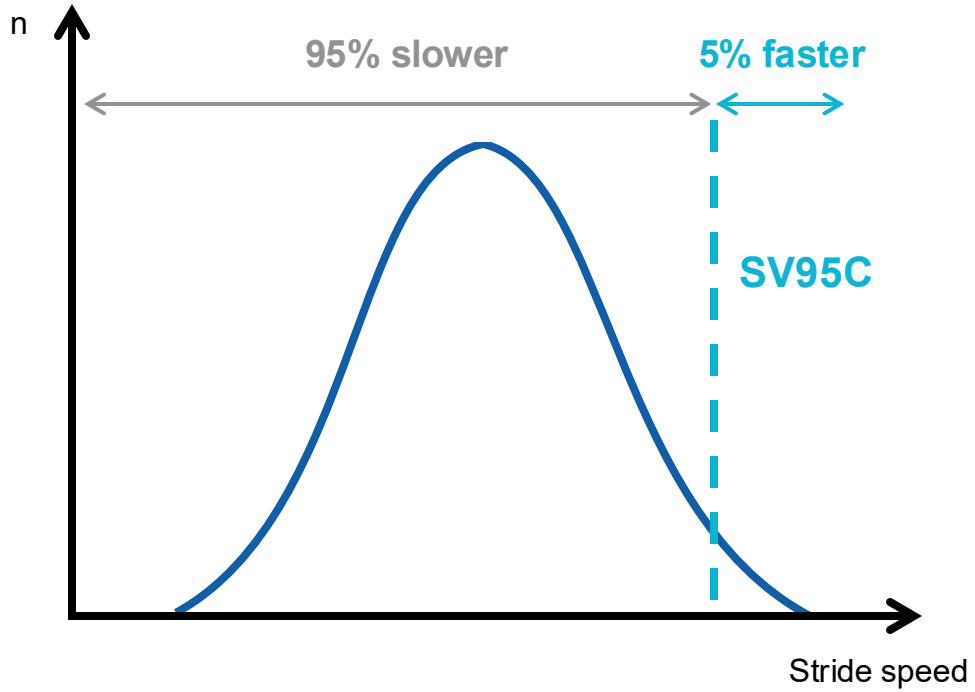
- An ankle-worn digital device (that meets EMA technical specifications*) passively collects raw sensor data continuously throughout the day over a defined recording duration (minimum 50 hours, optimum 180 hours)[1–3]
  - The EMA approved ActiMyo® device, **Syde**, was specifically designed for real-world use in patients with movement disorders. Data capture is enabled for up to 2 weeks without internet connection or battery charging[4]
- Stride-level data (stride length and stride speed) are uploaded to a server and processed to calculate SV95C.[1,2]

SV95C is a digital objective endpoint of ambulatory performance in patients' normal daily environment†[2,4]

*Any device may be used to capture SV95C if it meets regulatory standards outlined by EMA; †Adopted by EMA; under review by other regulatory authorities.
DMD, Duchenne muscular dystrophy; EMA, European Medicines Agency; SV95C, stride velocity 95th centile.
1. Servais L, et al. *Nat Med.* 2023;29(10):2391–92; 2. Servais L, et al. *Sci Rep*. 2024;14(1):29681; 3. EMA Qualification Opinion. July 2023. Accessed May 02, 2025. https://www.ema.europa.eu/en/documents/scientificguideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf;
4. Servais L, et al. *J Neuromuscul Dis*. 2022;9(2):335–46.

SV95C represents the speed of the fastest 5% of strides taken during everyday living over a pre-defined duration

- SV95C is the threshold at which 95% of strides are slower and 5% are faster[1,2]
- The 95th centile reflects a high activity level that is sensitive to disease progression and treatment effects, independent of external factors[1]
- SV95C is the first digital measure to receive regulatory body (EMA) qualification, for use as a primary endpoint in studies of boys with DMD ≥4 years old[1–3]
  - Under review for qualification by the US FDA[2]



The EMA has stated that SV95C may be used as a primary endpoint in studies of boys with DMD ≥4 years old[3]

EMA, European Medicines Agency; ICC, intraclass correlation coefficient; MCID, minimal clinically important difference; m, meter; m/s, meters per second; SEM, standard error of the measurement; SV95C, stride velocity 95th centile.

1. Servais L, et al. *Nat Med.* 2023;29(10):2391–92; 2. Servais L, et al. *Sci Rep*. 2024;14(1):29681; 3. EMA Qualification Opinion. July 2023. Accessed May 02, 2025. https://www.ema.europa.eu/en/documents/scientificguideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 4. Servais L, et al. *J Neuromuscular Dis*. 2022;9:335–46.

Contextualization of meaningful change in SV95C

MCID | **Used to assess change in clinical presentation and may be used to determine response to treatment or disease progression[1]**

EMA qualification opinion on SV95C

April 2019[2]

- Calculated using SEM in 40 patients, baseline SD, and ICC calculated from the first and last 15 days of a 1-month recording period
- Relative MCID **= 0.0985 m/s**

July 2023[3]

- Calculated using SEM in 103 patients, baseline SD, and ICC calculated from the first and last 15 days of a 1-month recording period
- MDC statistically measured based on SEM at 80–95% confidence levels, and by considering 0.2 SD, 0.5 SD, and 0.8 SD of the measurement
  - MCID based on SEM at 80–95% confidence intervals **= 0.127–0.194 m/s**
  - 0.5 SD estimate of MCID **= 0.191 m/s**

The proposed MCID for SV95C is estimated to be ~0.1 m/s (36 m in 6 min)[2,3]

The SV95C change of ~0.1 m/s corresponds to:*

- 6MWT MCID of 30 m[4]
- NSAA change of 2 to 3 points[4]

*Derived based on clinical worsening.

6MWT, 6-minute walk test; ICC, intraclass correlation coefficient; MCID, minimal clinically important difference; MDC, minimal detectable change; m, meter; m/s, meters per second; NSAA, North Star Ambulatory Assessment; SD, standard deviation; SV95C, stride velocity 95th centile.

1. Duong T, et al. *J Neuromuscul Dis.* 2021;8(6):939–48; 2. EMA Qualification Opinion. April 2019. Accessed May 02, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondary-endpoint-duchennemuscular-dystrophy-measured-valid-and-suitable-wearable-device_en.pdf; 3. EMA Qualification Opinion. July 2023. Accessed May 02, 2025. https://www.ema.europa.eu/en/documents/scientificguideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 4. Servais L, et al. *Sci Rep.* 2024;14(1):29681.

SV95C significantly correlates with established motor function assessments

Convergent validity

- SV95C significantly correlated with 6MWT, NSAA, and 4SC in 107 individuals with DMD at baseline and at follow-up over 12 months[1]

Spearman's correlation coefficients between absolute value of SV95C and established COAs in individuals with DMD[2]

	Baseline (N=107)	Month 3 (n=43)	Month 6 (n=20)	Month 9 (n=24)	Month 12 (n=15)
6MWT	0.657**	0.761**	0.524*	0.691**	0.835**
NSAA	0.644**	0.575**	0.396^{ns}	0.677**	0.753**
4SC	−0.634**	−0.603**	−0.536*	−0.651**	−0.749**

*p<0.05; **p≤0.001; ns, not significant.
The convergent validity reflects the degree to which one clinical outcome measure correlates with other tests that measure the same construct[2]

Other measures supporting the clinical validation of SV95C

Test-retest reliability

- ICC of 0.970 (95% CI: 0.947−0.983) based on two successive SV95C measurements taken 1 month apart in 52 individuals with DMD[1,2]

Known-groups validity

- Median SV95C scores are lower in individuals with DMD (N=125; 1.563 m/s) vs age-matched controls (N=66; 2.713 m/s; p<0.001)[1,2]

SV95C is a reliable outcome measure that is moderately/strongly correlated with other outcomes such as 6MWT, NSAA, and 4SC[2]

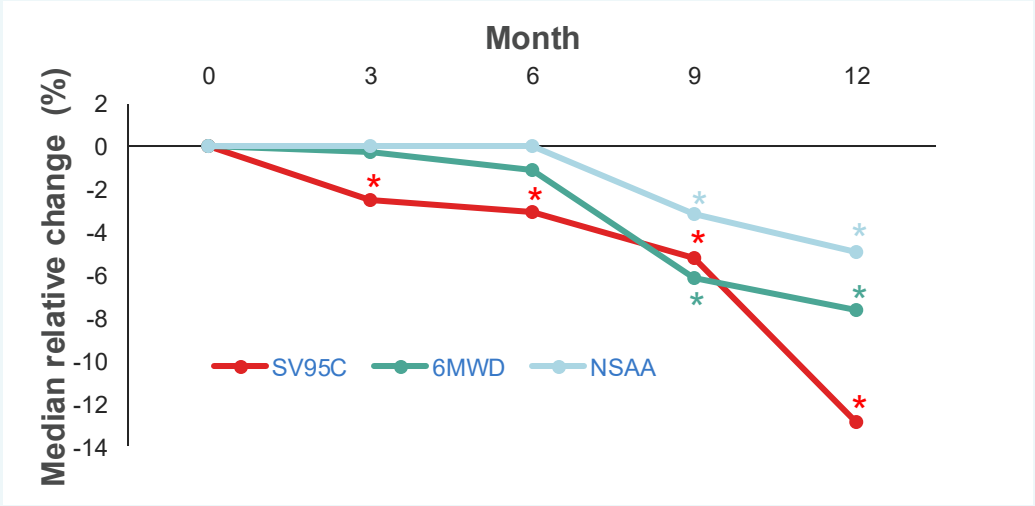
4SC, 4 stair climb; 6MWT, 6-minute walk test; CI, confidence interval; COA, clinical outcome assessment; DMD, Duchenne muscular dystrophy; ICC, intraclass correlation coefficient; NSAA, North Star Ambulatory Assessment; SV95C, stride velocity 95th centile.

1. Servais L, et al. *Sci Rep*. 2024;14(1):29681; 2. EMA Qualification Opinion. July 2023. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf (accessed April 30, 2025).

SV95C detects disease progression earlier than other ambulatory motor function assessments

- SV95C demonstrated a progressive loss of maximal speed that could be observed as early as ~3 months, vs 9 months with 6MWT and NSAA[1]

Median change from baseline and SRMs for SV95C, 6MWT, and NSAA in individuals with DMD on a stable steroid regimen[1*]



Asterisks denote statistically significant changes from baseline:
SV95C: 3 months: p=0.0019; 6 months: p=0.0009; 9 months: p=0.0005; 12 months: p=0.0003
6MWD: 9 months: p=0.0016; 12 months: p=0.0007
NSAA: 9 months: p=0.0153; 12 months: p=0.0192

SV95C has shown greater sensitivity to detect disease progression earlier than other established motor function assessments[1,2]

*Results from an analysis of individuals with DMD on stable steroid regimens from three natural history studies and two clinical trials.
6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; NSAA, North Star Ambulatory Assessment; SRM, standardized response mean, SV95C, stride velocity 95th centile.
1. Servais L, et al. *Sci Rep*. 2024;14(1):29681; 2. EMA Qualification Opinion. July 2023. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf (accessed April 30, 2025).

Survey results demonstrate the willingness of patients/families to use wearable devices in clinical trials of DMD

In an online survey distributed internationally to patients with DMD and their families through global patient organizations (October 2020–January 2021):

Walking was identified as the **key function that** non-ambulatory patients sought to have restored

58% (n=26/45) indicated that an **increase in top walking speed** reflects improved ambulation

Most respondents (69%) **preferred a wearable device** in a real-world setting rather than a regular assessment in a clinic-based setting for assessing mobility in a clinical trial

>70% (n=55/78) noted that a wearable device would make trial participation more attractive

>75% (n=61/78) were willing to use a wearable device

45% (n=33/74) were willing to a wearable device for the duration of a trial

The burden of wearing the device is less than the value of measuring ambulation precisely in a real-life setting

DMD, Duchenne muscular dystrophy; SV95C, stride velocity 95th centile.

1. EMA Qualification Opinion. July 2023. Accessed June 18, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf.

Digital wearable endpoints like SV95C address limitations of established DMD clinical outcome assessments

Advantages

- Represents an individual's real ambulatory capability, through real-world continuous monitoring[1]
- Does not rely on patient motivation or subjective assessment[1]
- Can reduce burden of traveling to the clinic[1]
- Highly correlated with 6MWT[1]

Limitations

- Requires adherence to wearing device[2,3]
- Technical reliability[3]
- Data privacy[3]
- Not used in routine clinical practice[4]
- Adopted by EMA but under review by other regulatory authorities[1]
- More data are needed to establish the threshold estimates and predictive value[1]

See slide 5 and 6 for cut-off values to predict loss of function/ambulation in commonly used functional assessments in DMD

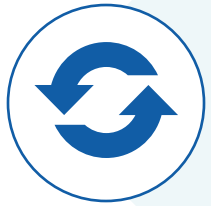
SV95C is a real-world, clinically meaningful outcome assessment that addresses some of the limitations of established motor function assessments in DMD[1]

6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; EMA, European Medicines Agency; SV95C, stride velocity 95th centile.

1. EMA Qualification Opinion. July 2023. Accessed May 1, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 2. Servais L, et al. *Nat Med.* 2023;29(10):2391–92;
3. Servais L, et al. *Sci Rep*. 2024;14(1):29681; 4. Servais L, et al. *Digit Biomark.* 2021;5:183–90.

Evidence supports the use of SV95C as a secondary endpoint in other progressive NMDs, including FSHD, in European trials

Clinical validation of SV95C in FSHD



Test-retest reliability

- ICC of 0.991 based on two successive SV95C measurements taken 1 month apart in 14 individuals

Known-groups validity

- Median SV95C scores are lower in individuals with FSHD (N=19; 1.284m/s) vs healthy controls (N=93; 2.500 m/s; p<0.001)

Convergent validity

- The convergent validity of SV95C was confirmed in FSHD (N=13) with a strong correlation between SV95C and 6MWT (ρ=0.770, p=0.002)

The EMA concluded that evidence supports the use of SV95C as a secondary endpoint in FSHD

6MWT, 6-minute walk test; FSHD, facioscapulohumeral muscular dystrophy; ICC, intraclass correlation coefficient; NMD, neuromuscular disease; NSAA, North Star Ambulatory Assessment; SV95C, stride velocity 95th centile. EMA Qualification Opinion. July 2023. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf (accessed July 14, 2025).

Summary

- Gait and functional ambulation are important markers of disease in NMDs and are relevant measures for assessing disease progression and as endpoints in studies of potential new treatments[1,2]
  - However, established functional assessments, for example those used in studies of ambulatory individuals with DMD, can be affected by external factors that impact reliability, and only provide a snapshot of an individual's maximal functional ability at a specific timepoint[3–5]
- SV95C is a digital ambulation measure derived from a wearable device that addresses some of these limitations by allowing the passive collection of continuous data in real-world settings[4]
- The EMA has stated that SV95C may be used as a primary endpoint in studies of boys with DMD ≥4 years old*[5]
  - The proposed MCID is estimated to be ~0.1 m/s (36 m in 6 min)[5]
  - SV95C has been shown to be a reliable outcome measure that correlates with established assessments (e.g., 6MWT, NSAA, and 4SC), while demonstrating greater sensitivity for detecting disease progression earlier[4,5]
  - Evidence also supports its use as a secondary endpoint in other progressive NMDs such as FSHD[5]
- Survey results demonstrate the willingness of patients/families to use wearable devices in clinical trials of DMD[5]

*Adopted by EMA; under review by other regulatory authorities.

4SC, 4 stair climb; 6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; EMA, European Medicines Agency; FSHD, facioscapulohumeral muscular dystrophy; MCID, minimal clinically important difference; NMD, neuromuscular disease; NSAA, North Star Ambulatory Assessment; SV95C, stride velocity 95th centile.

1. Kennedy RA, et al. *J Foot Ankle Res.* 2020;13:10; 2. Hadouiri N, *Eur J Phys Rehabil Med.* 2024;60:257-269; 3. Servais L, et al. *Nat Med.* 2023;29(10):2391–92; 4. Servais L, et al. *Sci Rep.* 2024;14(1):29681; 5. EMA Qualification Opinion. July 2023. Accessed May 1, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf