Walking speed during daily living, a systematic review

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Introduction : why do we need new endpoints ?

- Objective, quantifiable walking speed endpoints are lacking
- Real-life walking speed is a key factor of quality of life

Current walking speed evaluation compared to wearable devices :

	Dedicated labs	6-minute walking test	Wearable
Cost	+++	- - -	+
Availability	- - -	+++	+++
Workload	+++	++	- - -
Hawthorne effect (Patients perform better when observed)	+++	+++	- - -

Wearable devices offer :

- Cost-effective and available solutions
- Reduce workload
- Eliminate biais

➡ Endpoints have to be validated by regulatory agencies such as the EMA or FDA before clinical use.

What is the purpose of this poster ?

- Currently published data
- Focus on Duchenne Muscular Dystrophy
- What is missing for global validation ?
- Insights on clinical application

Methods :

We searched the MEDLINE database for studies on the assessment of real-life walking speed using a wearable device, in any population and for any disease.

503 papers Initial search → **66 papers** After screening by title/abstract → **10 papers** After screening by full-text

- Small academic studies ++
- No intent of achieving validation

Results divided into 5 categories :

Validity :
- Ability to distinguish patients from healthy controls

Reliability :
- Measurements are consistent for the same patient

Feasibility :
- Affordability and patient adherence

Accuracy :
- Comparison with validated gait assessment method

Sensitivity to change :
- Tracking patient performance changes

Results for Duchenne Muscular Dystrophy

Validity

Walking speed is significantly reduced in patients compared to controls

Sensitivity to change

Negative change was statistically significant as early as 3 months of follow-up

Reliability

Intraclass correlation coefficient of 0.97

Accuracy

Sv95c correlated with the 6-minute walk test

Sv95c correlated with movement laboratory measurements

Sv95c correlated with the North Star Ambulatory Assessment and the 4-stair climb test

Feasibility

Wearable devices are cost-effective

Patients, including children[6], show good compliance

What has been proposed so far :

Pediatric focus :

Duchenne Muscular Disease (DMD) :

- **Only disease with a validated digital endpoint** by the EMA
- Uses Sv95c : 95th percentile of walking speed

These results are displayed in the main circle [1,2]

Sv95c have also been used inFacioscapulohumeral dystrophy :

- Validity confirmed : compared to controls
- Good reliability : intraclass correlation coefficient > 0.9
- Sensitivity to change : confirmed

➡ Insufficient data for official validation

And beyond pediatrics :

	Validity	Reliability	Feasibility	Accuracy	Sensitivity to change	Letter of intent
Parkinson's [3]	YES	?	YES	+/- (medium bouts did not correlate to MDS-UPDRS III)	YES	YES (FDA)
Sarcopenia	?	?	YES	YES (Medium correlation with 6-MWT)	?	YES (FDA)
Multiple sclerosis [4,5]	?	?	YES	+/- (Real-walking speed overestimate)	?	YES (FDA)
Huntington disease	?	?	?	?	?	YES (but rejected by FDA)

Discussion :

Bridging the gap in digital endpoint validation :

There is a clear interest from regulators :

- EMA has validated Sv95c for DMD before 4 years old
- FDA has accepted multiple letters of intent

But what is missing ?

- **Limited large-scale initiatives** : mainly small, academic studies without clear interest or ressources for validation. Only MOBILISE-D and Sv95c generate extensive database
- **Costly and long validation process :** even MOBILISE-D, a $50 million-funded project faced significant challenges that limited its ability to develop and implement a digital mobility assessment solution

How can validation be facilitated ?

- **Streamlined regulatory pathways** : the EMA has fast-tracking pathways for pain medication approval across various diseases - why not digital endpoints ?
- **Improved study framework** : A unified approach would allow data integration across diseases, populations and devices

What does the future hold :

- **Early detection of decline** though a clinician-friendly app, prompting therapeutic changes
- **Tracking therapy impact** by the clinician and the patient through the app, enhancing motivation and engagement
- **Accelerate drug approvals** and improve patient's quality of life

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