



**Ataxia Global Conference 2022**

# **Capturing clinical progression in multisystemic genetic ataxias:** lessons from 1637 prospective assessments in patients with autosomal recessive or early-onset ataxia

*Andreas Traschütz, MD, PhD*



## The SARA - *generic scale, generic problems?*

- Regulatory and academic concerns
- Suggested modifications
- Better understanding of its metric properties as COA are urgently needed

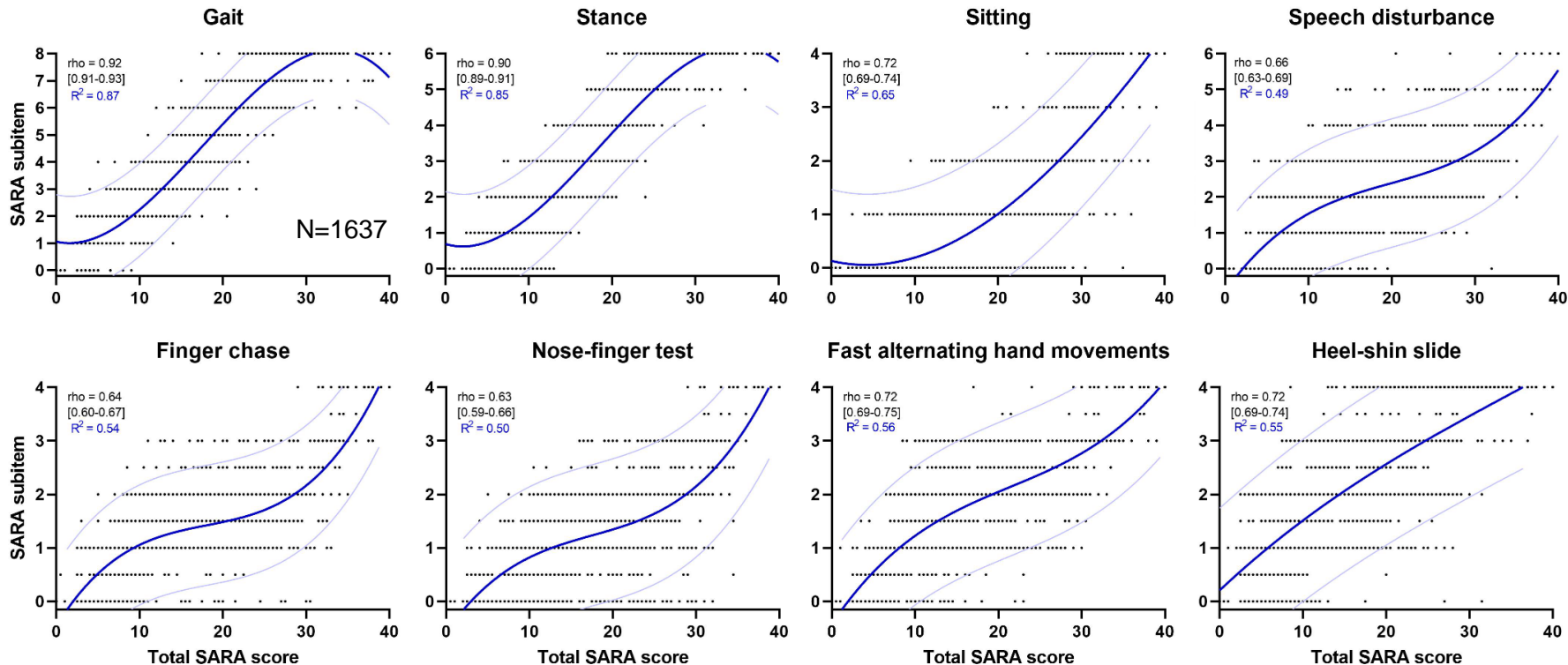
→ **Aim: Characterization of *generic* COA properties based on real-world prospective longitudinal data**

- EOA/ARCAs with 86 genotypes
- 1637 SARA assessments in 887 patients
- 370 patients with 2-8 longitudinal follow-up
- '*Common ARCAs*': FA, ARSACS, SPG7, AOA2, SYNE1, AVED, COQ8A, AT, POLG

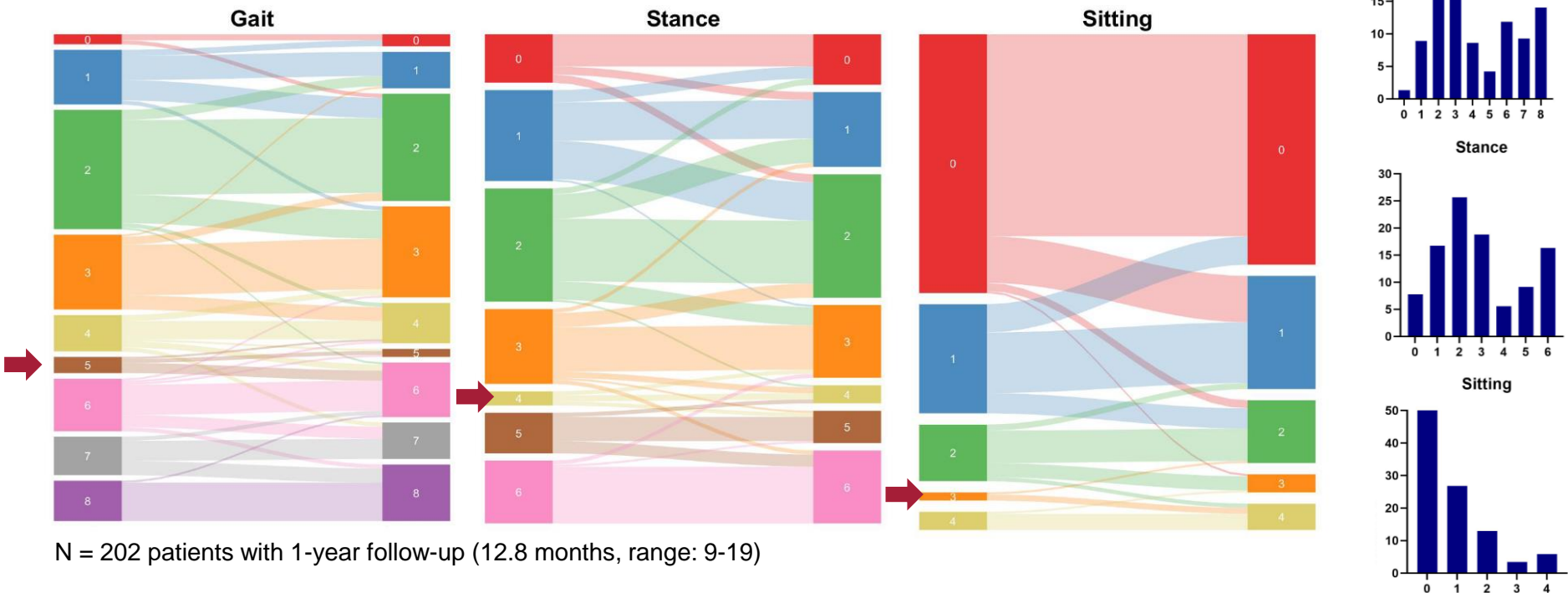


Traschütz et al., Front Neurol, 2021

# Subitem-level responsiveness



## Metric limitation: Incomplete use of subscore levels



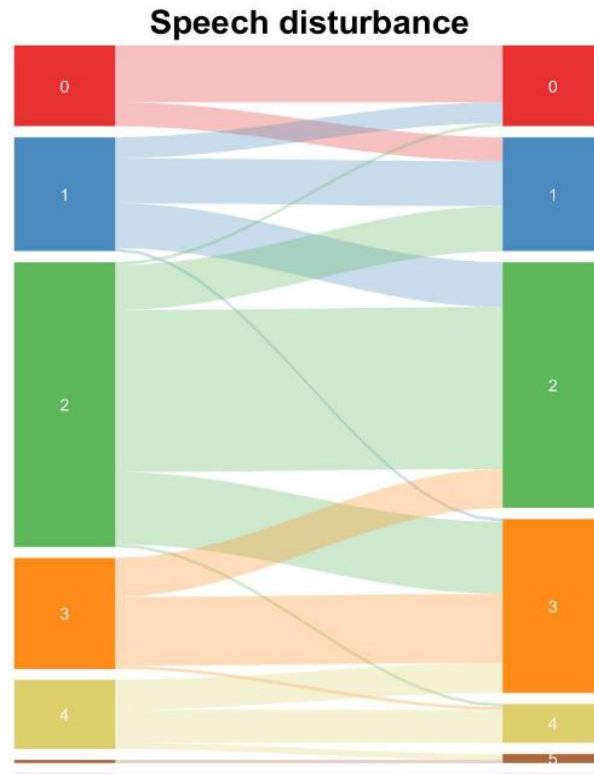


## Metric limitation: Non-progression

Hardly any progression from  
score level 3 to 4

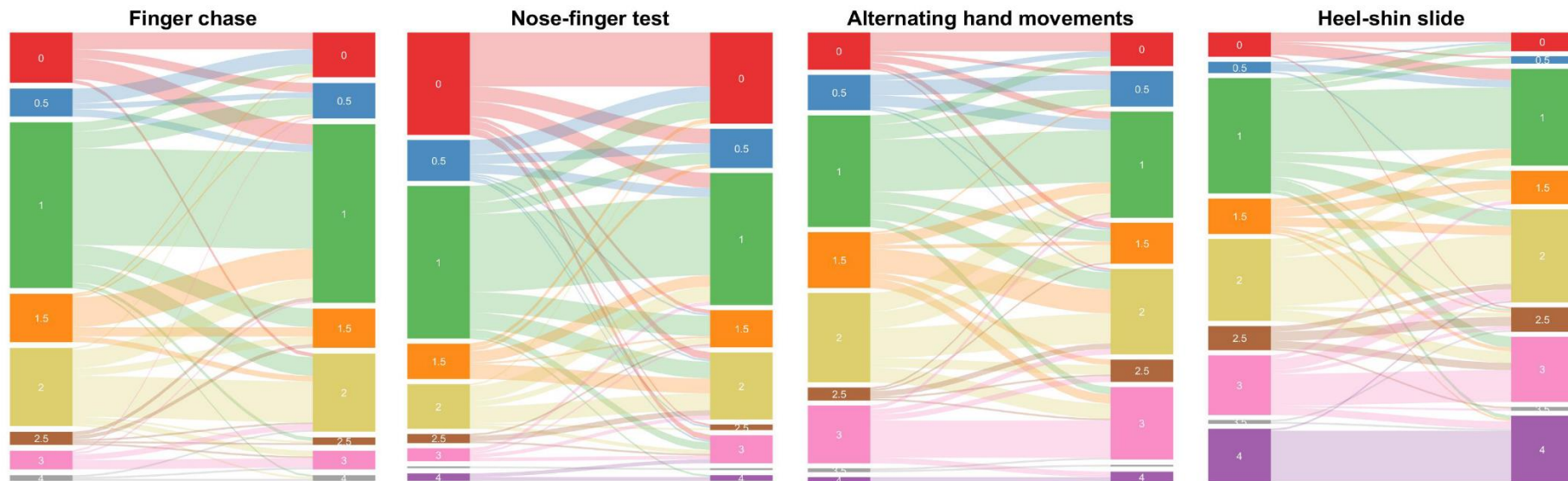
37% and 41% *improvement*  
from score level 3 and 4

Under-representation of  
score levels 5 and 6



N = 202 patients with ~1-year follow-up

## Metric limitation: Variability of appendicular subitems

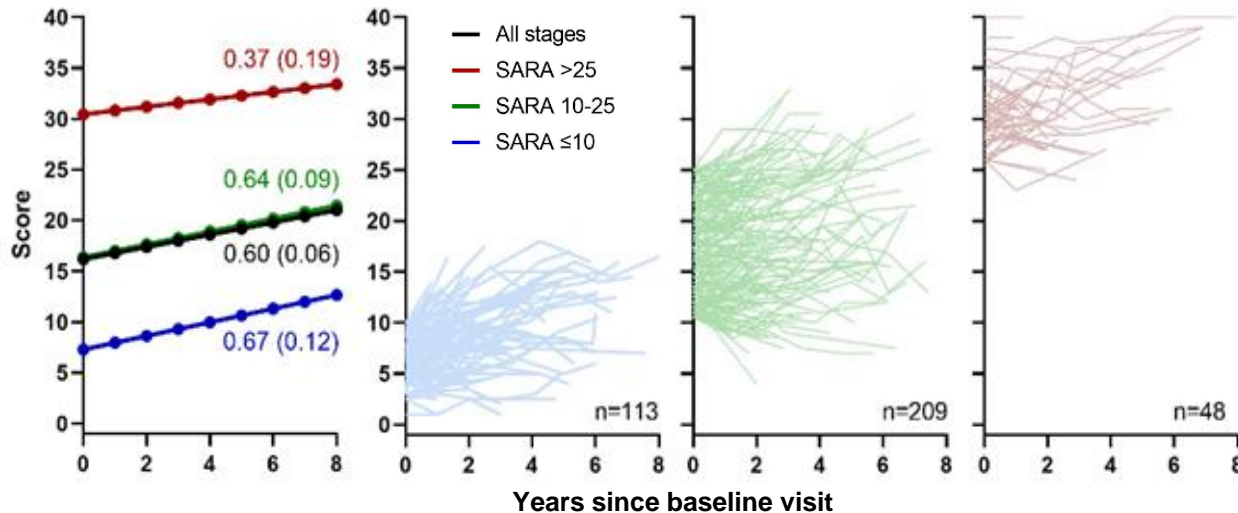


# Sensitivity to progression declines in advanced ataxia

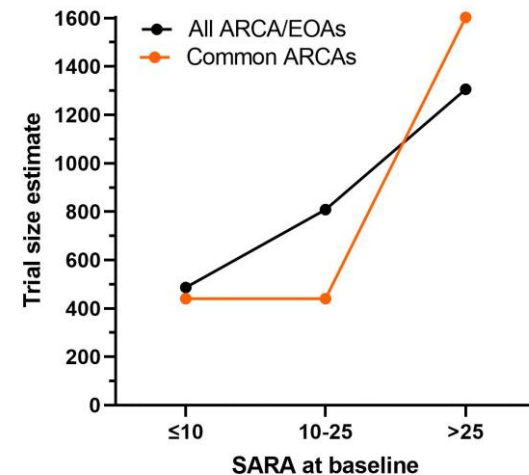
Ralf-Dieter Hilgers  
RWTH Aachen



Total SARA score

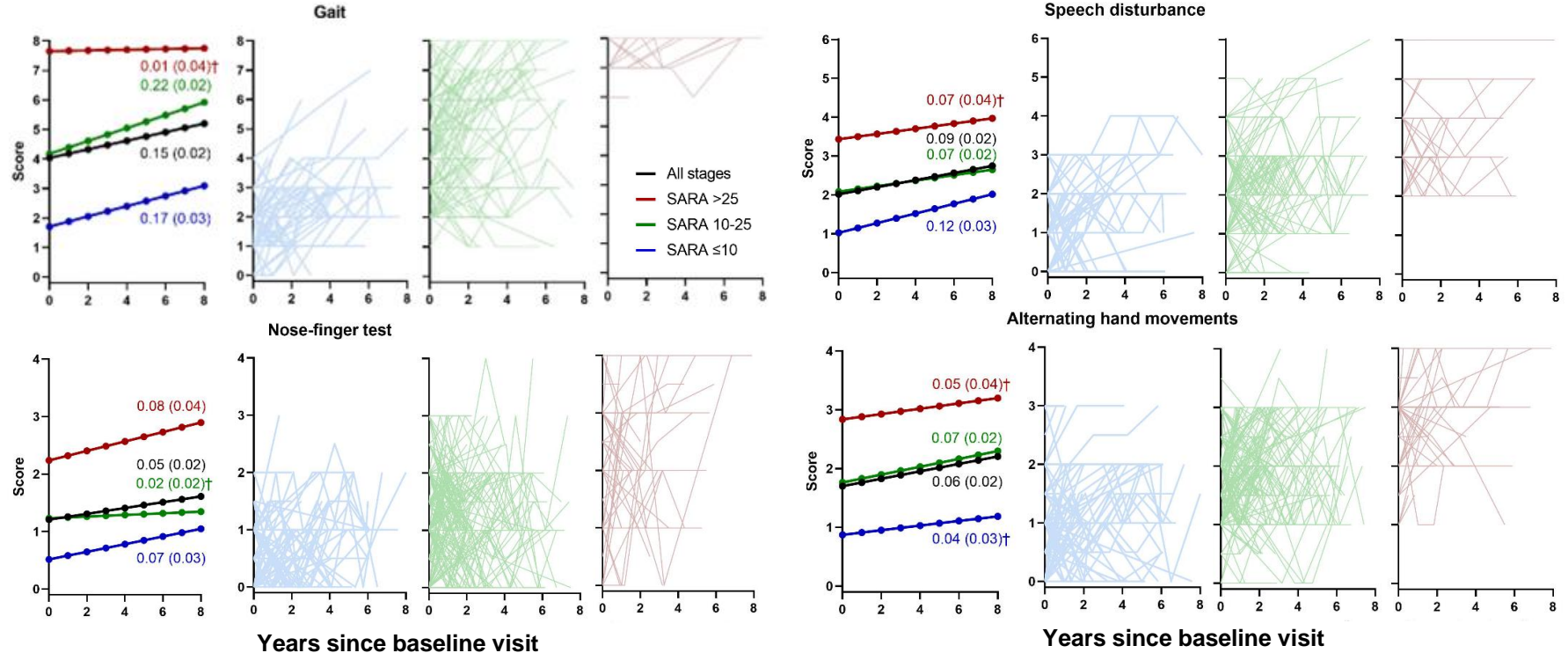


Disease stage





# Sensitivity to progression consistent with limited subitem responsiveness

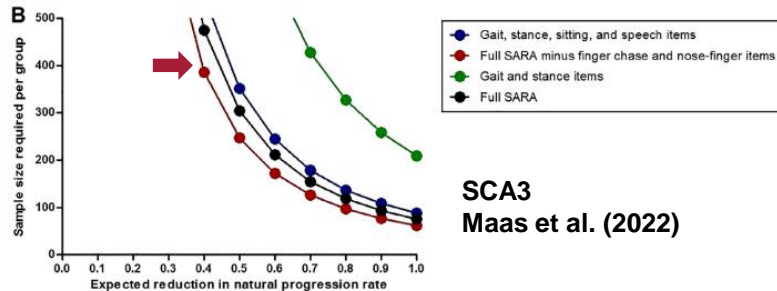




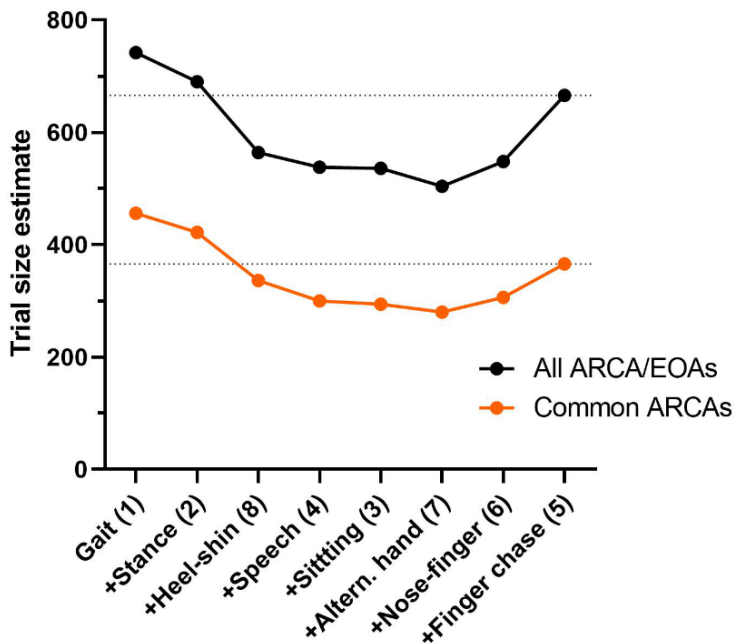
# Rank-optimized SARA generically reduces trial size by 20-25%

Optimal sensitivity without subitems  
*finger-chase* and *nose-finger*

Better, but still suboptimal sensitivity  
with selection of 3-4 subitems



## Rank-optimized SARA composites





Thank you for your attention.  
Questions?



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# Appendix



# Metric, not validity problems limit responsiveness

