

What's in an mFARS Score?

ADL-Based Interpretation of Rating Scales

Christian Rummey

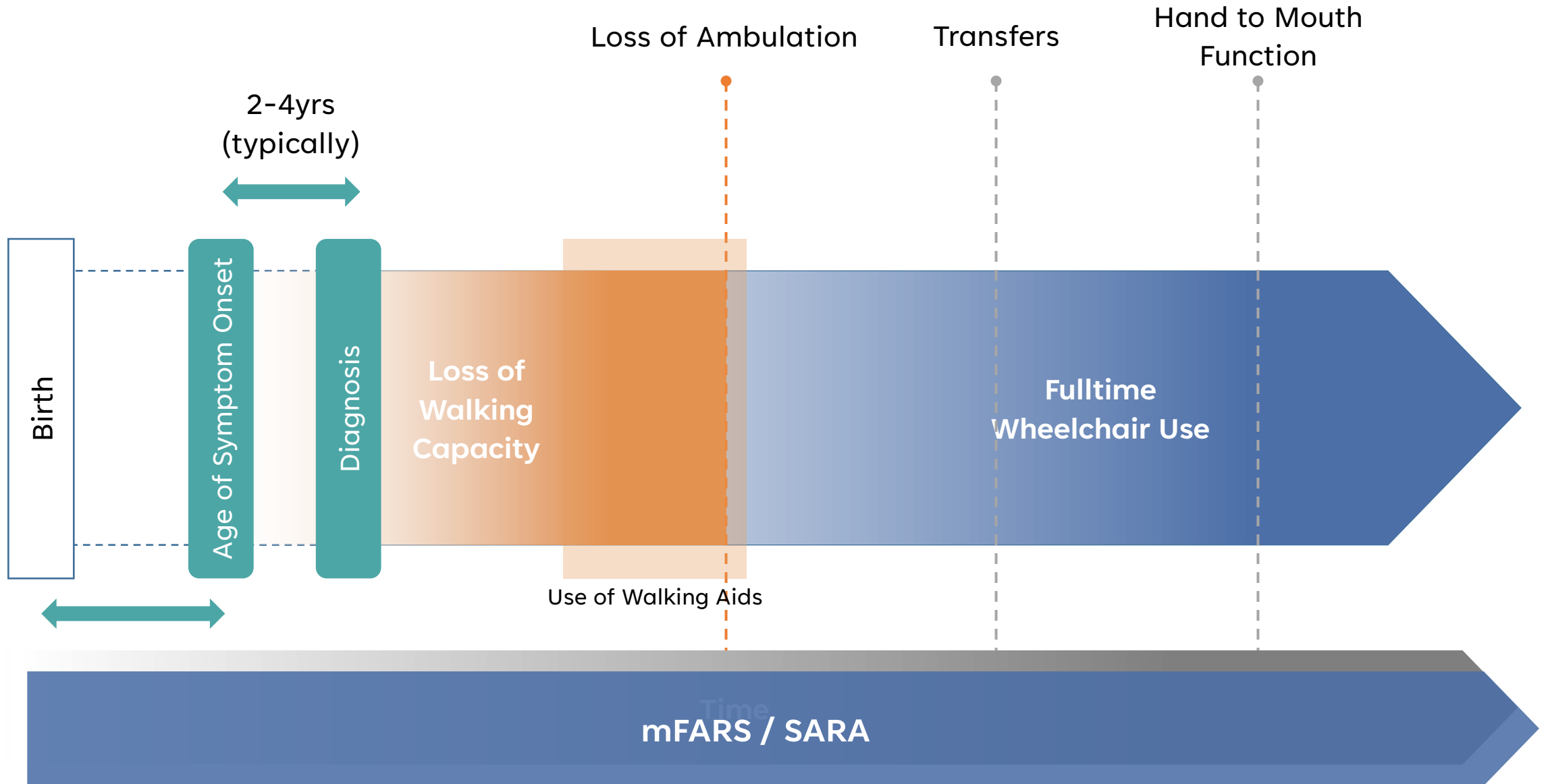
CTAX 2025, Amsterdam

Disclosures

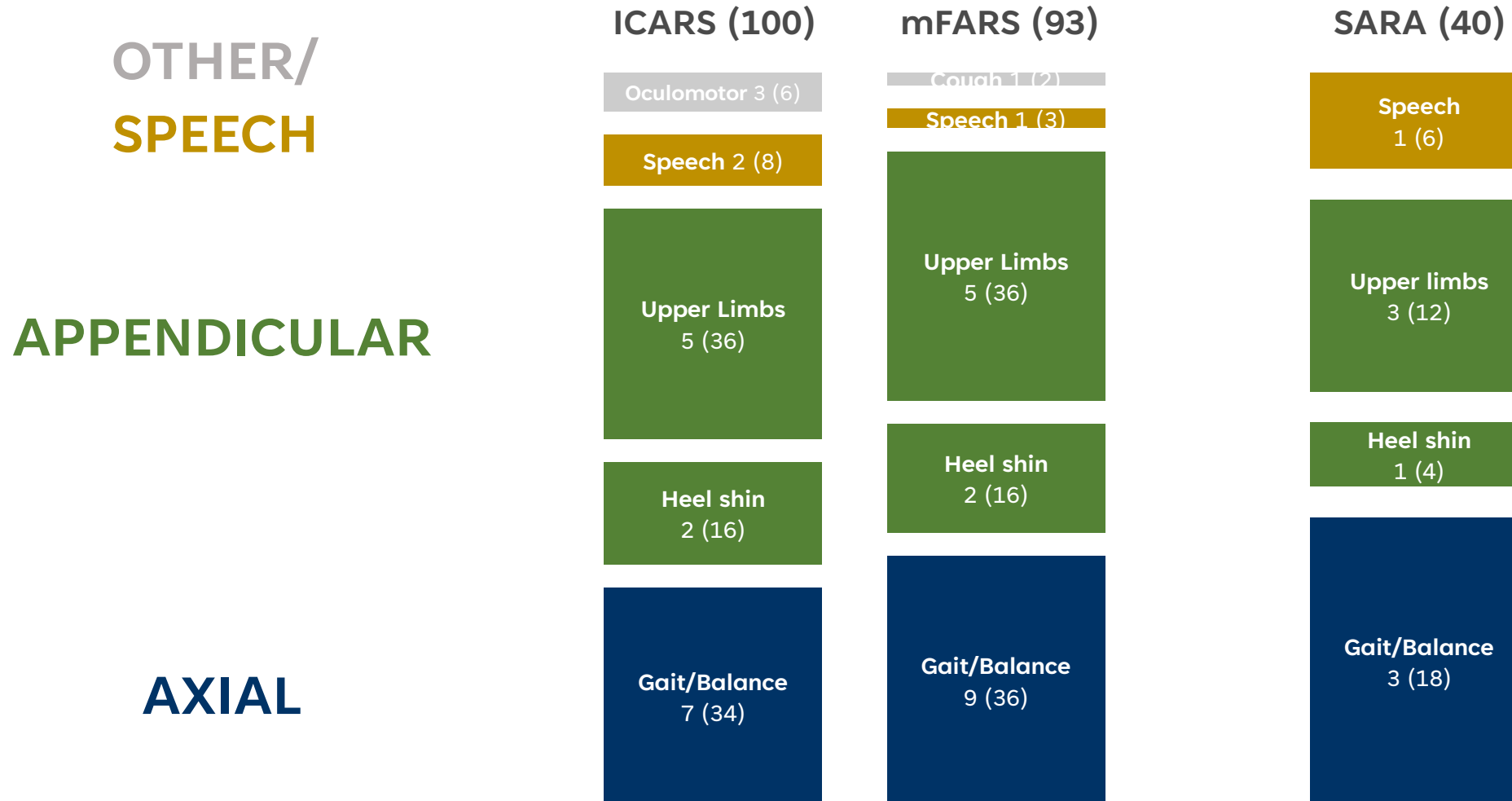
- Friedreich's Ataxia Research Alliance
- National Ataxia Foundation
- Ataxia UK

- Biogen, PTC, Larimar, Biohaven, Lexeo, Takeda, Solaxa

Disease Course - Ataxia



Domain Weights in Ataxia Rating Scales



Individual Items

	mFARS	SARA	ICARS
Bulbar Function	A3. (2) Cough	4. (6) Speech	15. (4) Fluency
	A4. (3) Speech		16. (4) Clarity
Appendicular Function	B1. (6) Finger/Finger	5. (4) Finger chase	8. (8) Knee-tibia test
	B2. (8) Nose/Finger	6. (4) Nose/Finger	9. (8) Heel to Knee
	B3. (8) Dysmetria	7. (4) Fast Altering Hand mov.	10. (8) Finger to Nose dysmetria
	B4. (6) Rapid Altering Mov.		11. (8) Finger to Nose tremor
	B5. (8) Finger Taps		12. (8) Finger/Finger
	C1. (8) Heel/shin slide	8. (4) Heel/shin slide	13. (8) Pron., sup., alter. Mov.
	C2. (8) Heel/shin tap		14. (4) Archimedes spiral
	Axial Function	E1. (4) Sitting	
E2A. (4) Stance Feet Apart			2. (4) Gait Speed
E2B. (4) – with eyes closed		1. (8) Gait	3. (6) Stand eyes open
E3A. (4) Stance Feet Together		2. (6) Stance	4. (4) Spread of feet, eyes open
E3B. (4) – with eyes closed		3. (4) Sitting	5. (4) Body sway eyes open
E4. (4) Tandem Stance			6. (4) Body sway eyes closed
E5. (4) Stance on Dominant Foot			7. (4) Sitting Position
E6. (3) Tandem Walk			
E7. (5) Gait			
Oculomotor Disorders			17. (3) Nystagmus
			18. (2) Ocular pursuit
			19. (1) Dysmetria of saccade

Loss of Ambulation: 2020 Paper

- First Data-based Estimation of Time to Loss of Ambulation
 - In Typical/Early FA, LoA occurs after 11.5y after Disease Onset
 - mFARS exam (standing positions) provide functional Mini-Milestones
 - Predictive for Loss of Ambulation

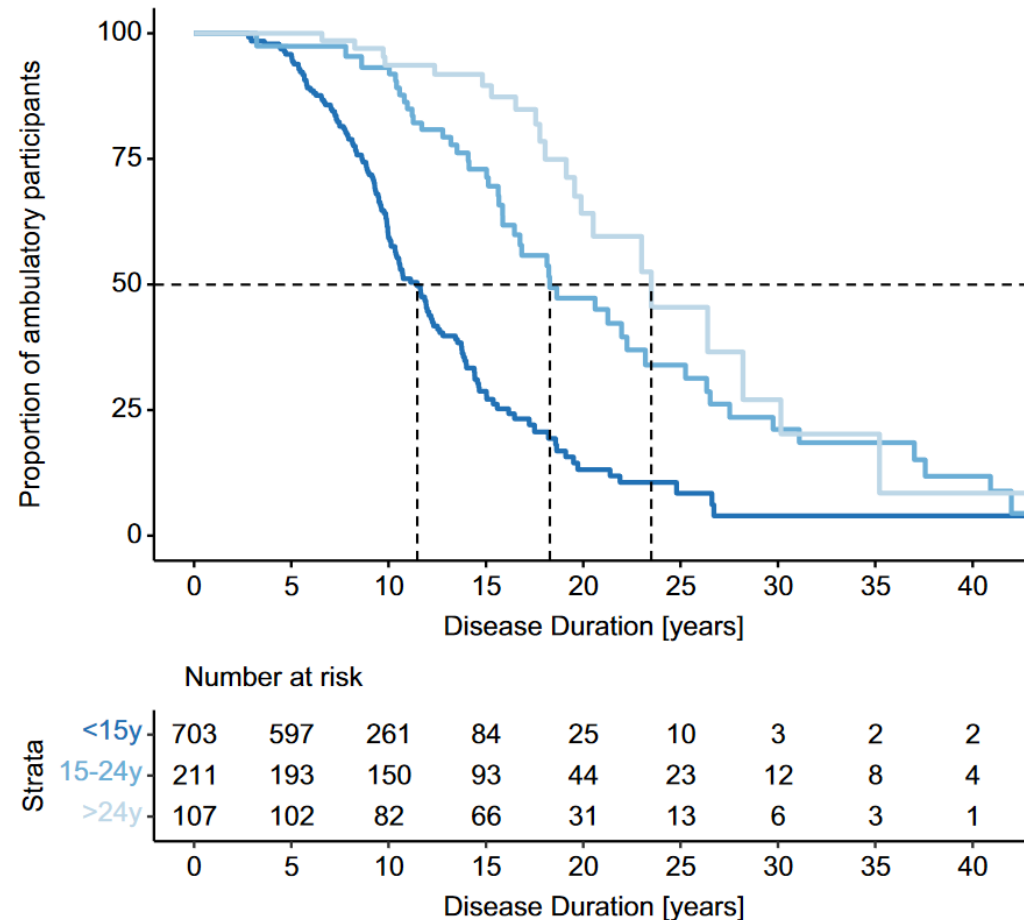
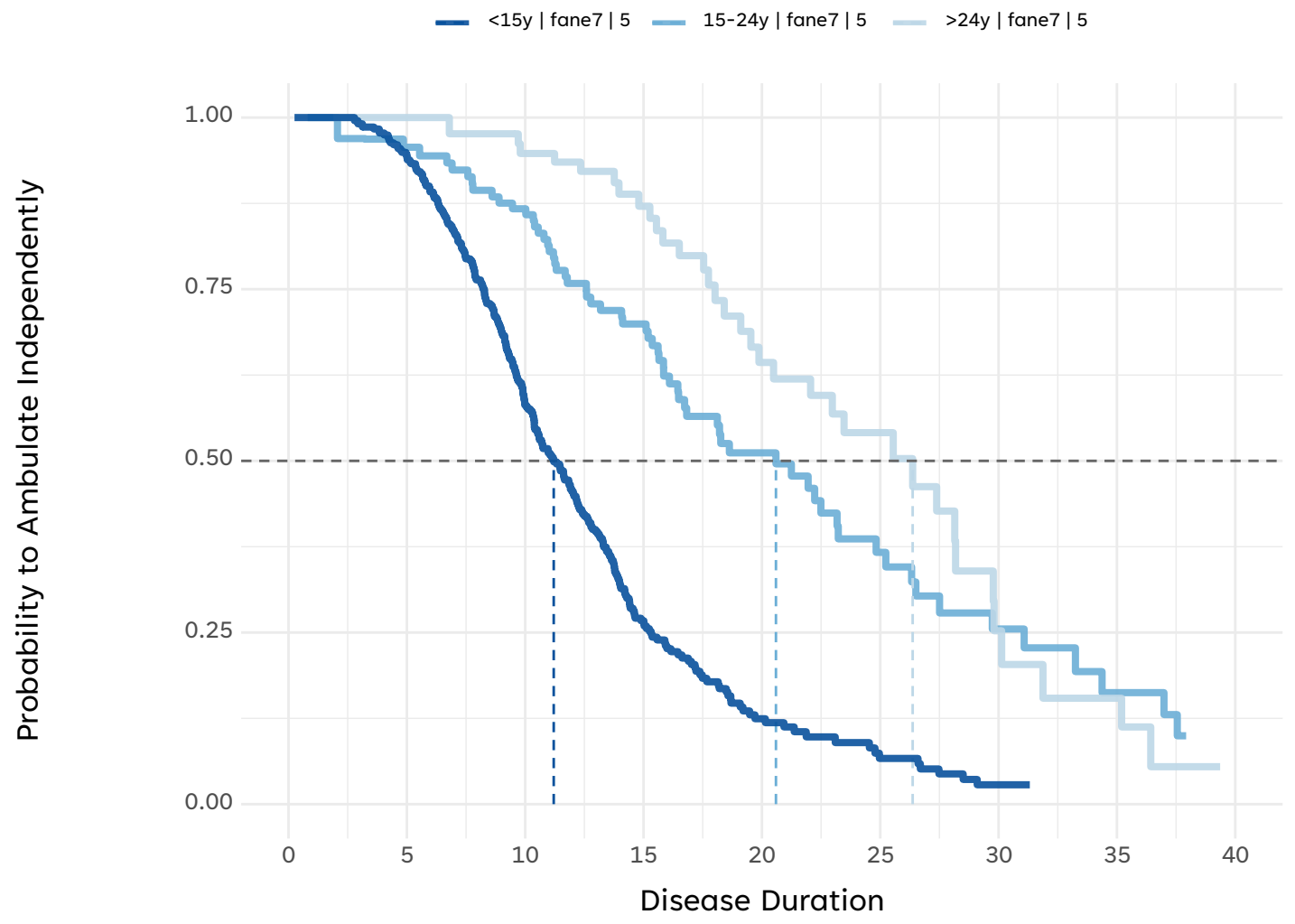


Fig. 2. Estimated proportion of ambulant participants over disease duration. Vertical dotted lines indicate the median disease duration at LoA by onset group.

LoA by Duration and Onset Group updated 2020 Analysis

strata (AOO)	parameter	threshold	N	events observed	median duration (y)	left censoring (%)	truncation bias (y)
<15y	fane7	5	999	292	11.2	31	2.2
15-24y	fane7	5	309	66	20.6	24	5.7
>24y	fane7	5	156	34	26.4	14	1.7

Stable Estimates upon larger Follow-Up

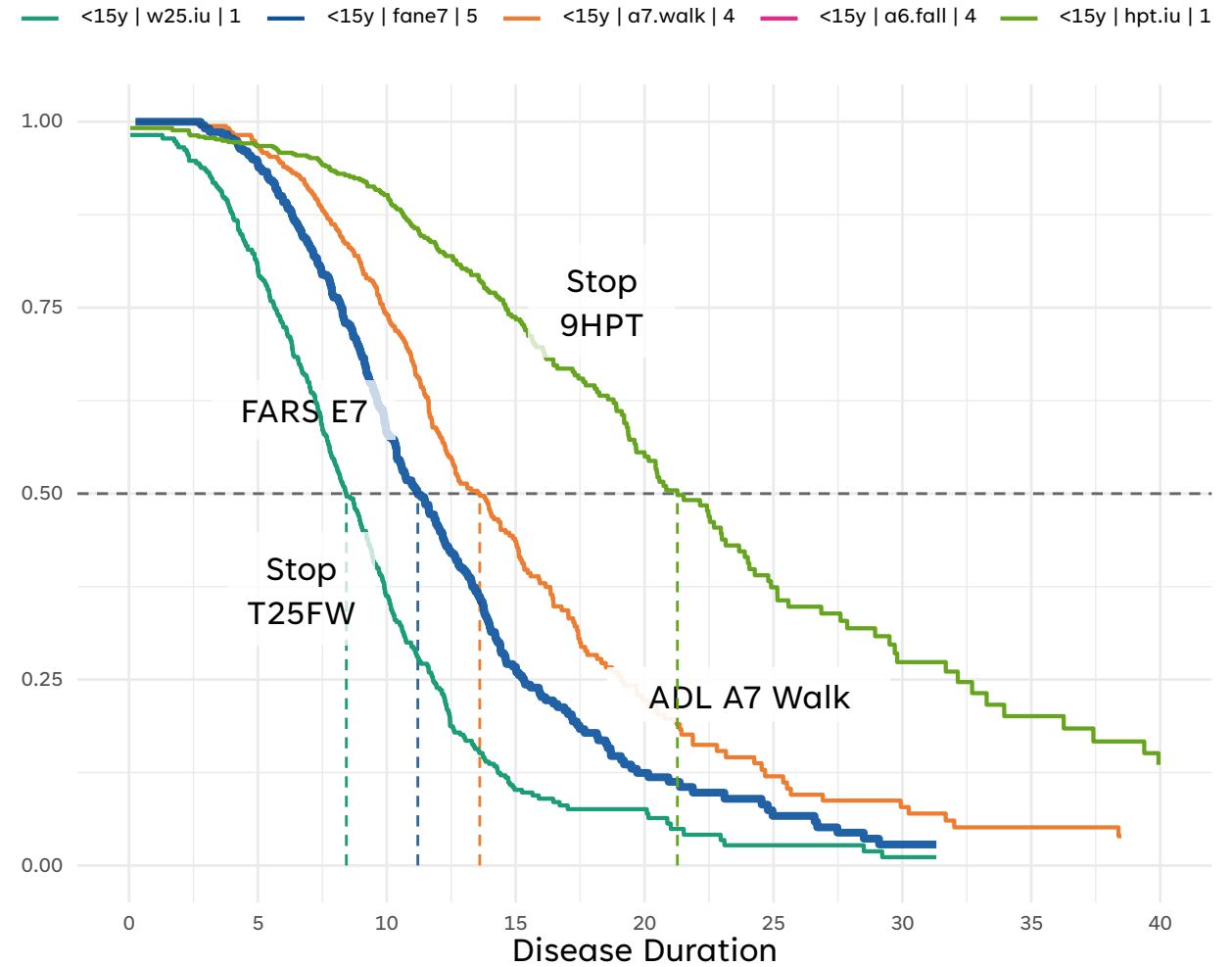


	<15y fane7 5	15-24y fane7 5	>24y fane7 5
999	874	401	130
292	130	40	14
309	279	208	134
66	63	35	17
156	145	115	80
34	46	25	7
31	3	2	2
24	8	4	
14	4	1	

Definitions for LoA by Duration

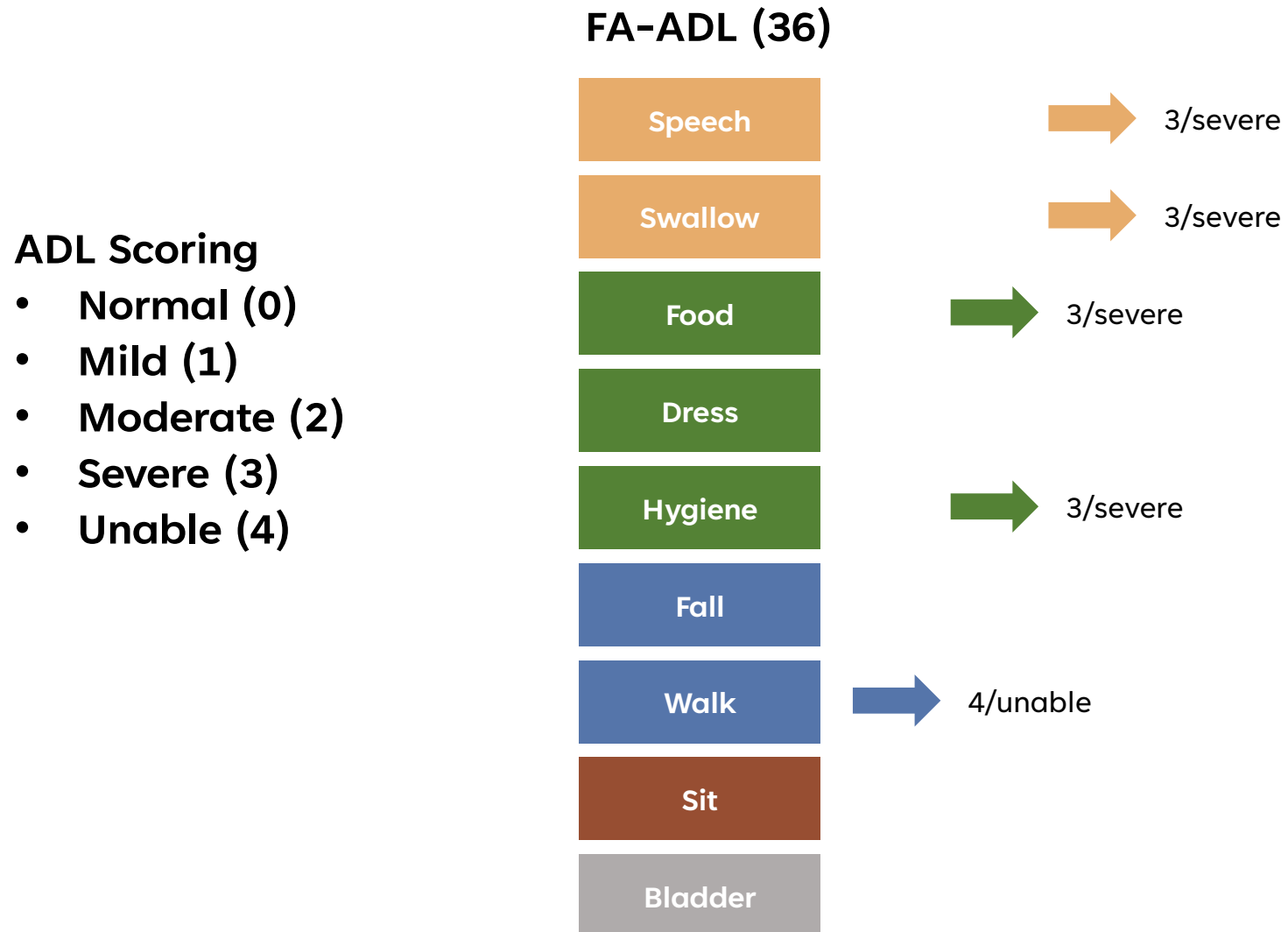
strata	par	thr	N	events.obs	median	lcn.pct	trunc.bias
<15y	w25.iu	1	1,009	345	8.4	41	1.5
<15y	fane7	5	999	292	11.2	31	2.2
<15y	a7.walk	4	1,002	253	13.6	26	2.8
<15y	a6.fall	4	1,002	241	15.6	23	3.3
<15y	hpt.iu	1	984	195	21.3	13	3.8

Probability to Retain Function / ADL



Strata	N	753	264	54	24	7	2	1	1
<15y w25.iu 1	1009	753	264	54	24	7	2	1	1
<15y fane7 5	999	874	401	130	40	14	3	2	2
<15y a7.walk 4	1002	898	507	206	66	24	12	5	4
<15y a6.fall 4	1002	891	527	255	98	42	19	8	6
<15y hpt.iu 1	984	876	612	353	169	72	35	18	10

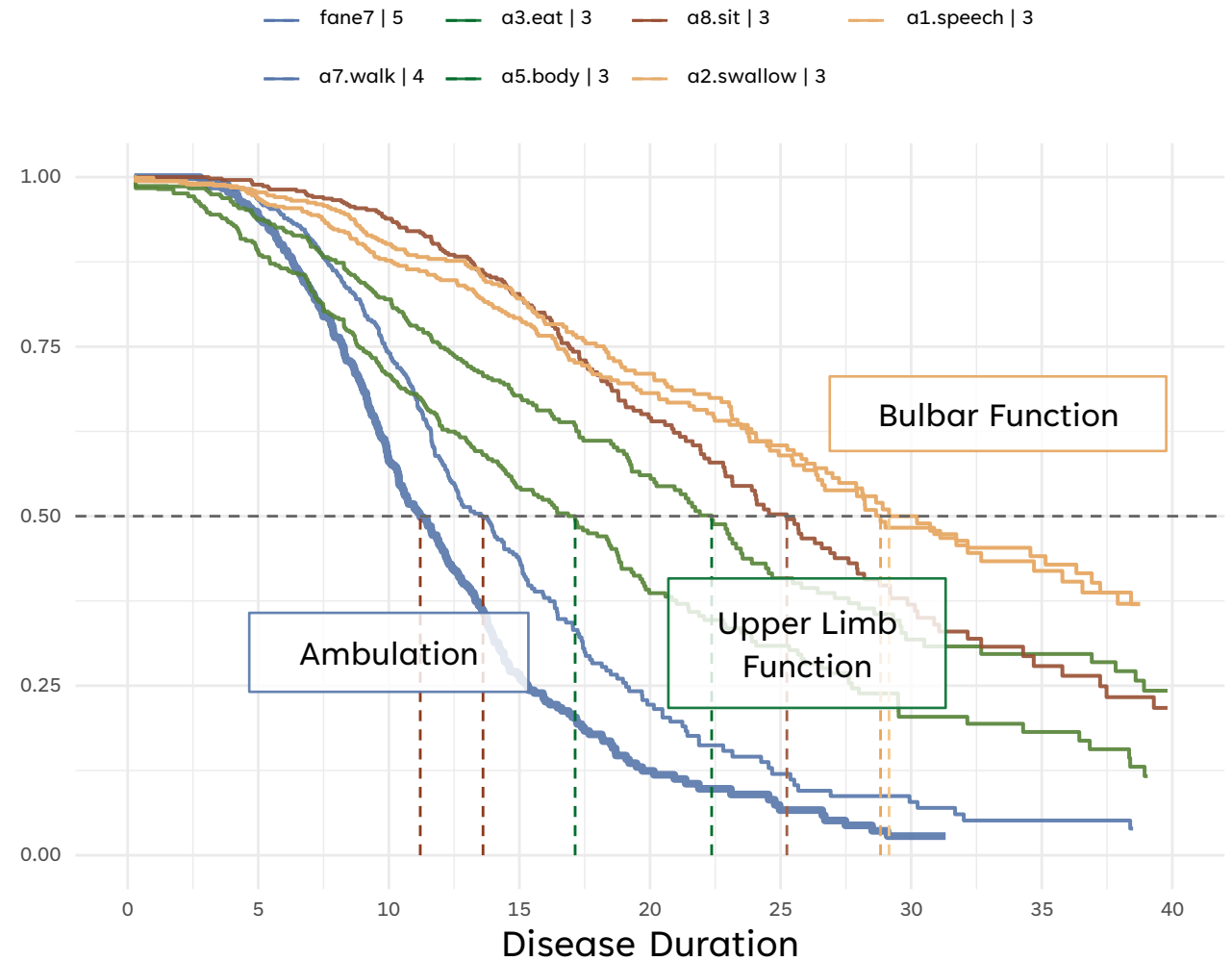
FA-ADL Items & Scoring



ADL Loss by Disease Duration

strata	par	thr	N	events.obs	median	lcn.pct	trunc.bias
<15y	fane7	5	999	292	11.2	31	2.2
<15y	a7.walk	4	1,002	253	13.6	26	2.8
<15y	a3.eat	3	1,001	237	17.1	22	5.7
<15y	a5.body	3	998	194	22.4	16	6.9
<15y	a8.sit	3	1,000	166	25.2	10	4.0
<15y	a2.swallow	3	995	151	28.8	10	8.1
<15y	a1.speech	3	1,000	142	29.2	9	7.4

Probability to Retain Function / ADL



fane7 5	999	874	401	130	40	14	3	2	2
a7.walk 4	1002	898	507	206	66	24	12	5	4
a3.eat 3	1001	823	498	271	125	70	30	19	10
a5.body 3	998	870	573	335	176	83	44	30	17
a8.sit 3	1000	915	648	405	199	101	50	25	15
a2.swallow 3	995	894	595	375	206	118	64	40	24
a1.speech 3	999	908	622	405	216	117	61	36	25

Disease Duration

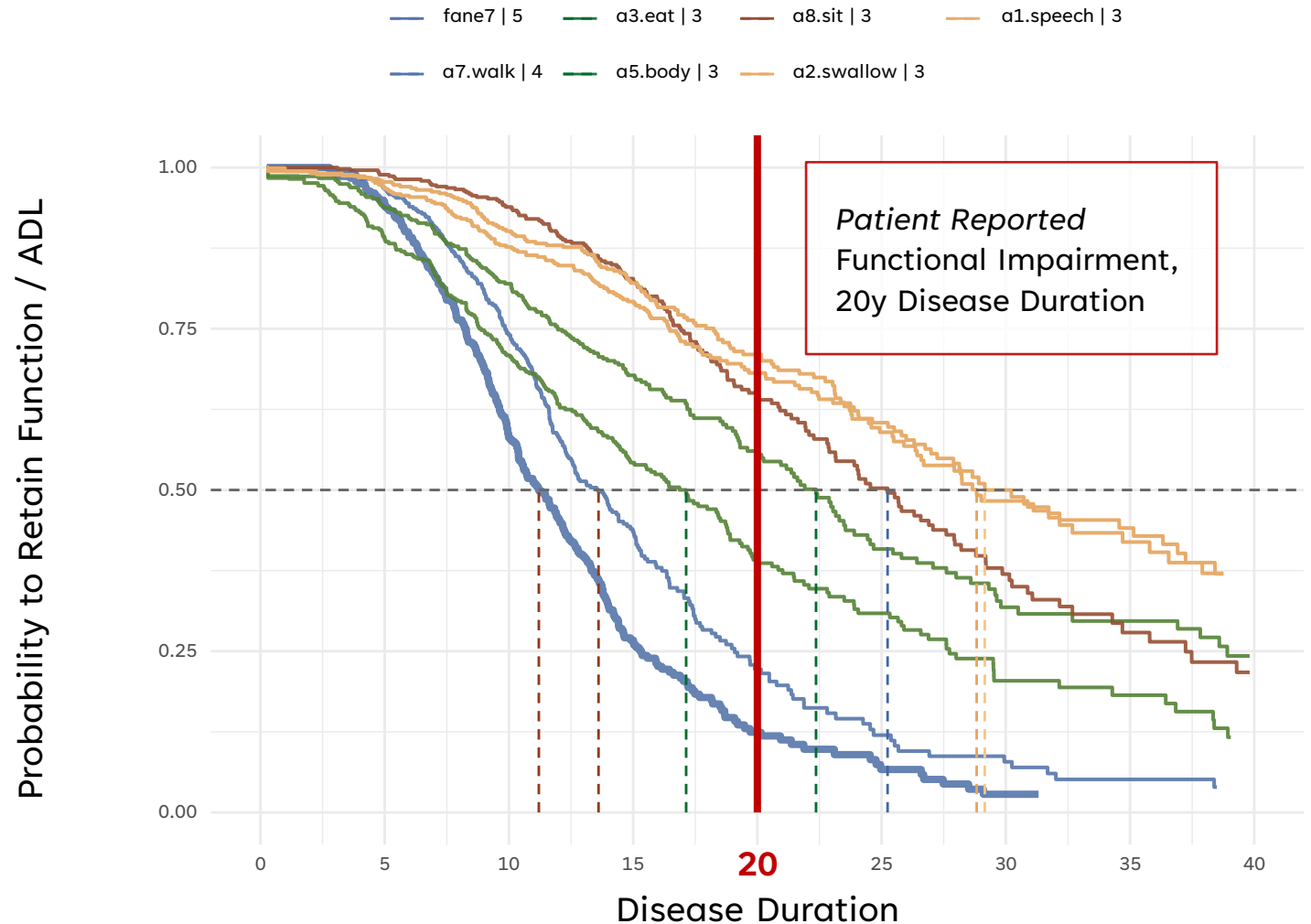
ADL Loss by Disease Duration

- Typical FRDA (onset <14y):
20y Disease Duration:

- 12% Ambulatory (FARS E7)
- 22% Ambulatory (FA-ADL 7 Walk)
- 38% moderate (or less) - cutting food
- 58% - personal hygiene

- From the Top

- 30% severe bulbar impairment

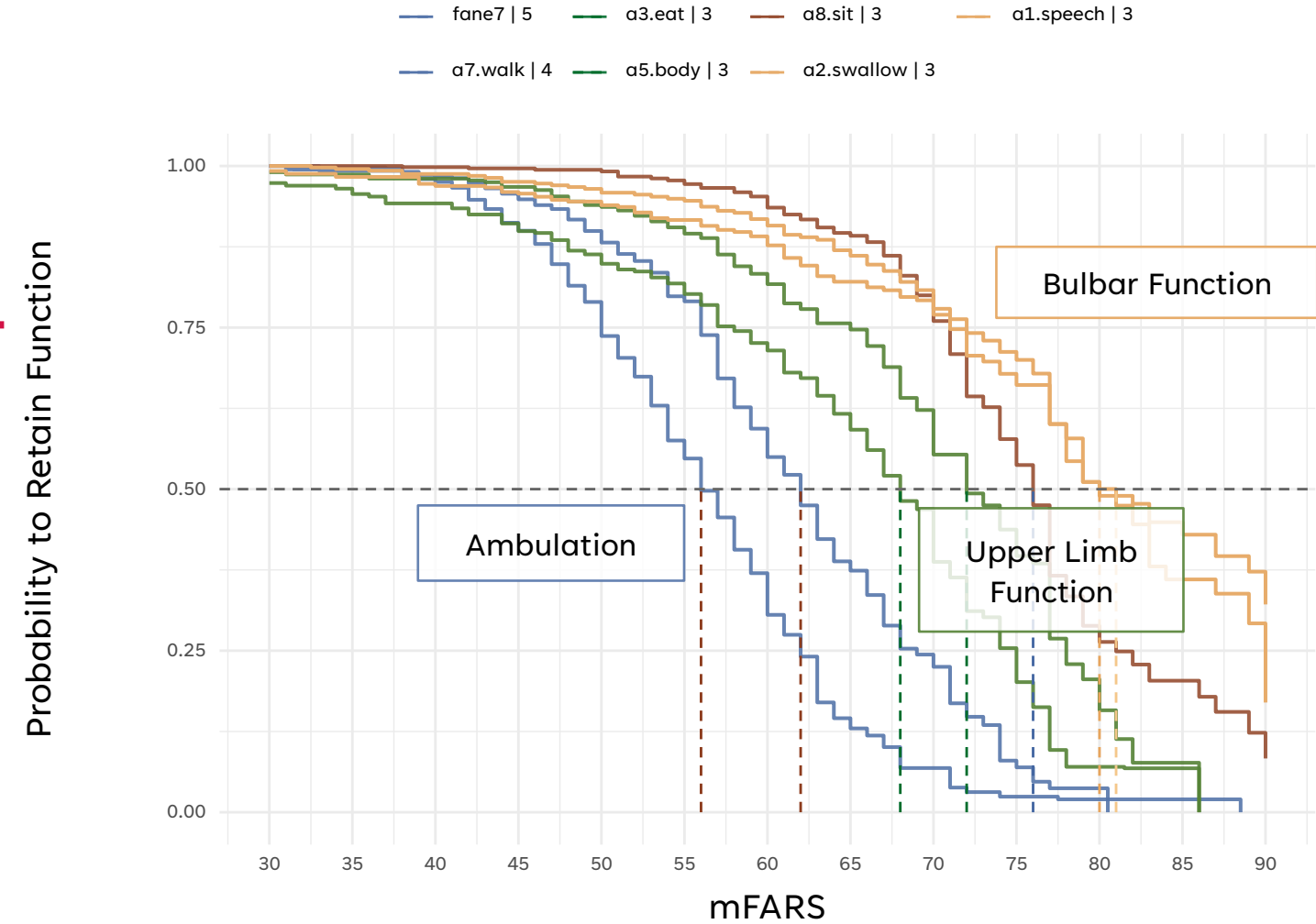


fane7 5	999	874	401	130	40	14	3	2	2
a7.walk 4	1002	898	507	206	66	24	12	5	4
a3.eat 3	1001	823	498	271	125	70	30	19	10
a5.body 3	998	870	573	335	176	83	44	30	17
a8.sit 3	1000	915	648	405	199	101	50	25	15
a2.swallow 3	995	894	595	375	206	118	64	40	24
a1.speech 3	999	908	622	405	216	117	61	36	25

Disease Duration

ADL Loss by mFARS Score

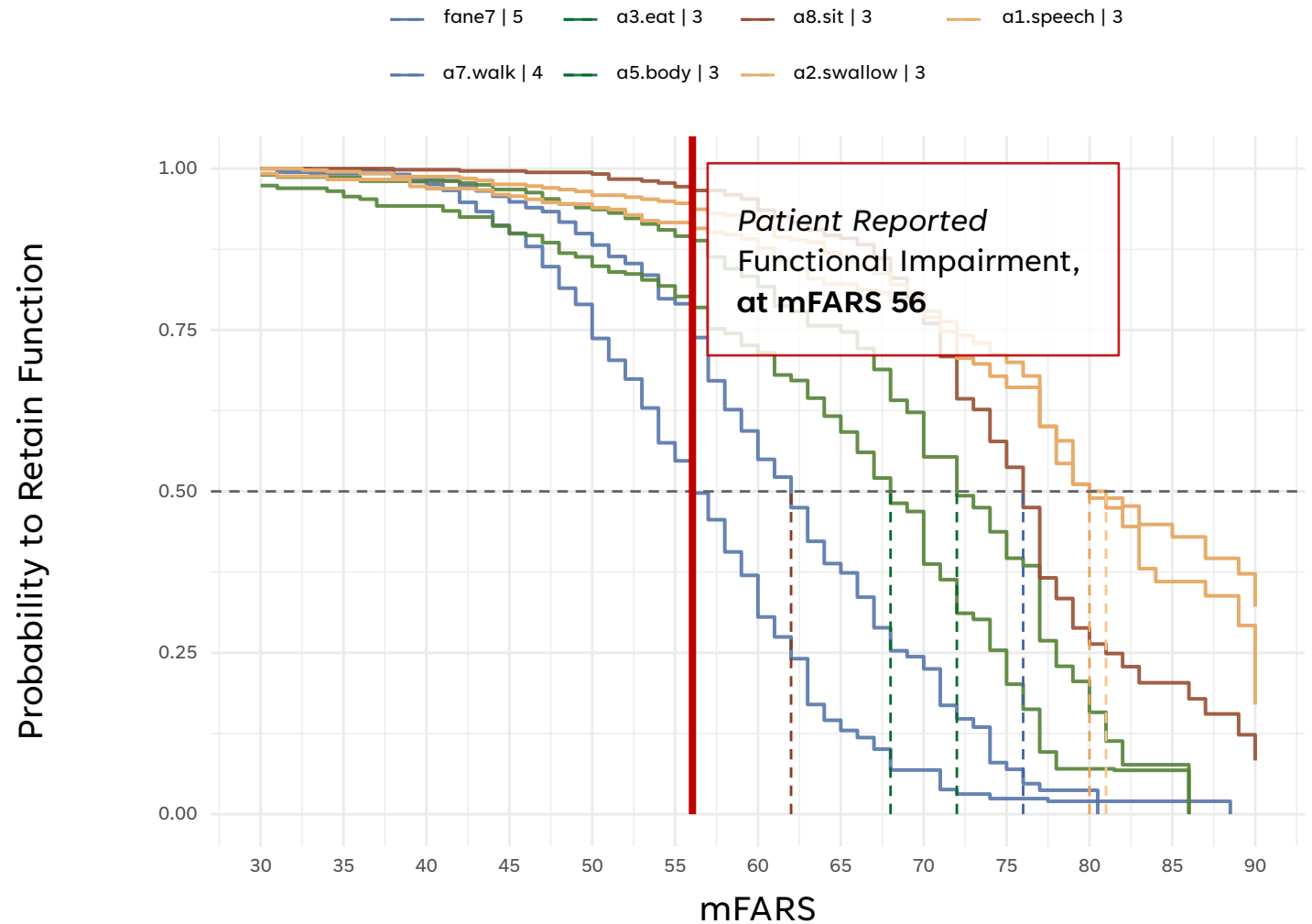
- **Loss of Ambulation**
 - 56 Median mFARS
- **Upper Limb Function (severe)**
 - 68-72 Range - mFARS
- **Loss of Bulbar Function (severe)**
 - 80-81 Range - mFARS



fane7 5	961	911	850	734	577	375	209	62	23	5	1	1	
a7.walk 4	835	793	733	653	547	418	260	129	63	15	2		
a3.eat 3	828	776	711	633	535	441	334	224	127	47	5	2	
a5.body 3	856	814	759	690	593	498	385	279	173	76	17	2	
a8.sit 3	884	845	792	730	649	556	458	340	226	110	34	12	4
a2.swallow 3	874	827	770	703	618	519	433	321	237	145	64	32	16
a1.speech 3	890	848	793	722	639	549	453	342	235	132	65	25	7

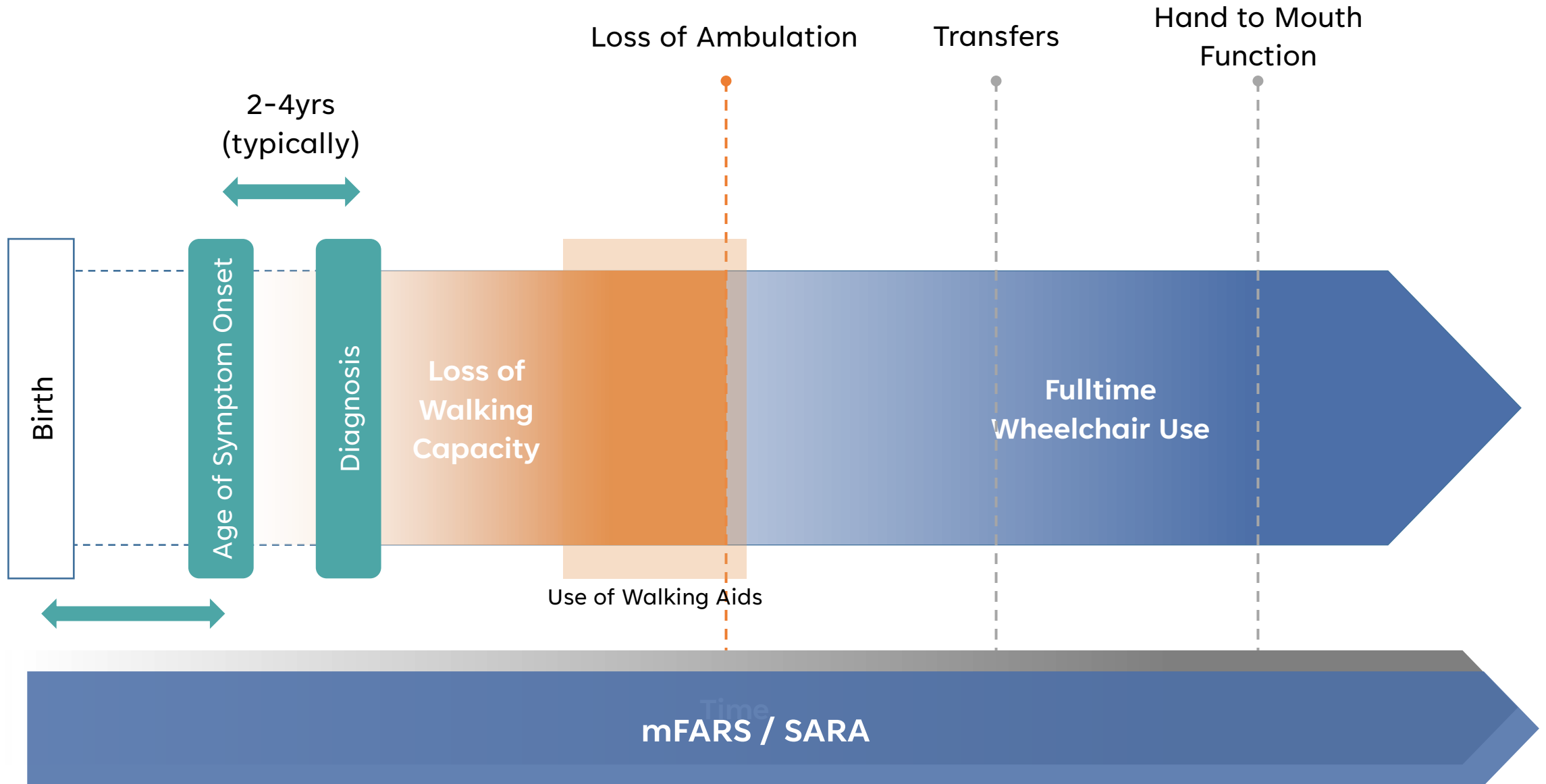
ADL Loss by mFARS Score

- Median mFARS Score at LoA: 56,
 - ➔ 50% Patients are non-ambulatory
 - ➔ 22% Ambulatory (FA-ADL 7 Walk)
- < 20% report severe upper limb impairment
- < 10% report severe bulbar function

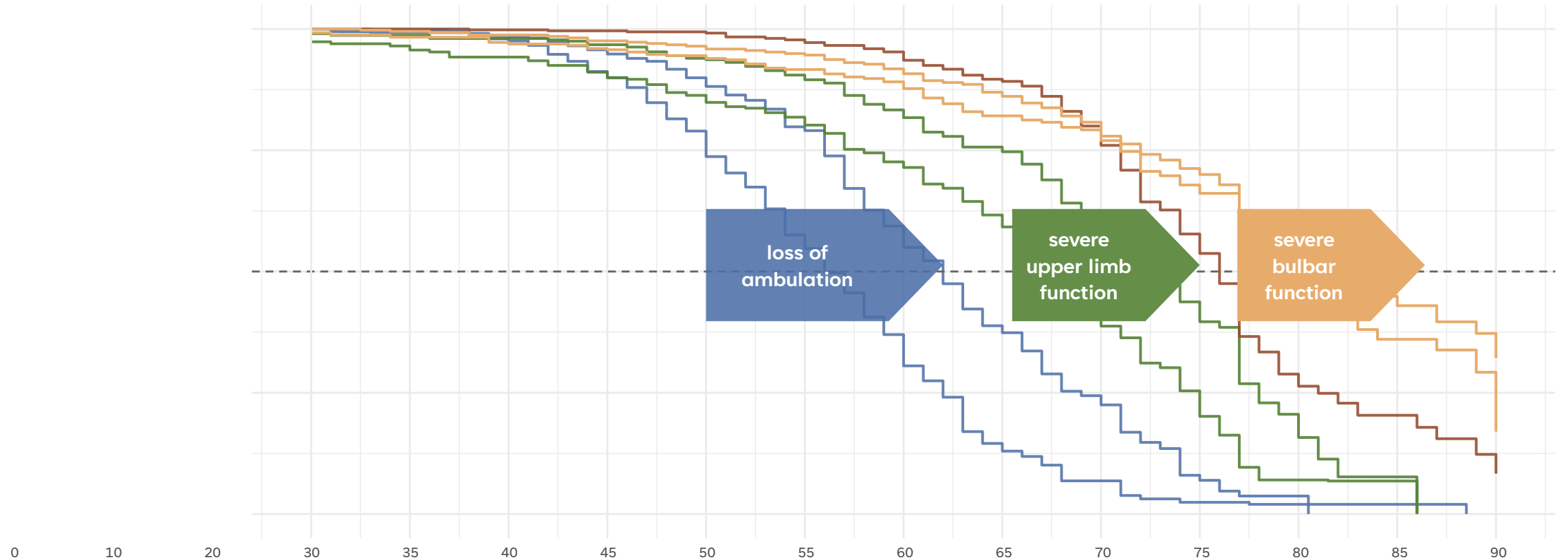


fane7 5	961	911	850	734	577	375	209	62	23	5	1	1	
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Disease Course - Ataxia

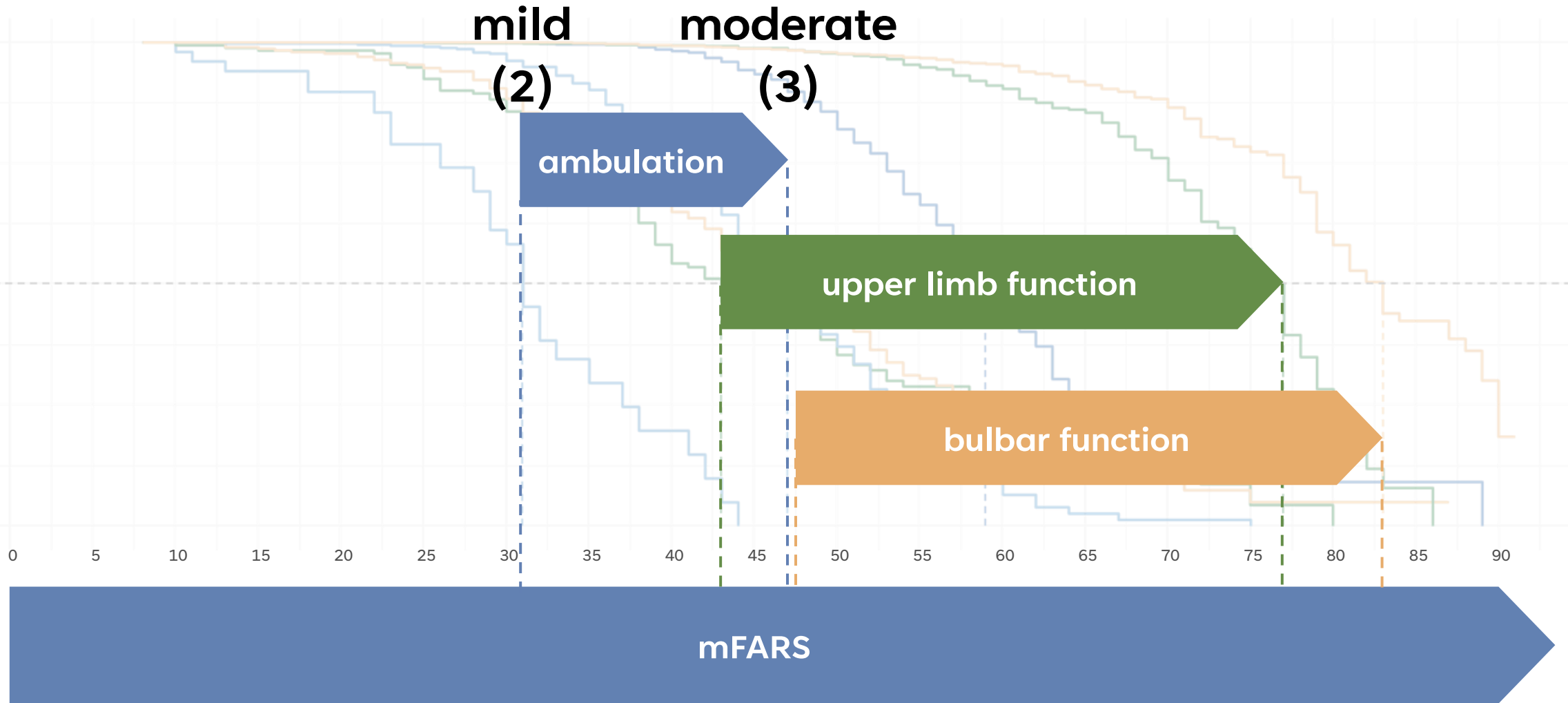


Disease Course - Ataxia



mFARS

Mild to Moderate Impairment by mFARS



Patient Reported Function Loss – along a Score-based axis

Idea: Assess Milestones on a “pseudo-time” Scale-axis

→ Link Score directly to patient reported function loss

- ADL-based “events” provide **patient centric interpretation**
- Supports the Understanding of Clinical Meaningfulness of Scores, and Score Changes