

Supplementary

Supplementary Figure 1 (A) FARS Disability Staging (FDS) and (B) Item and Sub score Overview of the neurological part of the FARS exam (FARSn). The mFARS is an abbreviated, used in contemporary clinical studies.³ Stance items within the FARS E/Upright stability sub score were marked in blue.

A

FARS Disability Staging (FDS)

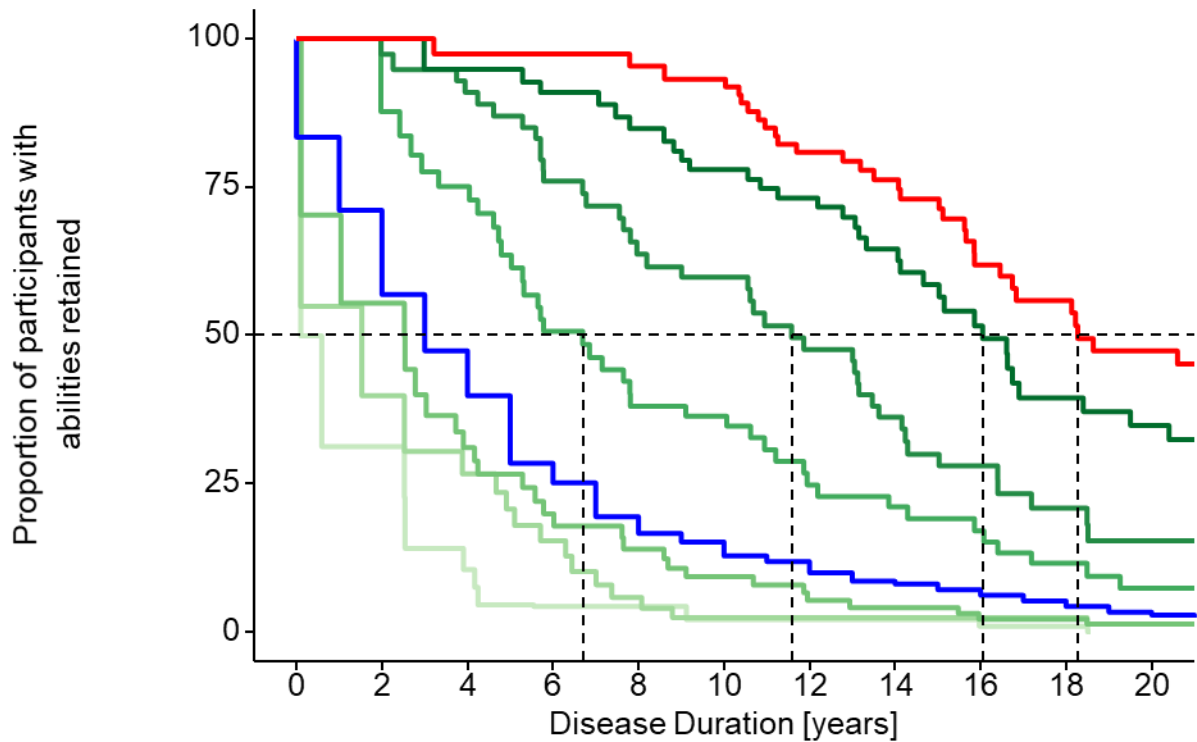
0	Normal.	
1	No disability.	Minimal signs detected by physician during screening. Can run or jump without loss of balance.
2	Minimal disability.	Symptoms present, recognized by subject, but still mild. Cannot run or jump without losing balance. The subject is physically capable of leading an independent life, but daily activities may be somewhat restricted.
3	Mild disability.	Symptoms are overt and significant. Requires regular or periodic holding onto wall/furniture or use of a cane for stability and walking. <small>(Note: Subjects postpone obtaining a cane by avoiding open spaces and walking with the aid of walls/people etc. These subjects are graded as stage 3.0.)</small>
4	Moderate disability.	Walking requires a walker, Canadian crutches or two canes. Or other aids such as walking dogs. Can perform several activities of daily living.
5	Severe disability.	Confined but can navigate a wheelchair. Can perform some activities of daily living that do not require standing or walking.
6	Total disability.	Confined to wheelchair or bed with total dependency for all activities of daily living.

B

	FARSn (125)	mFARS (93)
A1 (3) facial atrophy A3 (2) cough A2 (3) tongue atrophy A4 (3) speech	Bulbar	Bulbar
B1 (3+3) finger-finger B4 (3+3) rapid movements B2 (4+4) nose-finger B5 (4+4) finger taps B3 (4+4) dysmetria	Upper Limb	Upper Limb
C1 (4+4) heel shin slide C2 (4+4) heel shin tap	Lower Limb	Lower Limb
D1 (2+2) muscle atrophy D4 (2+2) position sense D2 (5+5) mus. weakness D5 (2+2) deep tendon reflexes D3 (2+2) vibratory sense	Peripheral Nerves	
E1 (4) sitting position E4 (4) tandem stance E2A (4) stance feet apart E5 (4) stance dom. foot E2B (4) - eyes closed E6 (3) tandem walk E3A (4) stance feet tog. E7 (5) gait E3B (4) - eyes closed	Upright Stability	Upright Stability

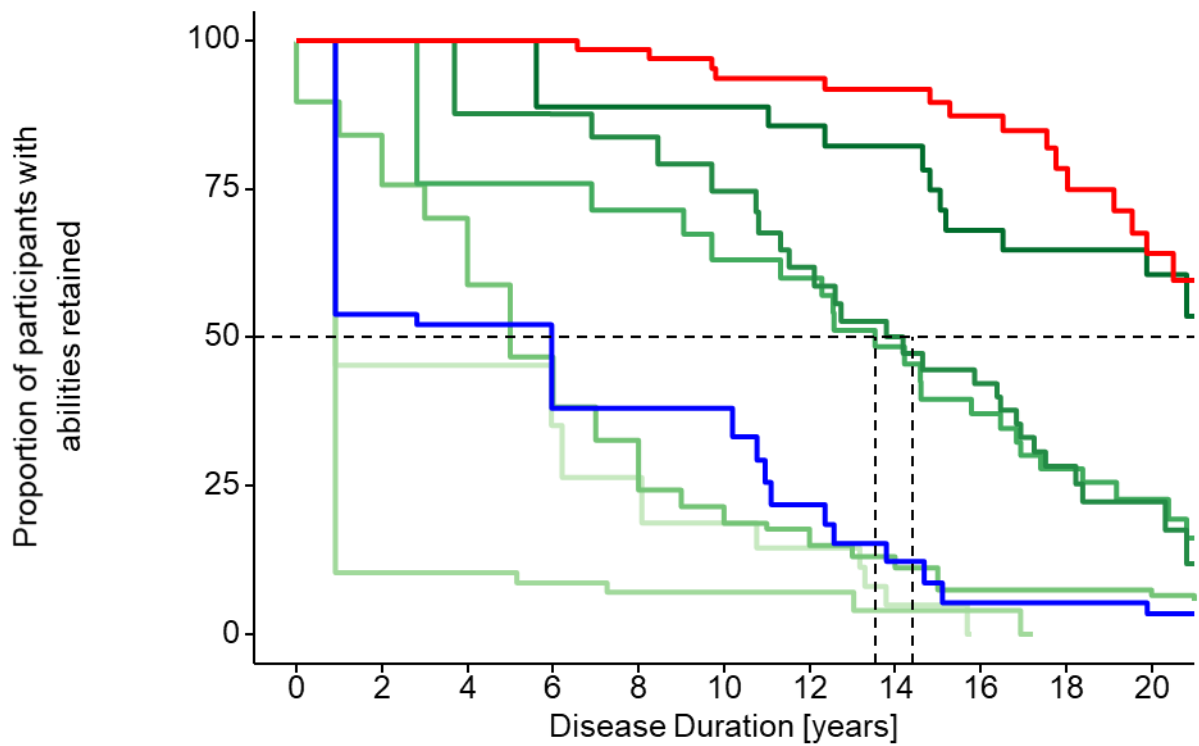
Supplementary Figure 2 Estimates for LoA and loss of function of FARS E stance items, onset group 15-24y (A) and >24y (B).

A



		Number at risk										
		0	2	4	6	8	10	12	14	16	18	20
LoA / Stance Items	E5	211	65	22	7	7	3	3	3	2	2	0
	E4	211	83	54	30	11	5	4	4	4	4	2
	E3B	211	117	65	40	26	17	9	7	4	4	2
	Diagnosis	211	150	100	60	41	32	25	18	15	11	7
	E2B	211	183	154	100	69	61	36	29	21	14	7
	E3A	211	204	183	146	114	97	70	48	32	22	14
	E2A	211	209	191	176	151	127	108	84	60	41	33
	LoA/E7	211	209	196	188	168	150	117	99	72	59	44

B



		Number at risk										
LoA / Stance Items		0	2	4	6	8	10	12	14	16	18	20
		E5	107	49	49	35	26	17	12	3	0	0
	E4	107	11	11	8	6	6	6	2	2	0	0
	E3B	107	90	75	50	35	23	19	14	8	8	8
	Diagnosis	107	58	54	38	36	34	18	9	4	4	3
	E2B	107	107	80	77	69	56	51	40	29	20	13
	E3A	107	107	92	87	80	66	53	42	34	18	11
	E2A	107	107	105	88	85	78	72	63	48	35	27
	LoA/E7	107	107	105	98	94	82	79	71	61	45	31

Supplementary Table 1: Number of Participants at Baseline visit with respective function loss patterns. A ‘0’ stands for able, a ‘1’ stands for unable. The expected pattern loss is E2B, E3A, E2A and E7. Percentages are based on onset groups.

N (%)	Onset Group	<15y	15-24y	>24y	All
Pattern					
Expected pattern of function loss					
All regular		676 (96)	204 (97)	101 (94)	981 (96)
000.0		202 (29)	76 (36)	49 (45)	327 (32)
100.0		96 (14)	35 (17)	10 (10)	141 (14)
110.0		101 (14)	22 (10)	11 (10)	134 (13)
111.0		51 (7)	21 (10)	14 (13)	86 (8)
111.1		226 (32)	50 (24)	17 (16)	293 (29)
Unusual patterns of function loss					
010.0		22 (3)	4 (2)	5 (5)	31 (3)
101.0		0	1 (0)	0	1 (0)
Non-ambulant, with some ability to stand					
110.1		4 (1)	2 (1)	1 (1)	7 (1)
010.1		1 (0)	0	0	1 (0)
011.1		0	0	0	0

Supplementary Table 2: Estimates for LoA by Onset group, and for loss of function of FARS E Items (Onset Groups 15-24y, >24y).

Onset Subgroup	Item	Description	Median Duration [y]	25, 75 percentiles	Subjects	Observed Events	left censored [%]	truncation bias* [y]
Loss of Stance Functions in the FARS E Sub score, Intermediate Onset Group (15-24y)								
15-24y	E5	Stance Dominant Foot	0.1	0.1, 2.5	211	9	95	6.6
15-24y	E3B	Stance Feet Together, Eyes Closed	1.5	0.1, 4.7	211	15	90	5.5
15-24y	E4	Stance, Tandem	2.5	0.1, 5.3	211	27	84	6.1
15-24y	-	Diagnosis of FRDA	3.0	1.0, 7.0	211	206	3	-
15-24y	E2B	Stance Feet Apart, Eyes Closed	6.7	4.0, 11.9	211	40	62	7.2
15-24y	E3A	Stance, Feet Together	11.6	6.7, 16.4	211	43	47	3.4
15-24y	E2A	Stance, Feet Apart	16	10.8, 23.6	211	41	34	7.6
15-24y	E7	LoA / Gait	18.3	14.1, 27.5	211	45	25	7
15-24y	FDS	Disease Stage	20.4	14.5, 28.2	211	41	25	4.5
Loss of Stance Functions in the FARS E Sub score, Late Onset Group (>24y)								
>24y	E5	Stance Dominant Foot	0.9	0.9, 0.9	107	3	95	16
>24y	E4	Stance, Tandem	0.9	0.9, 8.1	107	9	86	12.4
>24y	-	Diagnosis of FRDA	5.0	3.0, 8.0	107	104	4	-
>24y	E3B	Stance Feet Together, Eyes Closed	6.0	0.9, 11.1	107	14	79	7.8
>24y	E2B	Stance Feet Apart, Eyes Closed	13.5	6.9, 19.2	107	25	50	5.6
>24y	E3A	Stance, Feet Together	14.2	9.7, 18.4	107	26	45	3.3
>24y	E2A	Stance, Feet Apart	22.4	14.8, 30.1	107	14	29	7.7
>24y	FDS	Disease Stage	23.5	16.9, 30.1	107	15	22	6.7
>24y	E7	LoA / Gait	23.5	18, 30.1	107	21	17	4.7