SNUH 근신경계질환 심포지엄
ALS staging system: King's, MiToS and Beyond

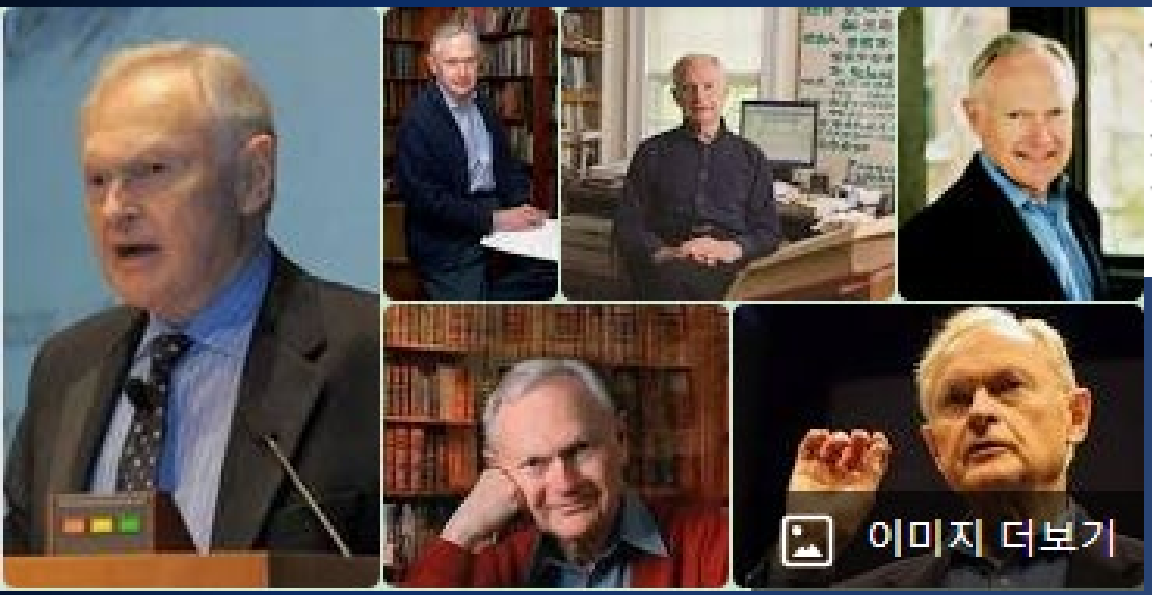
노원을지대학교 병원 신경과
유일한

Disease staging: Implications for hospital reimbursement and management

by Jonathan E. Conklin, John V. Lieberman, Cathleen A. Barnes, and Daniel Z. Louis

The current patient classification schemes used in case-mix reimbursement are not fully sensitive to variations in resource consumption that are associated with differential disease severity. Disease staging is a clinically based measure of severity that uses objective medical criteria to assess the stage of disease progression. Its availability in automated form increases its ease of implementation in hospital reimbursement and management. Results of recent studies demonstrate that staging is a useful case-mix reimbursement and management tool that explains significant variation in cost per discharge within current diagnosis-related groups.

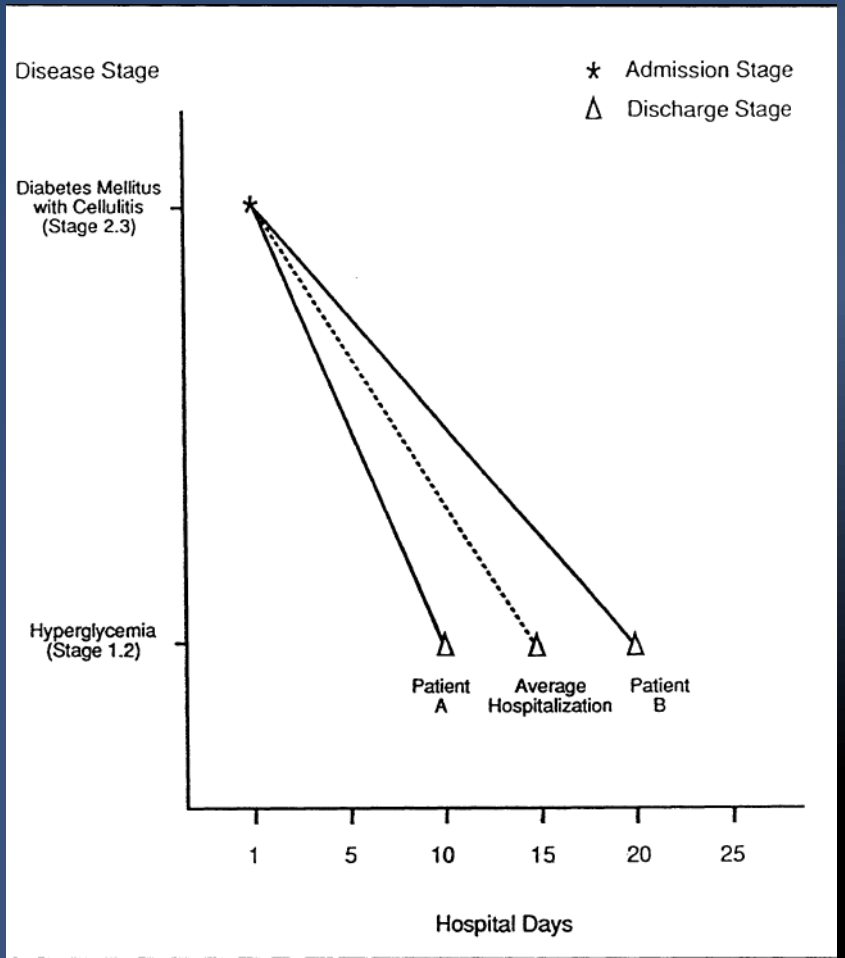
Health Care Financing Review/Nov. 1984/Annual Supplement



A disease can be effectively treated only when I as a doctor understand its causes in that particular patient, its site of origin, the internal havoc it creates, and the course which the process is likely to take whether treated or not. With that knowledge, I can make a diagnosis, prescribe a program of treatment, and predict an outcome. (p. xvii)

Role of staging system

1. Applied to Clinical trials
2. Evaluation of changes in severity as an outcome measure
3. Profiling practice patterns and clinical experience
4. Guidelines development
5. Evaluating clinical credentials



CLINICAL OUTCOMES MANAGEMENT AND DISEASE STAGING

LEONA E. MARKSON
DAVID B. NASH
DANIEL Z. LOUIS
JOSEPH S. GONNELLA
Jefferson Medical College

EVALUATION & THE HEALTH PROFESSIONS, Vol. 14 No. 2, June 1991 201-227

Amyotrophic Lateral Sclerosis

- Progressive upper and lower motor neuron degeneration,
- Poor (median survival 3-5 years) and variable prognosis.
- Staging system for informing disease progression and prognosis

Neuromuscular

RESEARCH PAPER

Evidence of multidimensionality in the ALSFRS-R Scale: a critical appraisal on its measurement properties using Rasch analysis

Franco Franchignoni,[1] Gabriele Mora,[2] Andrea Giordano,[3] Paolo Volanti,[4] Adriano Chiò[5]

Table 2 Factor analysis for a three factor solution, as suggested by parallel analysis

	Varimax rotated loadings		
Item	Factor 1	Factor 2	Factor 3
1. Speech	**0.92**	0.16	0.12
2. Salivation	**0.87**	0.18	0.12
3. Swallowing	**0.86**	0.32	0.18
4. Handwriting	0.15	0.18	**0.84**
5. Cutting food and handling utensils	0.15	0.22	**0.86**
6. Dressing and hygiene	0.11	0.28	**0.91**
7. Turning in bed and adjusting bedclothes	0.17	0.23	**0.92**
8. Walking	0.10	0.29	**0.78**
9. Climbing stairs	0.10	0.31	**0.79**
10. Dyspnoea	0.28	**0.82**	0.32
11. Orthopnoea	0.31	**0.74**	0.39
12. Respiratory insufficiency	0.21	**0.75**	0.32

King's system

- Based on the number of affected regions of the body.
- Stage 1: first region involvement
- Stage 2A: diagnosis
- Stage 2B: second region involvement
- Stage 3: third region involvement


doi:10.1093/brain/awr351 Brain 2012: 135; 847–852 | 847

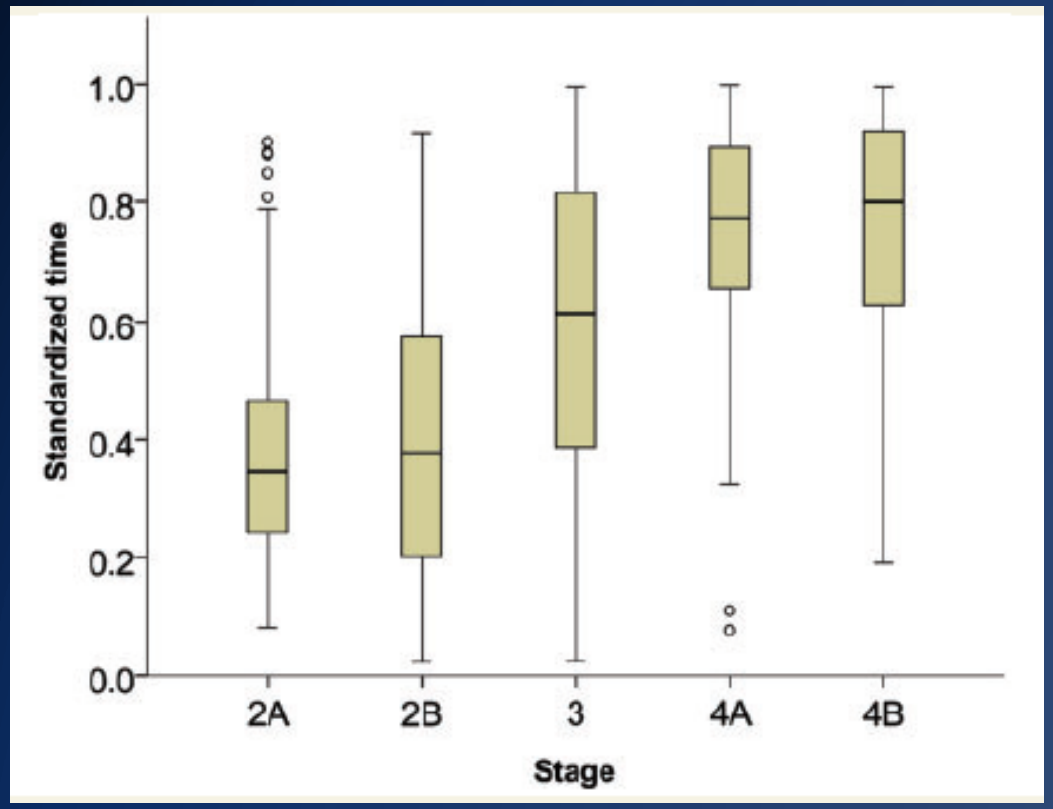
BRAIN
A JOURNAL OF NEUROLOGY

A proposed staging system for amyotrophic lateral sclerosis

Jose C. Roche,[1,2] Ricardo Rojas-Garcia,[1,3] Kirsten M. Scott,[1] William Scotton,[1] Catherine E. Ellis,[4] Rachel Burman,[5] Lokesh Wijesekera,[1] Martin R. Turner,[6] P. Nigel Leigh,[1,7] Christopher E. Shaw[1] and Ammar Al-Chalabi[1]

- Stage 4A: need for gastrostomy / Stage 4B: need for noninvasive ventilation
- Stage 5: death

King's system



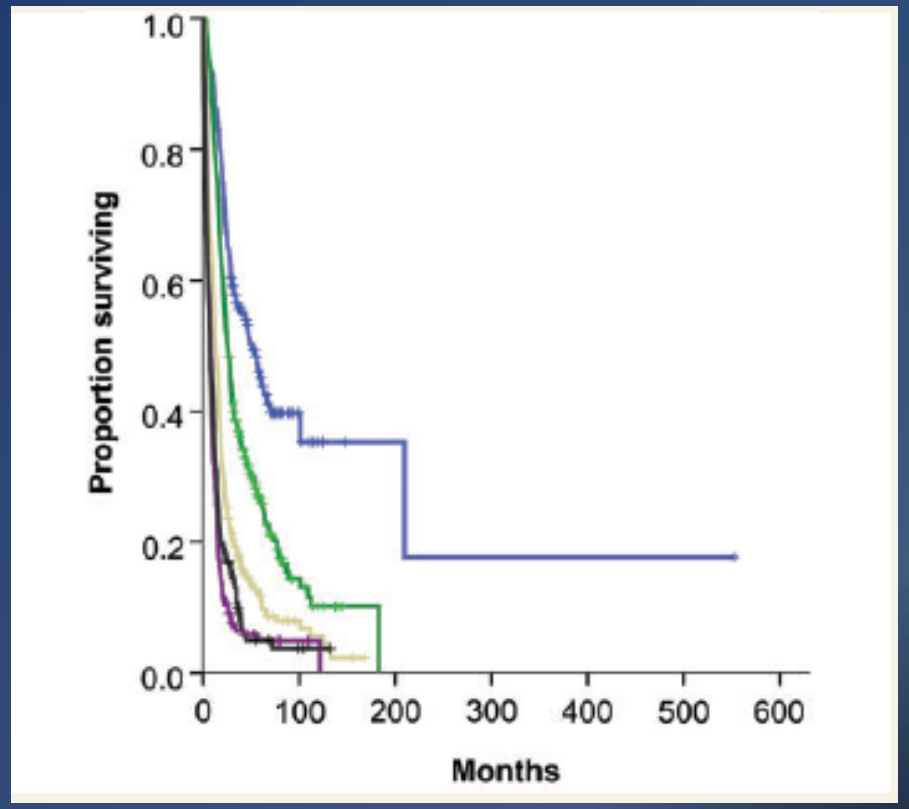
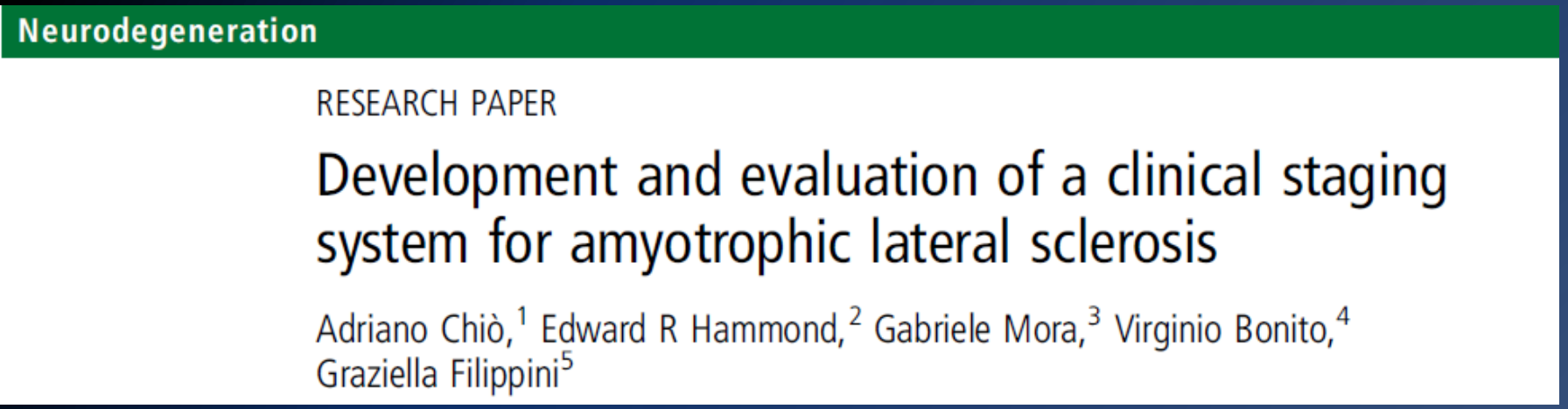


Table 3 Kaplan–Meier analysis of survival from each milestone

Last recorded milestone	Bulbar onset ALS		Limb onset ALS	
	Median (months)	5 year (%)	Median (months)	5 year (%)
Diagnosis	19	20.5	59	49.9
Involvement of second region	19	17.5	28	29.0
Involvement of third region	13	9.8	13	12.3
Need for gastrostomy	9	6.4	6	4.2
Need for non-invasive ventilation	3	5.9	8	6.0

Milano-Torino system (MiToS)



- Based on a clinical scale.
- Stage 0: symptoms only, loss of independence (-)
- Stage 1-4: loss of independence in a number of 4 domains from ALS Functional Rating Scale-Revised (ALSFRS-R)
- Stage 5: death

Table 1 Functional domains and stages

ALSFRS domain	Item	Score	Functional score*
Movement (walking/self-care)†	8	4 Normal	0
	Walking	3 Early ambulation difficulties	
		2 Walks with assistance	
		1 Non-ambulatory functional movement only	1
	OR	0 No purposeful leg movement	
	6	4 Normal function	0
	Dressing and hygiene	3 Independent and complete self-care with effort or decreased efficiency	
		2 Intermittent assistance or substitute methods	
		1 Needs attendant for self-care	1
		0 Total dependence	
Swallowing	3	4 Normal eating habits	0
	Swallowing	3 Early eating problems; occasional choking	
		2 Dietary consistency changes	
		1 Needs supplemental tube feeding	1
		0 NPO (exclusively parenteral or enteral feeding)	
Communicating†	1	4 Normal speech processes	0
	Speech	3 Detectable speech with disturbances	
		2 Intelligible with repeating	
		1 Speech combined with non-vocal communication	1
	AND	0 Loss of useful speech	
	4	4 Normal	0
	Handwriting	3 Slow or sloppy; all words are legible	
		2 Not all words are legible	
		1 Able to grip pen but unable to write	1
		0 Unable to grip pen	
Breathing†	10	4 None	0
	Dyspnea	3 Occurs when walking	
		2 Occurs with one or more of: eating, bathing, dressing	
		1 Occurs at rest, difficulty breathing when either sitting or lying	1
	OR	0 Significant difficulty, considering using mechanical respiratory support	
	12	4 None	0
	Respiratory insufficiency	3 Intermittent use of NIPPV	
		2 Continuous use of NIPPV during the night	1
		1 Continuous use of NIPPV during the night and day	
		0 Invasive mechanical ventilation by intubation or tracheostomy	

8. 걷기	정상	경한 걷기 장애가 있습니다.	보조기(워커walker, 지팡이, 족부보장구AFO)를 사용해서 걸을 수 있습니다.	다리를 움직일 수는 있으나 걸을 수 없습니다.	다리를 의도대로 움직일 수 없습니다.
6. 옷입기와 위생	정상 기능	느리고 어둔하지만 도움을 받지 않고 옷 입기와 몸씻기가 가능합니다.	간헐적으로 도움이 필요하거나 타인의 도움을 대신할 대체 방법을 사용합니다.	자발적인 옷 입기와 몸씻기 동작이 일부 가능하나 지속적인 도움이 필요합니다.	전적으로 타인의 도움이 필요합니다.

OR

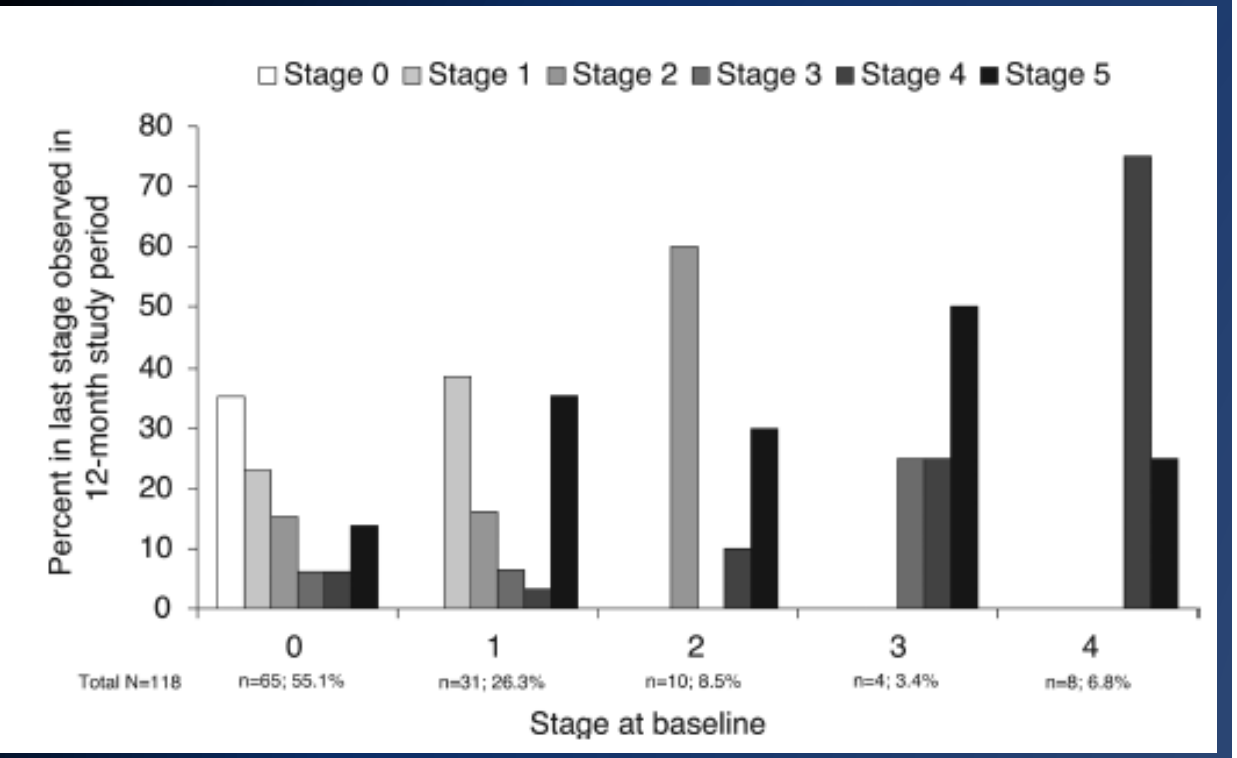
3. 삼키기	정상	경한 삼키기 장애가 있습니다. 가끔 사래가 들립니다.	음식물을 삼키기 위해 연식이나 유동식이 필요합니다.	위관의 사용이 필요합니다.	입으로는 음식물을 섭취할 수 없습니다(비경구적, 또는 장으로 직접 주입해야 합니다).

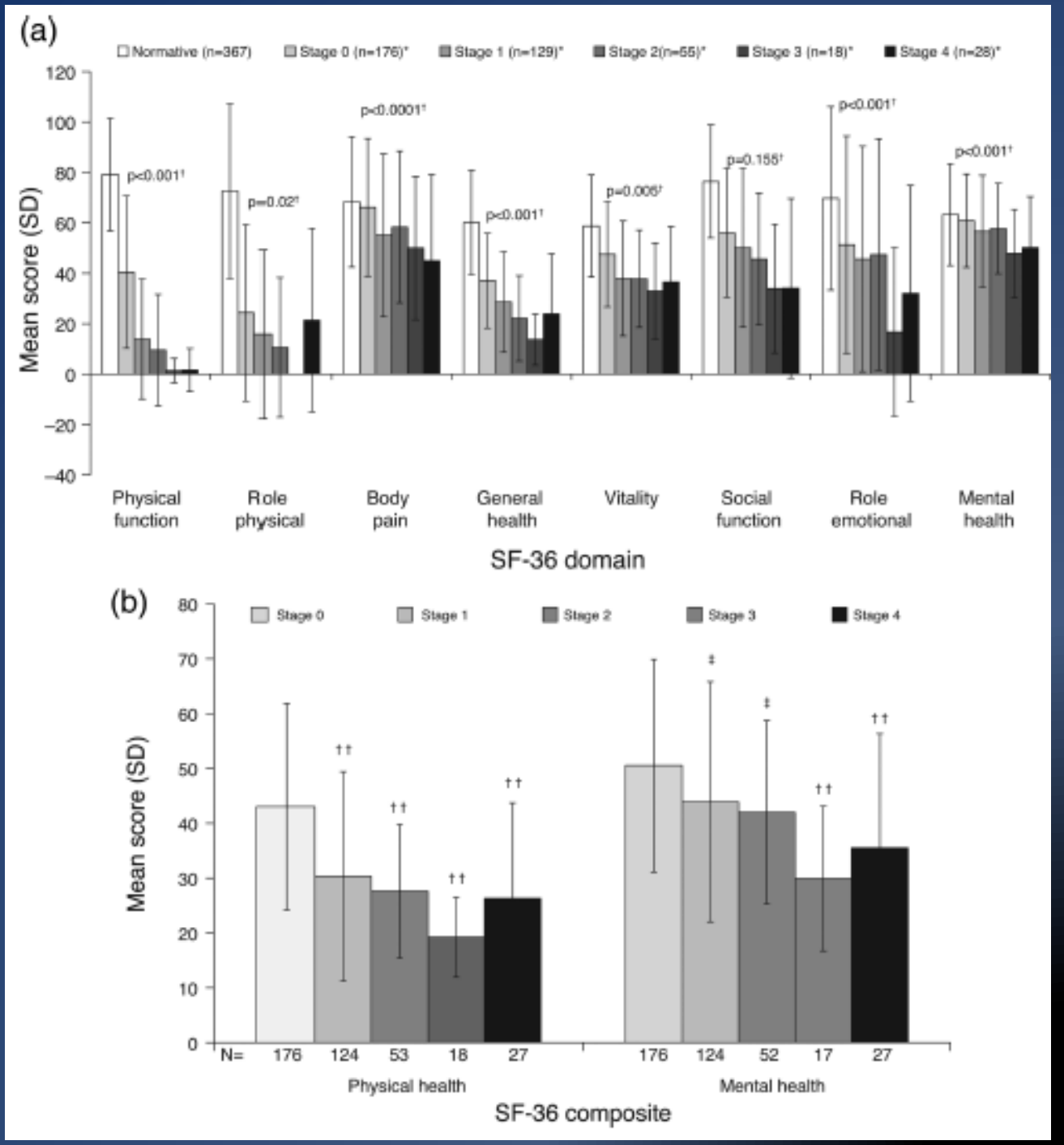
1. 말하기	정상	검사자가 인지할 만한 말하기 장애를 가지고 있습니다.	환자가 반복해서 말을 해야 의미를 알 수 있습니다.	비언어적인 방법 (몸짓 등)을 사용해야 의사소통이 가능합니다.	의미 있는 말하기 능력을 소실했습니다.
4. 쓰 기 (오른손잡이는 오른손, 왼손잡이는 왼손 기준)	정상	글쓰기가 느려지거나 글씨가 번져서 지저분해 집니다 ; 모든 글씨는 알아볼 수 있습니다.	일부 글씨는 읽기 어렵습니다.	펜을 잡을 수는 있지만 글쓰기는 불가능합니다.	펜을 잡기가 불가능합니다.

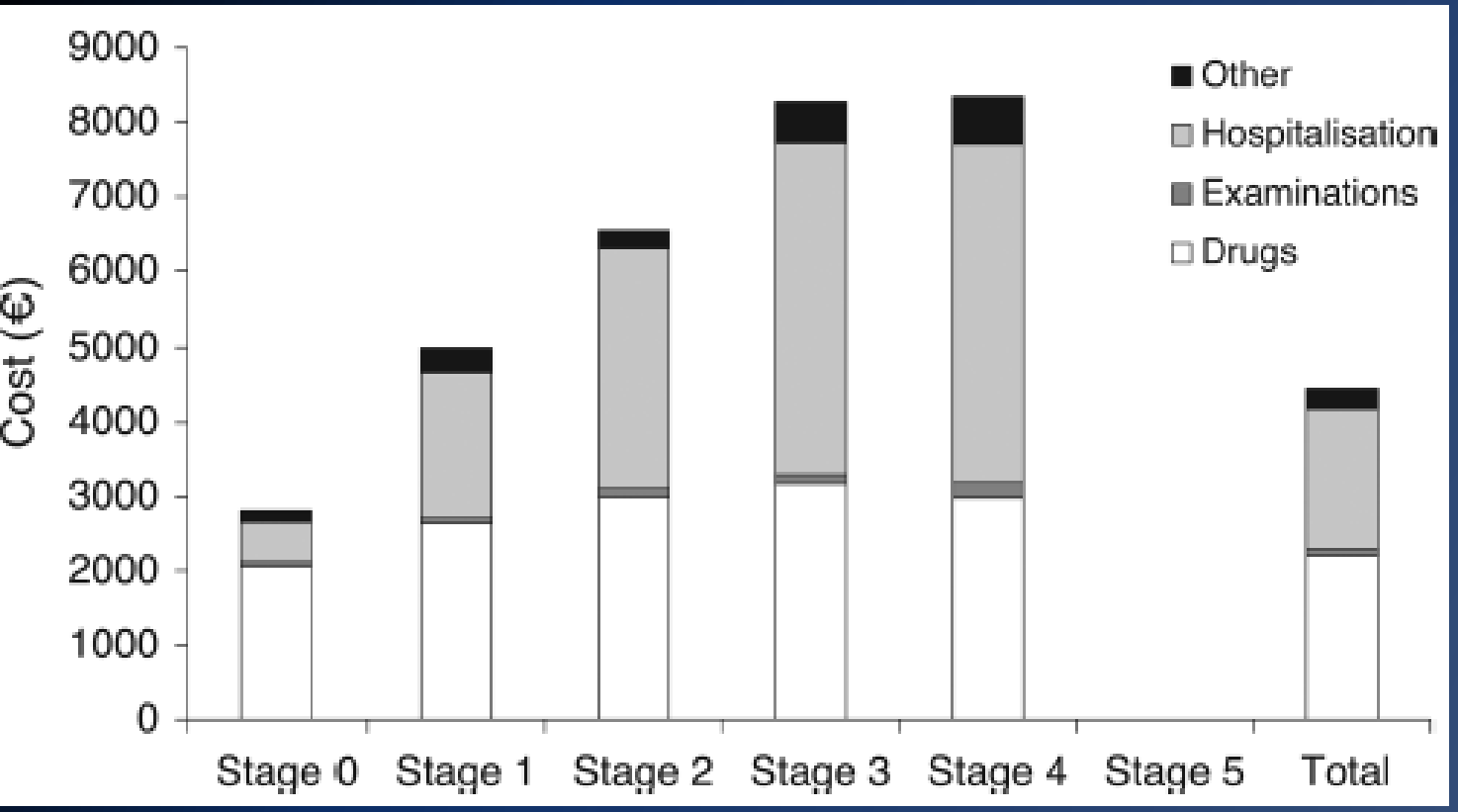
AND

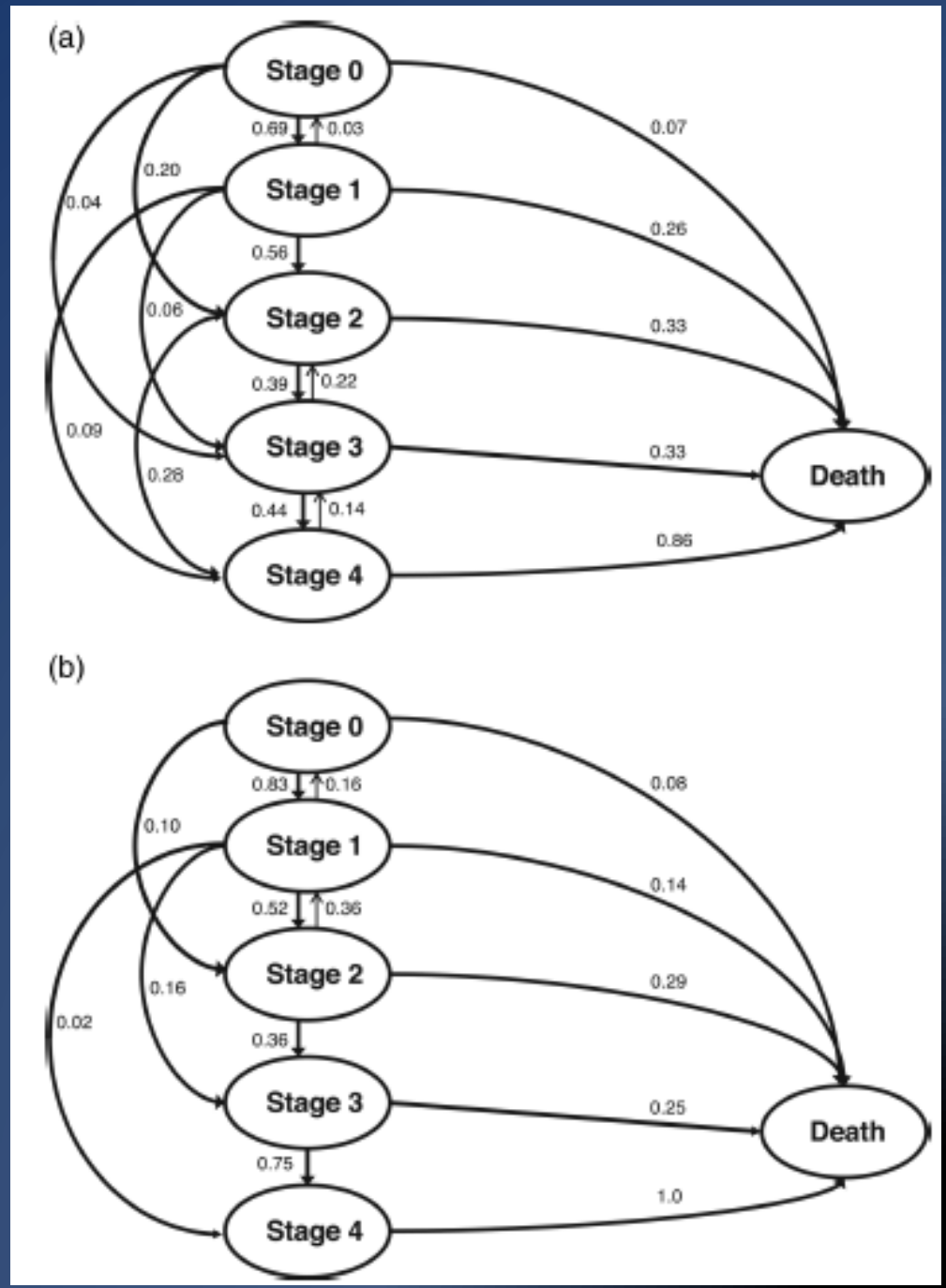
10. 호흡곤란 Dyspnea (기관절개술 시 0점)	없음	보행시에 숨이 가쁩니다.	식사시, 목욕시, 옷갈아 입을 때 중 1가지 이상에서 숨이 가쁩니다.	휴식시에 생기며 앉거나 누울 때 숨쉬기가 힘이 듭니다.	뚜렷한 호흡 장애가 있으며 인공호흡기 착용을 고려하게 됩니다.
12. 호흡부전 Respiratory insufficiency (기관절개술 시 0점)	없음	때때로 코나 입을 통해서 압력을 주는 기계호흡기(BiPAP)를 사용합니다.	밤에는 지속적으로 코나 입을 통해서 압력을 주는 기계호흡기(BiPAP)를 사용합니다.	하루 종일 코나 입을 통해서 압력을 주는 기계호흡기(BiPAP)를 사용합니다.	기관내삽관이나 기관절개술에 의한 인공호흡기(Invasive mechanical ventilation)를 사용합니다

OR


Stage 0
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Percent in last stage observed in 12-month study period
80
70
60
50
40
30
20
10
0
0
1
2
3
4
Total N=118
n=65; 55.1%
n=31; 26.3%
n=10; 8.5%
n=4; 3.4%
n=8; 6.8%
Stage at baseline


(a)
Normative (n=367)
Stage 0 (n=176)*
Stage 1 (n=129)*
Stage 2(n=55)*
Stage 3 (n=18)*
Stage 4 (n=28)*
Mean score (SD)
120
100
80
60
40
20
0
−20
−40
p<0.001†
p=0.02†
p<0.0001†
p<0.001†
p=0.005†
p=0.155†
p<0.001†
p<0.001†
Physical function
Role physical
Body pain
General health
Vitality
Social function
Role emotional
Mental health
SF-36 domain
(b)
Stage 0
Stage 1
Stage 2
Stage 3
Stage 4
Mean score (SD)
80
70
60
50
40
30
20
10
0
††
‡
N=
176
124
53
18
27
176
124
52
17
27
Physical health
Mental health
SF-36 composite


9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Cost (€)
Other
Hospitalisation
Examinations
Drugs
Stage 0
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Total


(a)
Stage 0
Stage 1
Stage 2
Stage 3
Stage 4
Death
0.69
0.03
0.07
0.20
0.04
0.26
0.56
0.06
0.33
0.39
0.22
0.09
0.33
0.28
0.44
0.14
0.86
(b)
Stage 0
Stage 1
Stage 2
Stage 3
Stage 4
Death
0.83
0.16
0.08
0.10
0.14
0.52
0.36
0.16
0.29
0.02
0.36
0.25
0.75
1.0

Comparison between two staging

- King's system
  - occurred at predictable times, evenly spaced out
  - Stage↑: survival↓, deaths↑
- MiToS system: skewed towards later phases.
  - Survival curves overlapped, homogenous deaths throughout most stages.

ORIGINAL ARTICLE

Amyotrophic lateral sclerosis: a comparison of two staging systems in a population-based study

D. Ferraro[a], D. Consonni[b], N. Fini[a], A. Fasano[a], C. Del Giovane[c], Emilia Romagna Registry for ALS (ERRALS) Group* and J. Mandrioli[a]

[a]*Department of Biomedical Metabolic and Neurosciences, Nuovo Ospedale Civile S. Agostino Estense, University of Modena and Reggio Emilia, Modena;* [b]*Epidemiology Unit, Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Milan; and* [c]*Department of Diagnostic and Clinical Medicine and Public Health, University of Modena and Reggio Emilia, Modena, Italy*

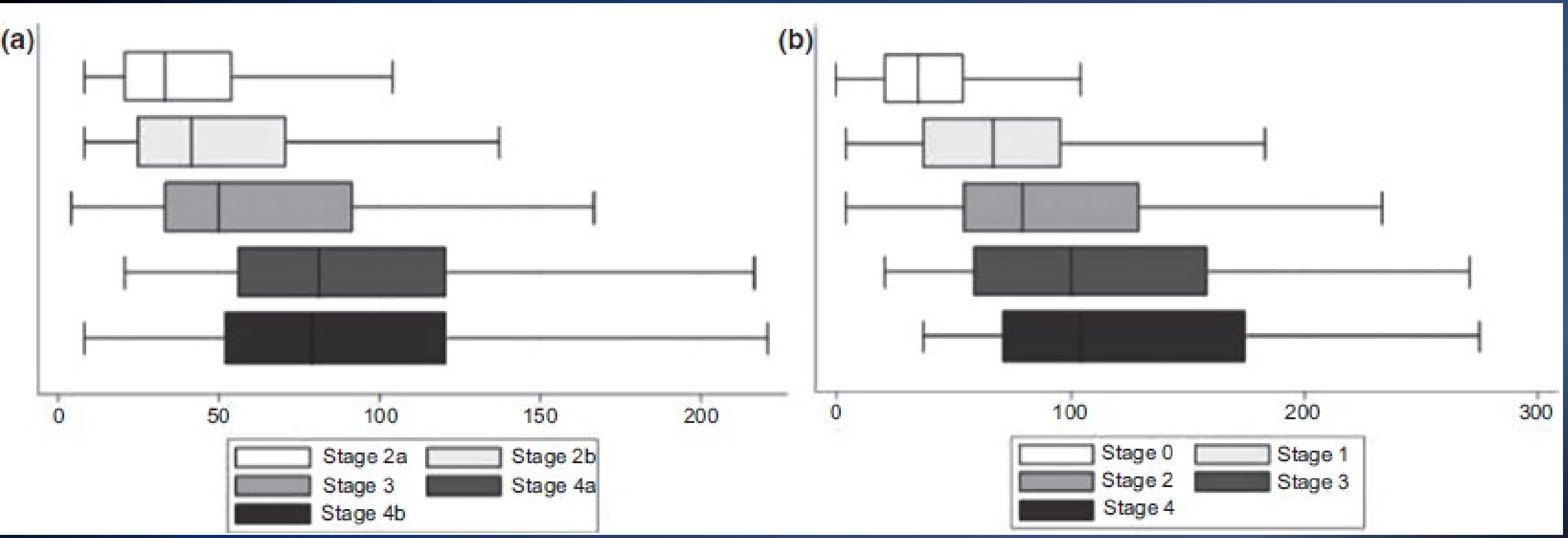
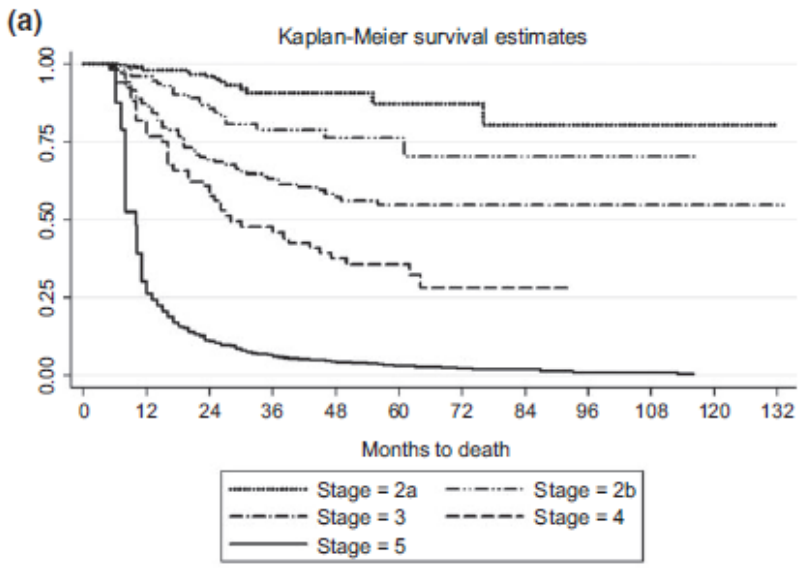

(a)
0
50
100
150
200
Stage 2a
Stage 2b
Stage 3
Stage 4a
Stage 4b
(b)
0
100
200
300
Stage 0
Stage 1
Stage 2
Stage 3
Stage 4

Table 3 Median and standardized median times (SMTs) from onset to each milestone

King's College staging system	Months (median) from onset (IQR)	SMT	Equality of medians test	Milano-Torino staging system	Months (median) from onset (IQR)	SMT	Equality of medians test
Stage 2a (n = 90)	8 (5–13)	33		Stage 0 (n = 192)	9 (5–13)	35	
Stage 2b (n = 123)	10 (6–17)	42	(onset-stage 2a vs. onset-stage 2b) ***P* < 0.01**	Stage 1 (n = 143)	16 (9–23)	67	(onset-stage 0 vs. onset-stage 1) ***P* < 0.01**
Stage 3 (n = 130)	12 (8–22)	50	(onset-stage 2b vs. onset-stage 3 ***P* < 0.01**	Stage 2 (n = 95)	19 (13–31)	79	(onset-stage 1 vs. onset-stage 2) ***P* < 0.01**
Stage 4a (n = 112)	20 (14–29)	81	(onset-stage 3 vs. onset-stage 4a/b) ***P* < 0.01**	Stage 3 (n = 51)	24 (14–38)	100	(onset-stage 2 vs. onset-stage 3) ***P* < 0.01**
Stage 4b (n = 148)	19 (13–29)	79	(onset-stage 4a vs. onset-stage 4b) P = 0.28	Stage 4 (n = 43)	25 (17–42)	104	(onset-stage 3 vs. onset-stage 4) ***P* < 0.01**
Death (n = 272)	24 (16–37)	100	(onset-stage 4a/b vs. onset death) ***P* < 0.01**	Death (n = 272)	24 (16–37)	100	(onset-stage 4 vs. onset death) ***P* < 0.01**

IQR, interquartile range.
Significant results in bold.



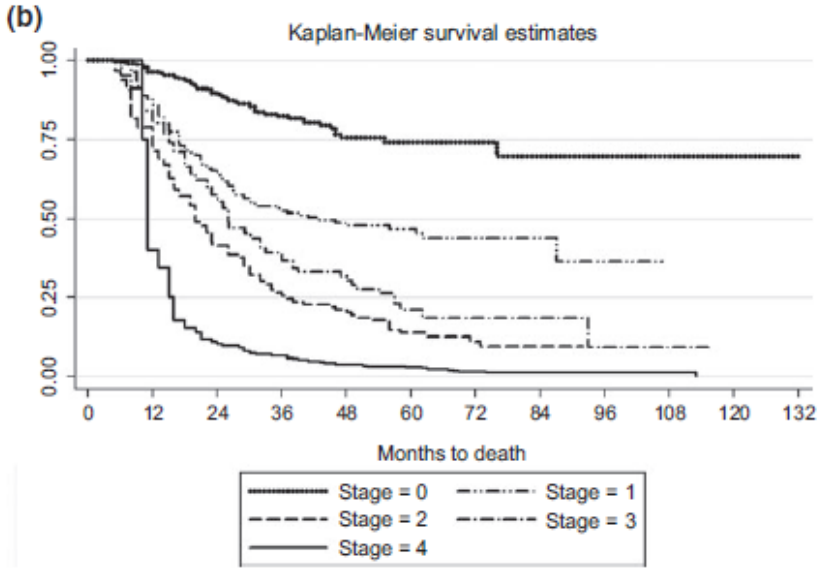


Table 4 Discriminatory ability and homogeneity for prediction of time to death/last observation

Staging system	Discriminatory ability linear trend χ^2	Homogeneity LR χ^2 test
Milano-Torino	31	166
King's College	178	290

Comparison between two staging

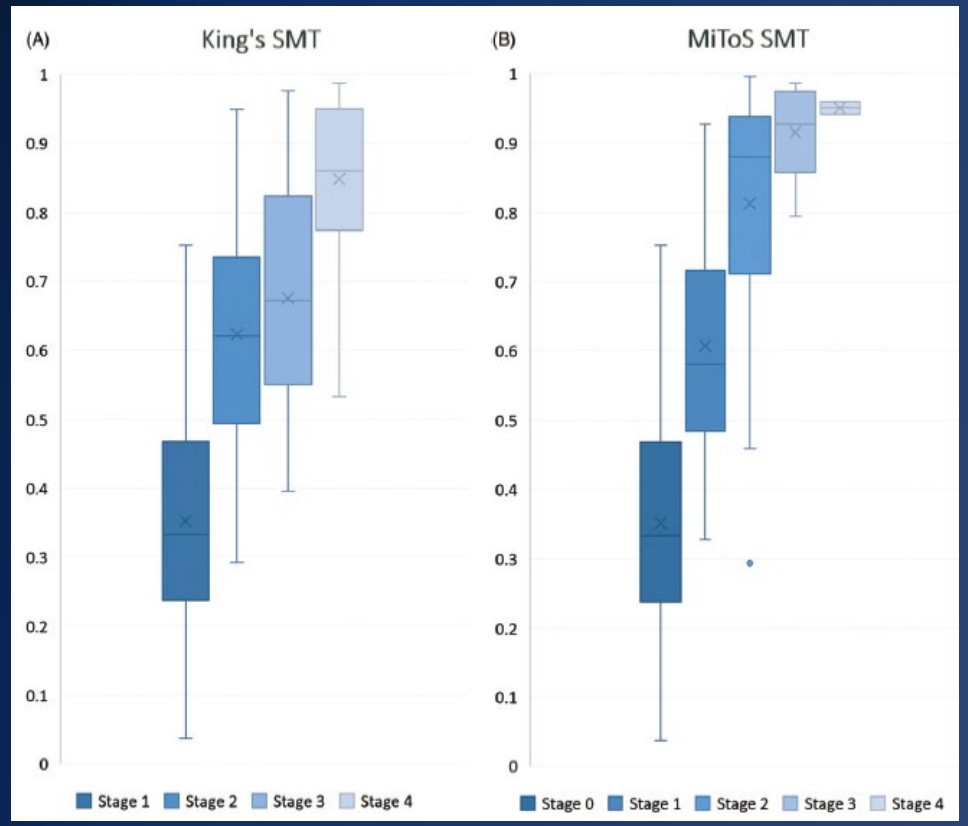
Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2017; 18: 227–232

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Comparison of the King's and MiToS staging systems for ALS

TON FANG[1]*, AHMAD AL KHLEIFAT[1]*, DANIEL R STAHL[2], CLAUDIA LAZO LA TORRE[3], CAROLINE MURPHY[2], UK-MND LICALS, CAROLYN YOUNG[4] PAMELA J SHAW[5], P NIGEL LEIGH[6] & AMMAR AL-CHALABI[1]

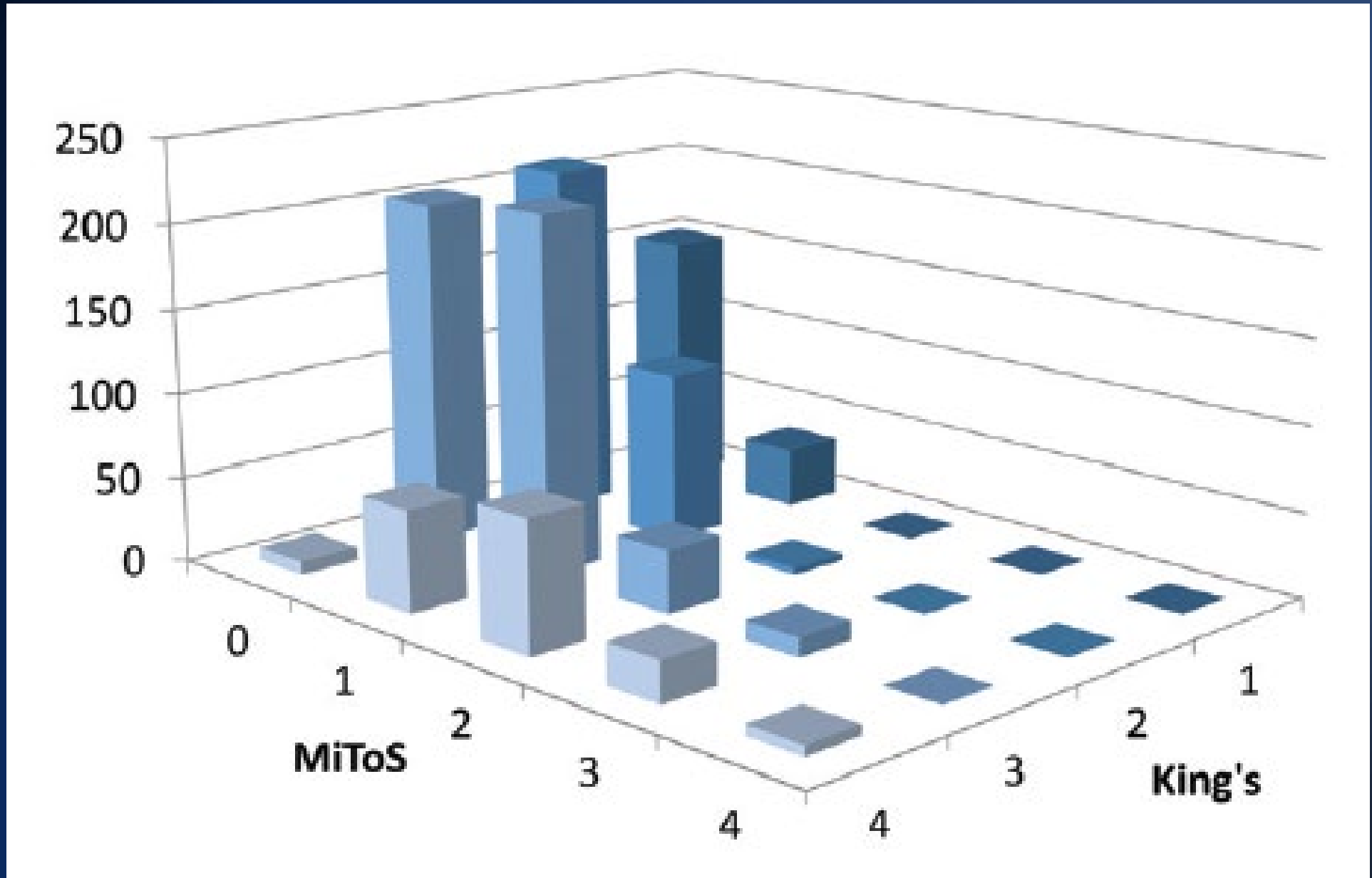


A)

King's staging system (*n*)	Median number of months from onset (IQR)	SMT (IQR)
1 (95)	9.0 (5.4–13.0)	0.33 (0.24–0.46)
2 (49)	18.4 (12.8–22.6)	0.62 (0.51–0.73)
3 (67)	18.9 (12.6–24.6)	0.67 (0.55–0.82)
4 (32)	24.8 (17.4–30.9)	0.86 (0.79–0.95)
5 (95)	27.7 (22.0–34.0)	1.00 (1.00–1.00)

B)

Milano-Torino staging system (*n*)	Median number of months from onset (IQR)	SMT (IQR)
0 (95)	9.0 (5.4–12.9)	0.33 (0.24–0.46)
1 (94)	16.5 (11.9–22.1)	0.58 (0.49–0.71)
2 (37)	25.0 (20.0–31.7)	0.88 (0.72–0.93)
3 (12)	25.1 (21.0–30.0)	0.93 (0.86–0.97)
4 (2)	27.0 (24.1–29.8)	0.95 (0.95–0.96)
5 (95)	27.7 (22.0–34.0)	1.00 (1.00–1.00)


250
200
150
100
50
0
0
1
2
MiToS
3
4
4
3
2
1
King's

Variable clinical course

- 4 domains in ALSFRS-R
  - Bulbar: speech, swallowing, sialorrhea
  - Fine motor: handwriting, cutting foot, dressing/hygiene
  - Gross motor: walking, climbing stairs, turning in bed
  - Respiratory function: dyspnea, orthopnea, respiratory insufficiency

TRAJECTORIES OF IMPAIRMENT IN AMYOTROPHIC LATERAL SCLEROSIS: INSIGHTS FROM THE POOLED RESOURCE OPEN-ACCESS ALS CLINICAL TRIALS COHORT

NIMISH J. THAKORE, MD, DM,[1] BRITTANY R. LAPIN, PhD, MPH,[2] ERIK P. PIORO, MD, PhD,[1,3] and POOLED RESOURCE OPEN-ACCESS ALS CLINICAL TRIALS CONSORTIUM

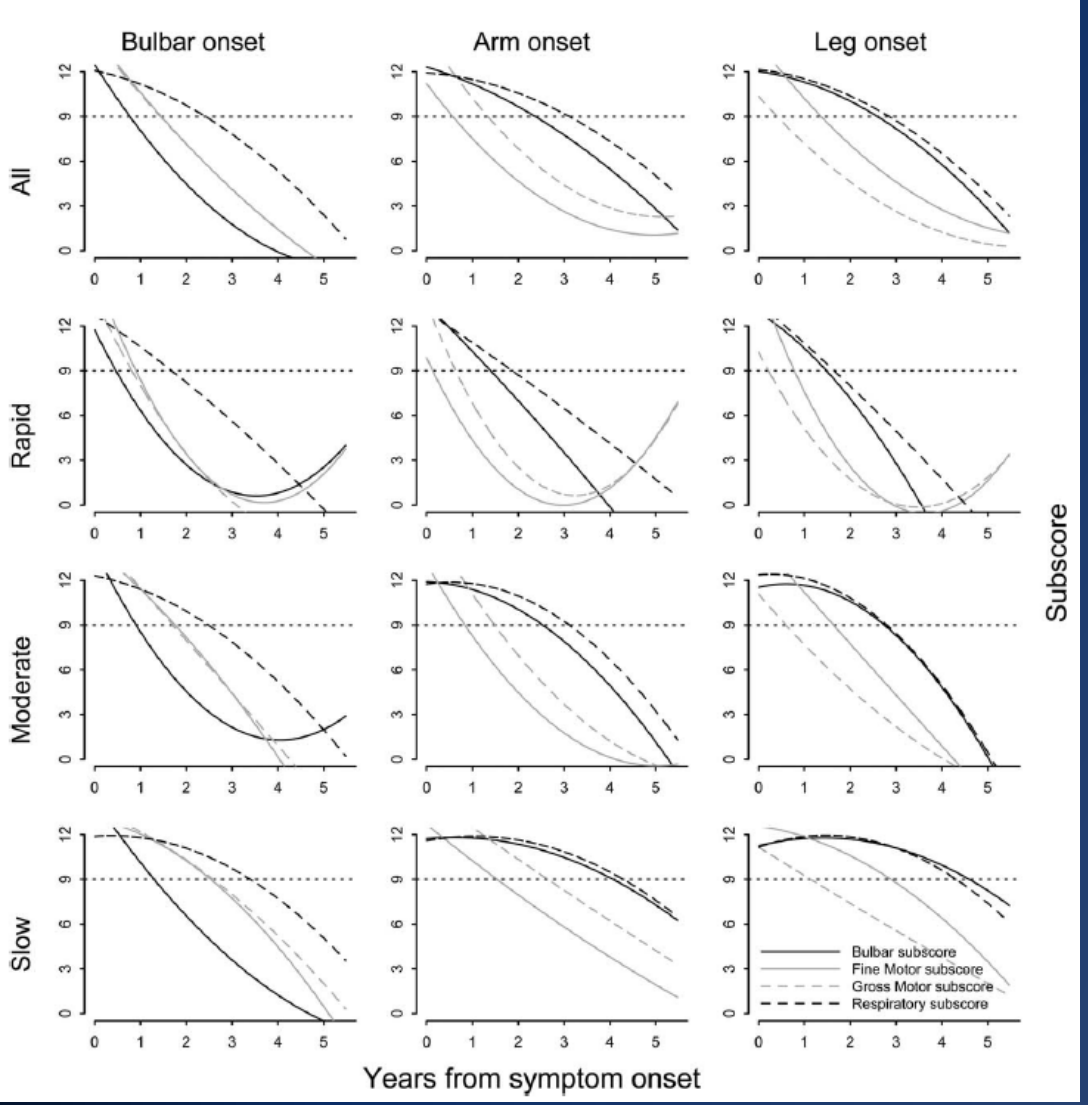


Table 4. Months from symptom onset when average quadratic time subscore trajectory crossed the threshold of 9 points, by site of onset*

Onset site	Bulbar subscore	Fine motor subscore	Gross motor subscore	Respiratory subscore
Bulbar	9.2 (8.6–9.8)	17.5 (16.5–18.5)	17.2 (16.4–18.1)	29.0 (27.5–30.7)
Arm	28.5 (27.0–30.6)	6.9 (5.6–7.9)	16.0 (15.1–16.8)	37.4 (35.3–40.5)
Leg	31.1 (29.6–32.7)	16.4 (15.6–17.2)	4.9 (3.6–6.0)	34.2 (32.8–35.8)