Motor neuron disease: Hope from despair through multidisciplinary care

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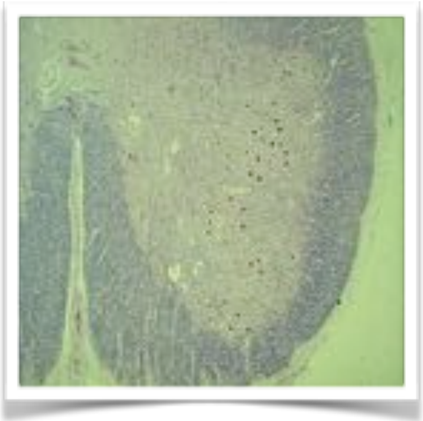
UNIVERSITY OF OXFORD

La sclérose amyotrophique
Amyotrophic Lateral Sclerosis = MND

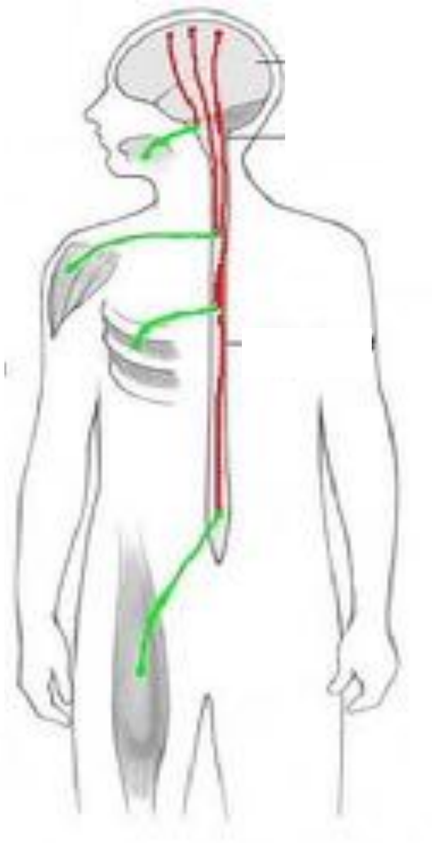
Jean-Martin Charcot
(1825-1893)

LMN

spinal cord anterior horn cell loss

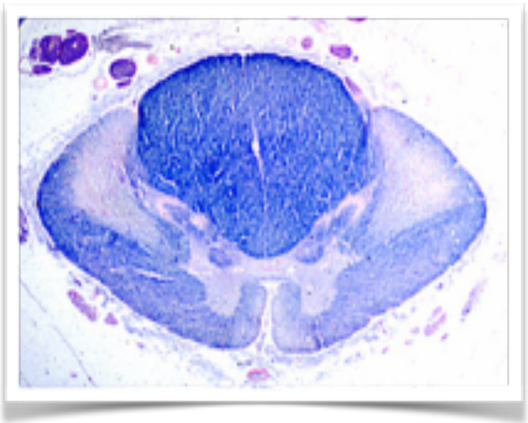


muscle wasting = amyotrophy



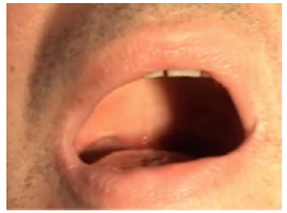
UMN

corticospinal (lateral) tract scarring

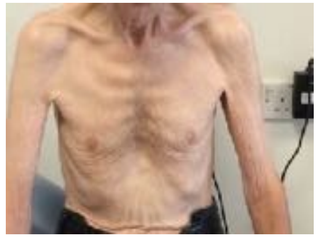


spasticity, hyperreflexia due to 'lateral sclerosis'

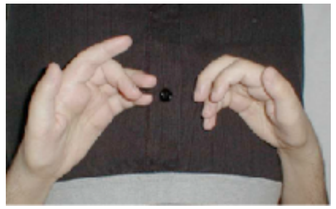
secretions
nutrition
communication

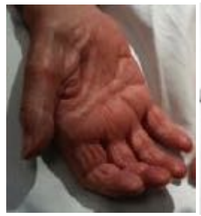


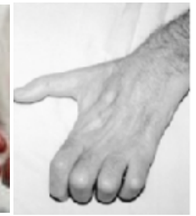
hypermetabolism

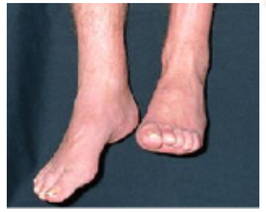


disability
loss of
independence









upper motor neurons

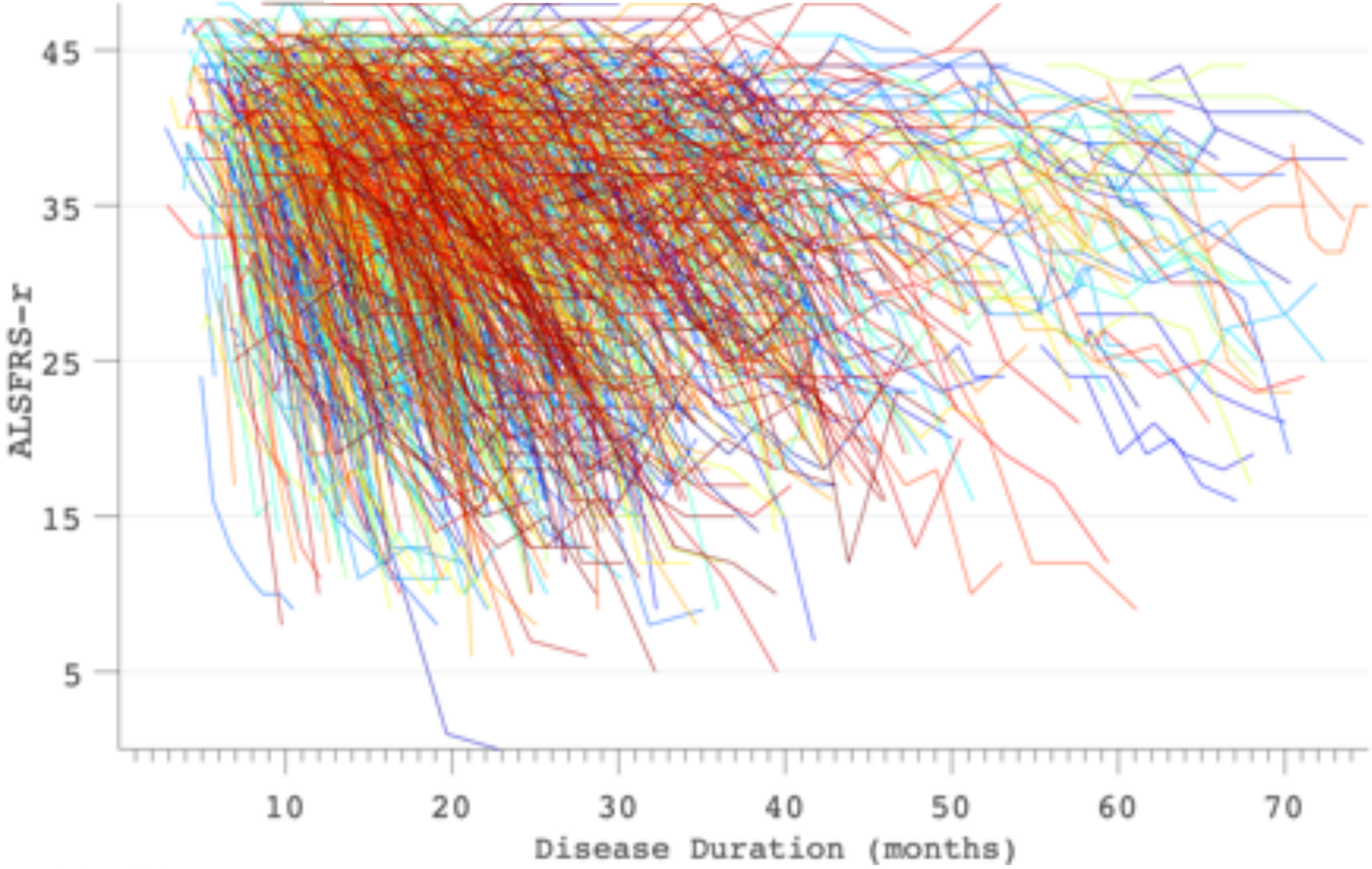
lower motor neurons

cognition and behaviour

corticobulbar
emotionality

respiratory
insufficiency = median
survival 30 months

The heterogeneity problem in MND



To assess efficacy:

1. Insensitive
2. Needs 12 months

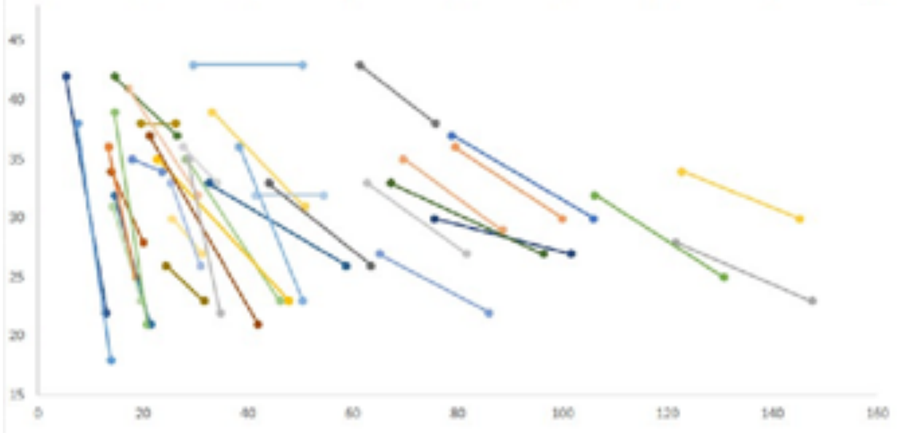
Proudfoot M *et al.* ALS-FTD 2016

Rate of decline individually fixed

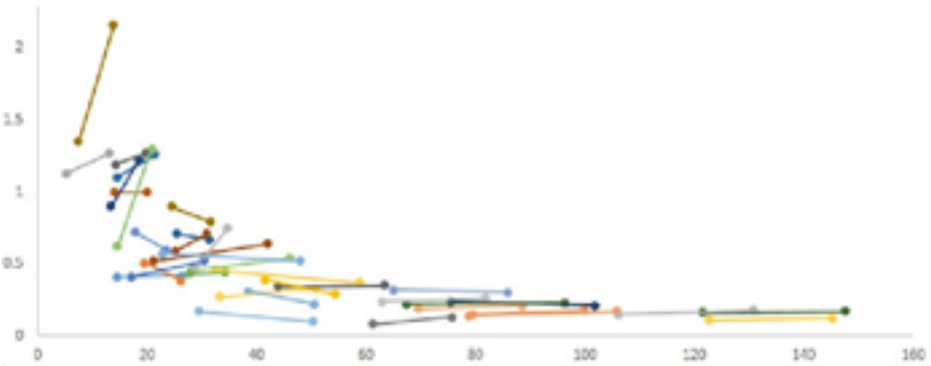
When the progress at the commencement is rapid, it usually continues rapid, until the disease has attained a wide extent, although the acute local onset mentioned below may be followed by slow extension. When it begins slowly, it is usually slow throughout.

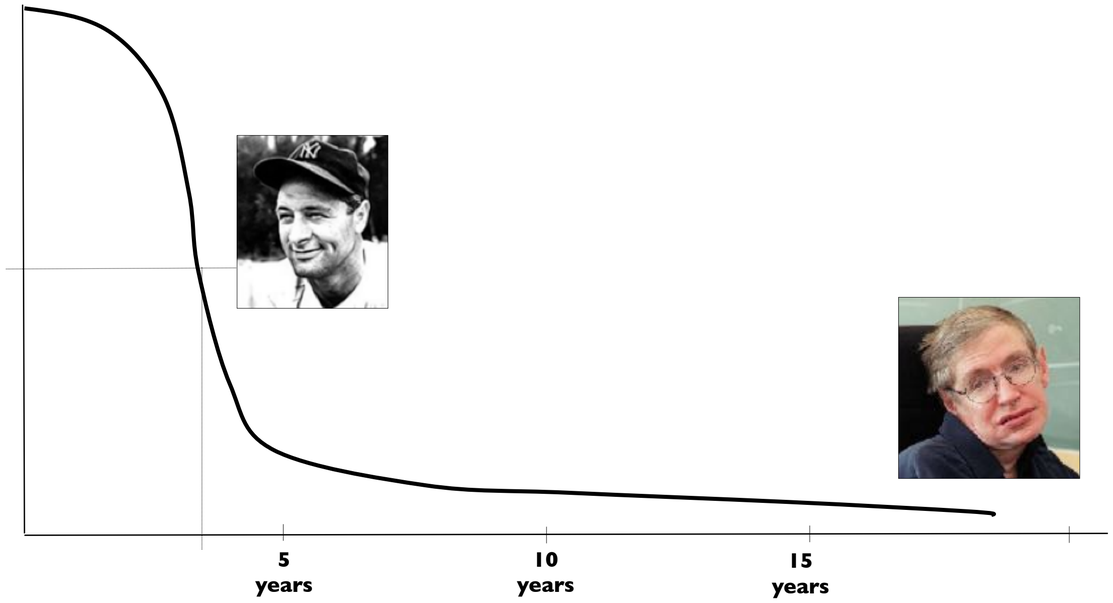
Gowers WR. A Manual of Diseases of the Nervous System. 1886

Variable decline in revised ALSFRS-R (48 to 0)



Rate of decline in ALSFRS-R





Prognosis for patients with amyotrophic lateral sclerosis: development and validation of a personalised prediction model

Henk-Jan Westeneng, Thomas P A Debray, Anne E Visser, Ruben P A van Eijk, James P K Rooney, Ancuta Calvo, Sarah Martin, Christopher J McDermott, Alexander G Thompson, Susana Pinto, Nina A Kobeleva, Angela Rosenbohm, Beatrice Stubendorff, Selma Sommer, Eva M Middelkoop, Annelot M Dekker, Jakv J F A van Vugt, Wouter van Rheenen, Alice Vajda, Mark Heverin, Alberto Kazoka, Hannah Hollinger, Maria Gromicho, Sanja Körner, Thomas M Ringer, An Jacobs Rodger, Anne Gunkel, Christopher E Shaw, Annelot Bruneteau, Michael Argyriou, Philippe Corcia, Philippe Couratier, Markus Weber, Julian Gonzalez-de-Olano, Albert C Ludolph, Susanne Petri, Mamede de Carvalho, Philip Van Damme, Kevin Talbot, Martin R Turner, Pamela J Shaw, Ammar Al-Chalabi, Adriano Chiò, Orla Hardiman, Kimmo J M Verstraete, Jan H Veldink, Leonard H van den Berg

Summary

Background Amyotrophic lateral sclerosis (ALS) is a relentlessly progressive, fatal motor neuron disease with a variable natural history. There are no accurate models that predict the disease course and outcomes, which complicates risk assessment and counselling for individual patients, stratification of patients for trials, and timing of interventions. We therefore aimed to develop and validate a model for predicting a composite survival endpoint for individual patients with ALS.

Methods We obtained data for patients from 14 specialised ALS centres (each one designated as a cohort) in Belgium, France, the Netherlands, Germany, Ireland, Italy, Portugal, Switzerland, and the UK. All patients were diagnosed in the centres after excluding other diagnoses and classified according to revised El Escorial criteria. We assessed 16 patient characteristics as potential predictors of a composite survival outcome (time between onset of symptoms and non-invasive ventilation for more than 23 h per day, tracheostomy, or death) and applied backward elimination with bootstrapping in the largest population-based dataset for predictor selection. Data were gathered on the day of diagnosis or as soon as possible thereafter. Predictors that were selected in more than 70% of the bootstrap resamples were used to develop a multivariable Royston-Parmar model for predicting the composite survival outcome in individual patients. We assessed the generalisability of the model by estimating heterogeneity of predictive accuracy across external populations (ie, populations not used to develop the model) using internal-external cross-validation, and quantified the discrimination using the concordance (c) statistic (area under the receiver operator characteristic curve) and calibration using a calibration slope.

Findings Data were collected between Jan 1, 1992, and Sept 22, 2016 (the largest data-set included data from 1535 patients). The median follow-up time was 97·5 months (IQR 52·9–168·5). Eight candidate predictors entered the prediction model: bulbar versus non-bulbar onset (univariable hazard ratio [HR] 1·71, 95% CI 1·63–1·79), age at onset (1·03, 1·03–1·03), definite versus probable or possible ALS (1·47, 1·39–1·55), diagnostic delay (0·51, 0·51–0·51), forced vital capacity (HR 0·93, 0·99–0·99), progression rate (6·13, 5·93–6·76), frontotemporal dementia (1·34, 1·20–1·50), and presence of a *C9orf72* repeat expansion (1·45, 1·31–1·61), all p<0·0001. The *c* statistic for external predictive accuracy of the model was 0·75 (95% CI 0·77–0·80; 95% prediction interval [PI] 0·74–0·82) and the calibration slope was 1·01 (95% CI 0·95–1·07; 95% PI 0·83–1·18). The model was used to define five groups with distinct median predicted (SE) and observed (SE) times in months from symptom onset to the composite survival outcome: very short 17·7 (0·20), 16·5 (0·23); short 25·3 (0·06), 25·2 (0·15); intermediate 32·2 (0·09), 32·1 (0·46); long 43·7 (0·21), 44·6 (0·74); and very long 91·0 (1·84), 85·6 (1·96).

Interpretation We have developed an externally validated model to predict survival without tracheostomy and non-invasive ventilation for more than 23 h per day in European patients with ALS. This model could be applied to individualised patient management, counselling, and future trial design, but to maximise the benefit and prevent harm it is intended to be used by medical doctors only.

Funding Netherlands ALS Foundation.

Introduction

Neurodegenerative diseases impose an enormous clinical and economic burden on patients and health systems.[1] Development of disease-modifying therapies and strategies for effective palliative care have been limited by disease heterogeneity and the presence of overlapping phenotypes.[2] Therefore, models that can reliably predict outcomes at an individual patient level

Lancet Neurol 2018
Published Online
March 26, 2018
http://dx.doi.org/10.1016/S1474-4422(18)30089-9
See Online/Comment
http://dx.doi.org/10.1016/S1474-4422(18)30111-X

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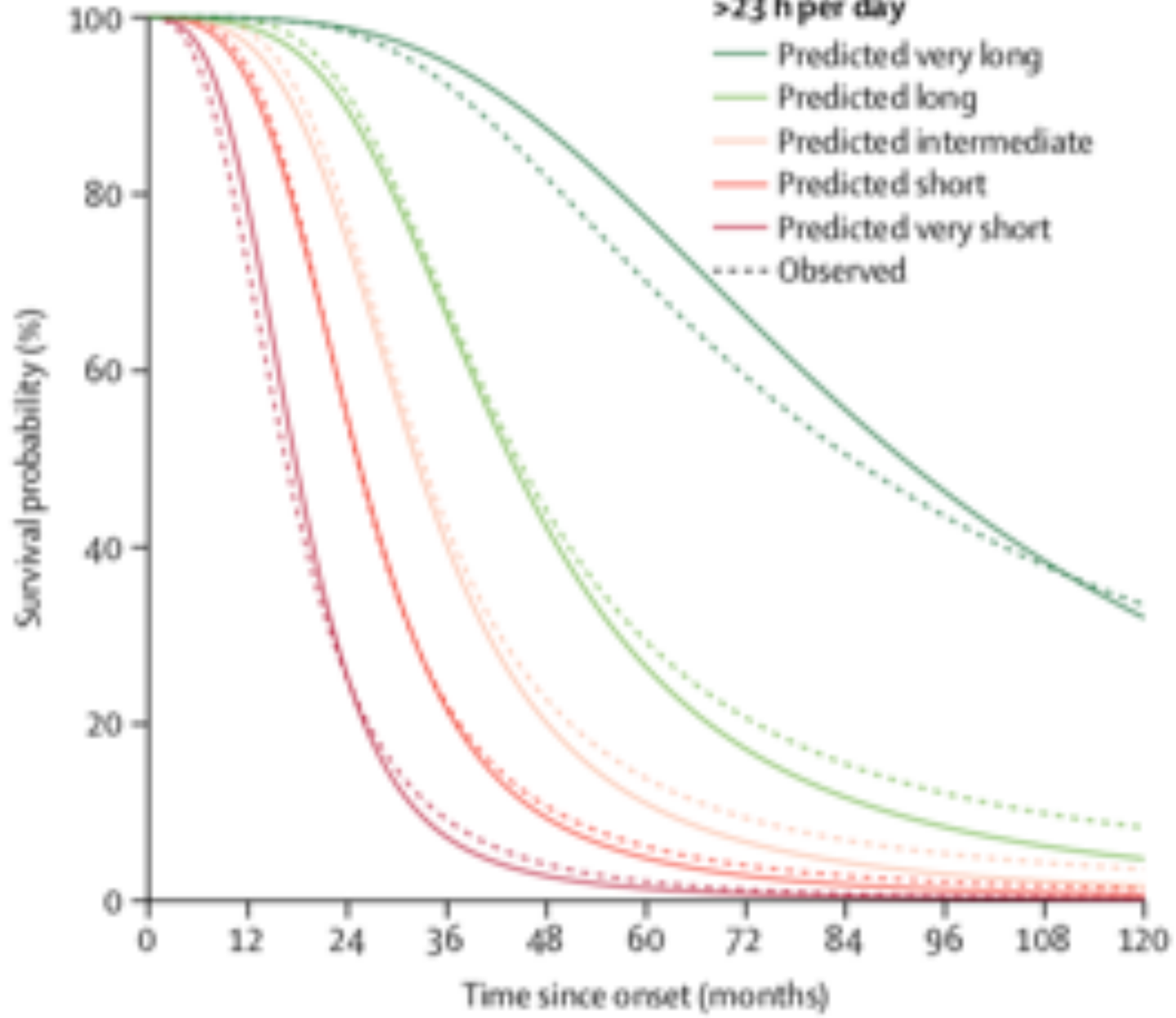
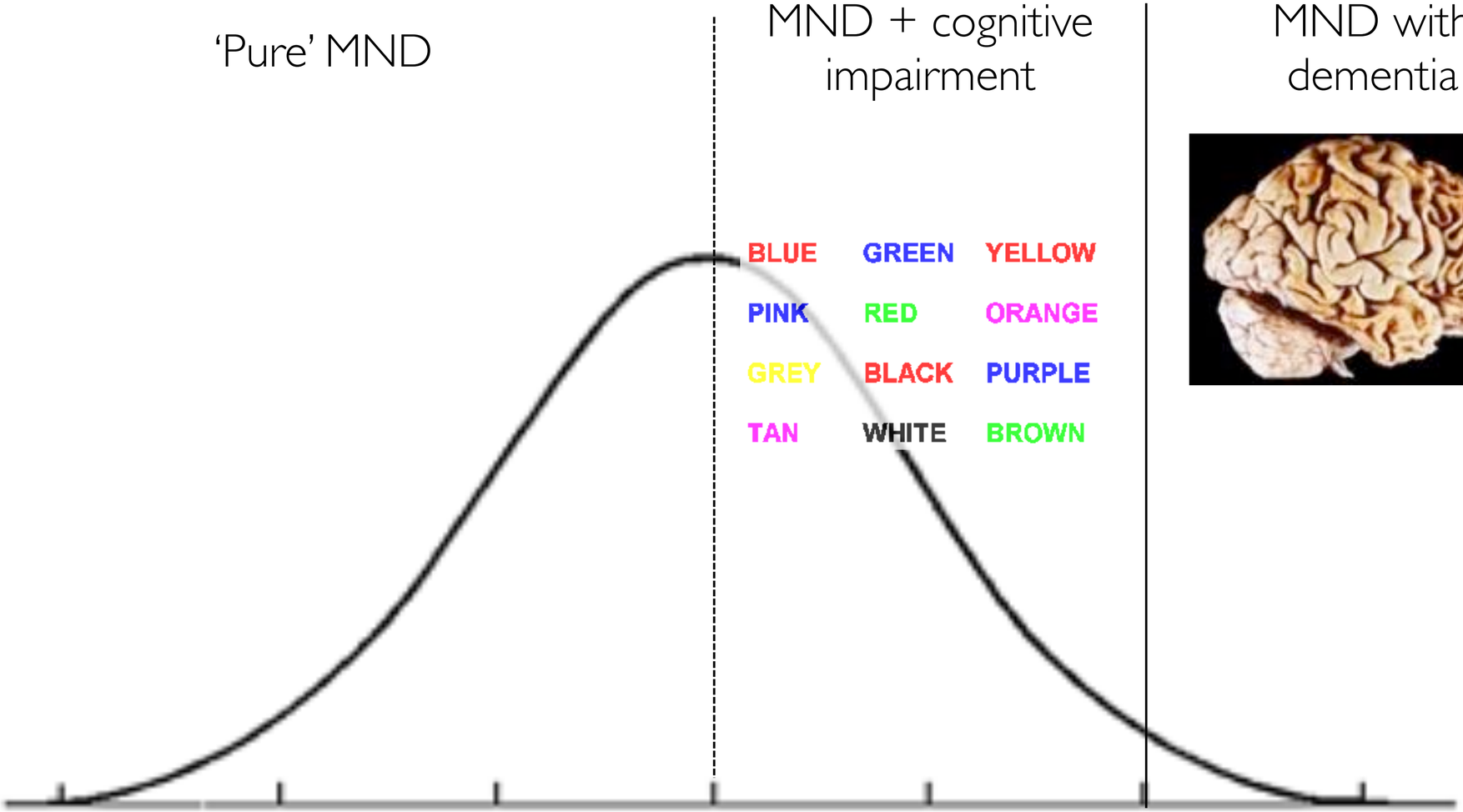


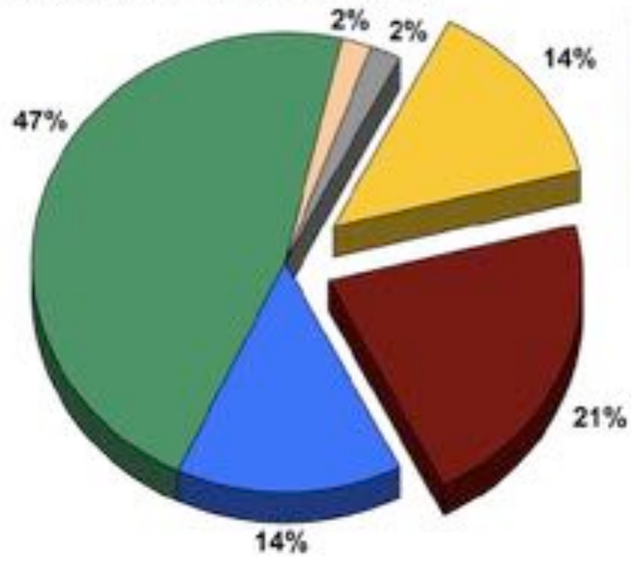
MND patients show changes that overlap with frontotemporal dementia

The syndrome of cognitive impairment in amyotrophic lateral sclerosis: a population-based study

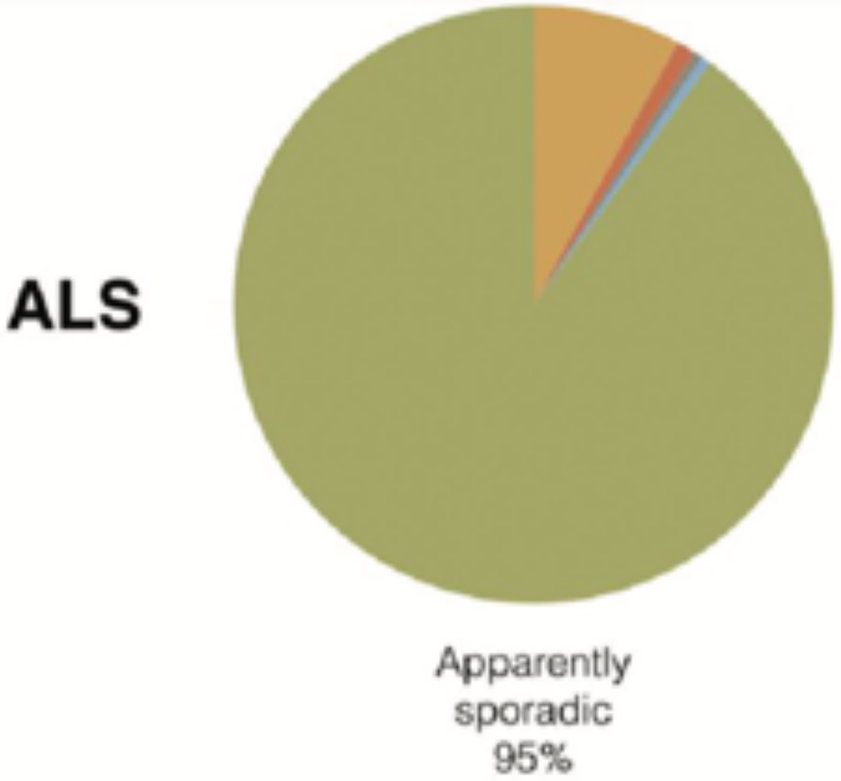
Julie Phukan,[1] Marwa Elamin,[1] Peter Bede,[1] Norah Jordan,[2] Laura Gallagher,[2] Susan Byrne,[1] Catherine Lynch,[1] Niall Pender,[2] Orla Hardiman[1,3]

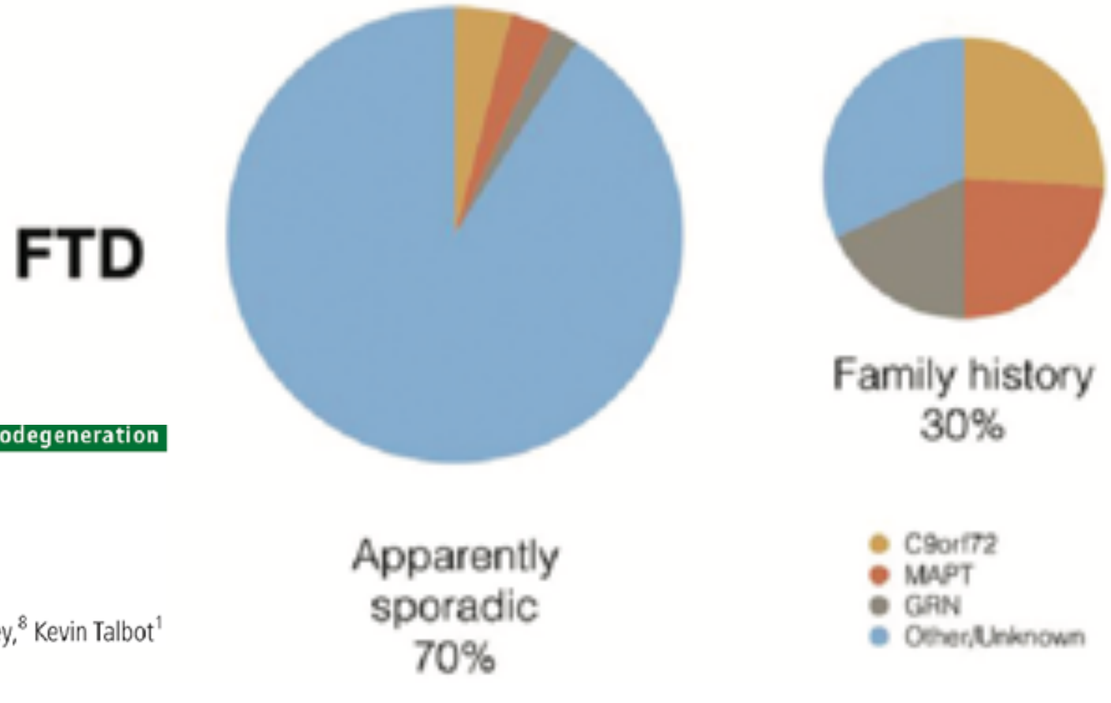
J Neurol Neurosurg Psychiatry 2012;**83**:102–108.





The genetics of ALS and FTD





Why family history is unreliable:

- Variable penetrance
- Early death
- Adoption
- Non-paternity
- Hidden disease

Neurodegeneration

VIEWPOINT

Genetic screening in sporadic ALS and FTD

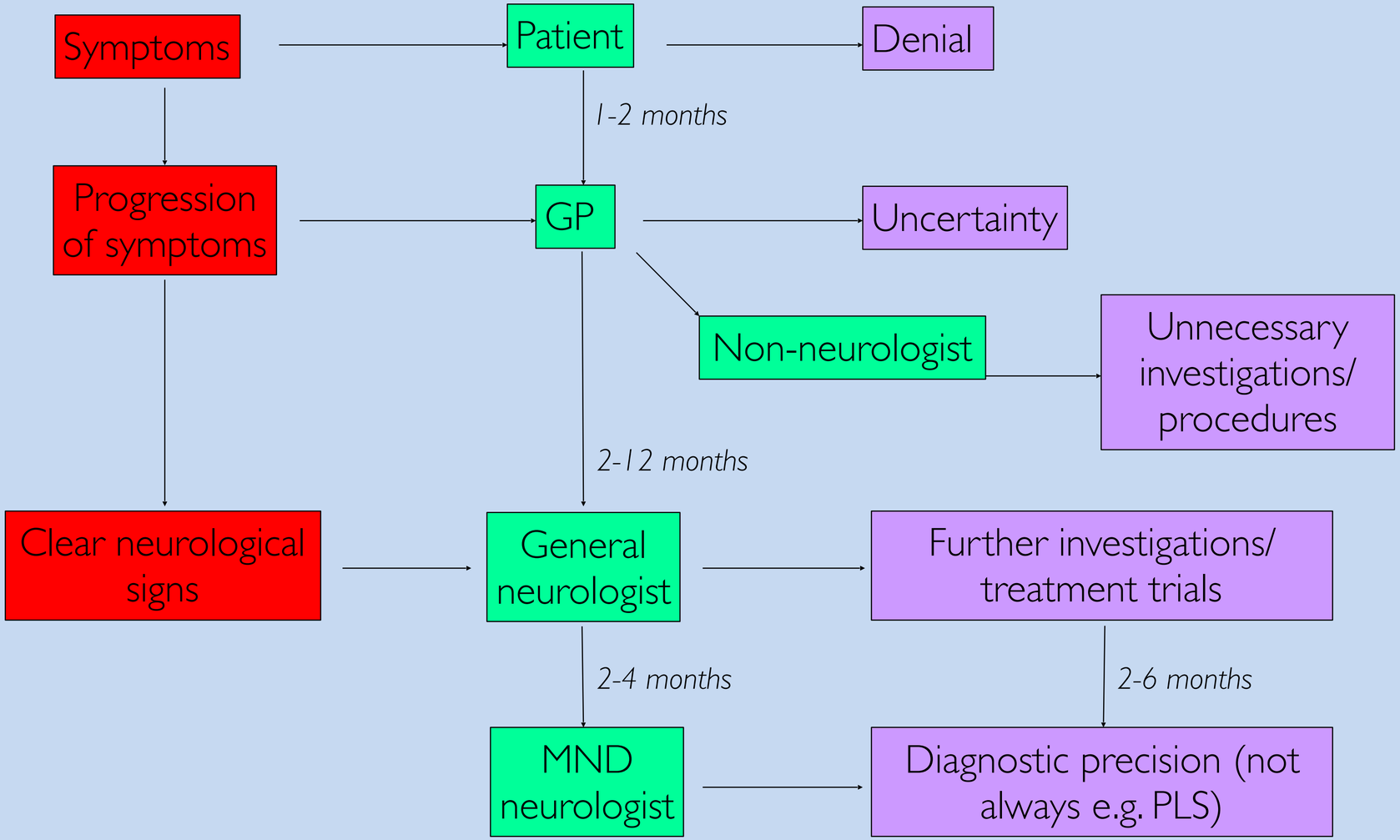
Martin R Turner,[1] Ammar Al-Chalabi,[2] Adriano Chio,[3] Orla Hardiman,[4] Matthew C Kiernan,[5] Jonathan D Rohrer,[6] James Rowe,[7] William Seeley,[8] Kevin Talbot[1]

J Neurol Neurosurg Psychiatry 2017

Time for MND specialist to make diagnosis:

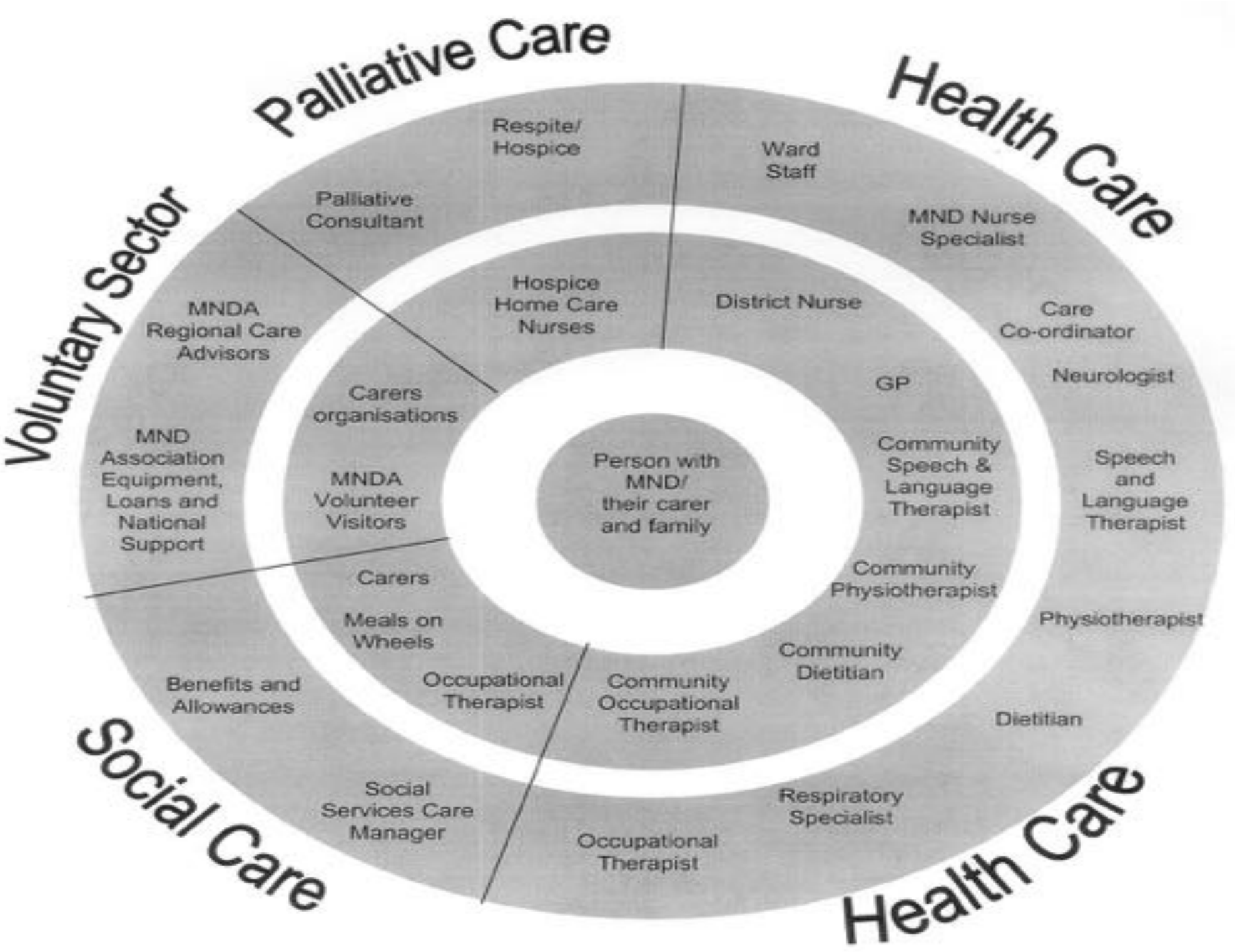
Average years for patient to reach specialist:

Diagnostic delay (mean 12 months)



Predictors of prognosis at presentation

- POOR:
  - Short referral latency
  - Respiratory-onset
  - Marked cognitive impairment
  - Bulbar-onset
- BETTER:
  - Pure LMN or UMN syndromes
  - Regional isolation for > 12 months
  - Younger age (<45)


Palliative Care
Health Care
Voluntary Sector
Social Care
Health Care
Respite/
Hospice
Ward
Staff
Palliative
Consultant
MND Nurse
Specialist
Hospice
Home Care
Nurses
District Nurse
Care
Co-ordinator
MNDA
Regional Care
Advisors
GP
Neurologist
Carers
organisations
MND
Association
Equipment,
Loans and
National
Support
Person with
MND/
their carer
and family
Community
Speech &
Language
Therapist
Speech
and
Language
Therapist
MNDA
Volunteer
Visitors
Community
Physiotherapist
Carers
Physiotherapist
Meals on
Wheels
Community
Dietitian
Benefits and
Allowances
Occupational
Therapist
Community
Occupational
Therapist
Dietitian
Social
Services Care
Manager
Respiratory
Specialist
Occupational
Therapist

mnda

motor neurone disease association

MND REGISTER

England, Wales & Northern Ireland

Oxford referral base

120 new patients/annum; 250 in regular FU

The Clinic Coordinator

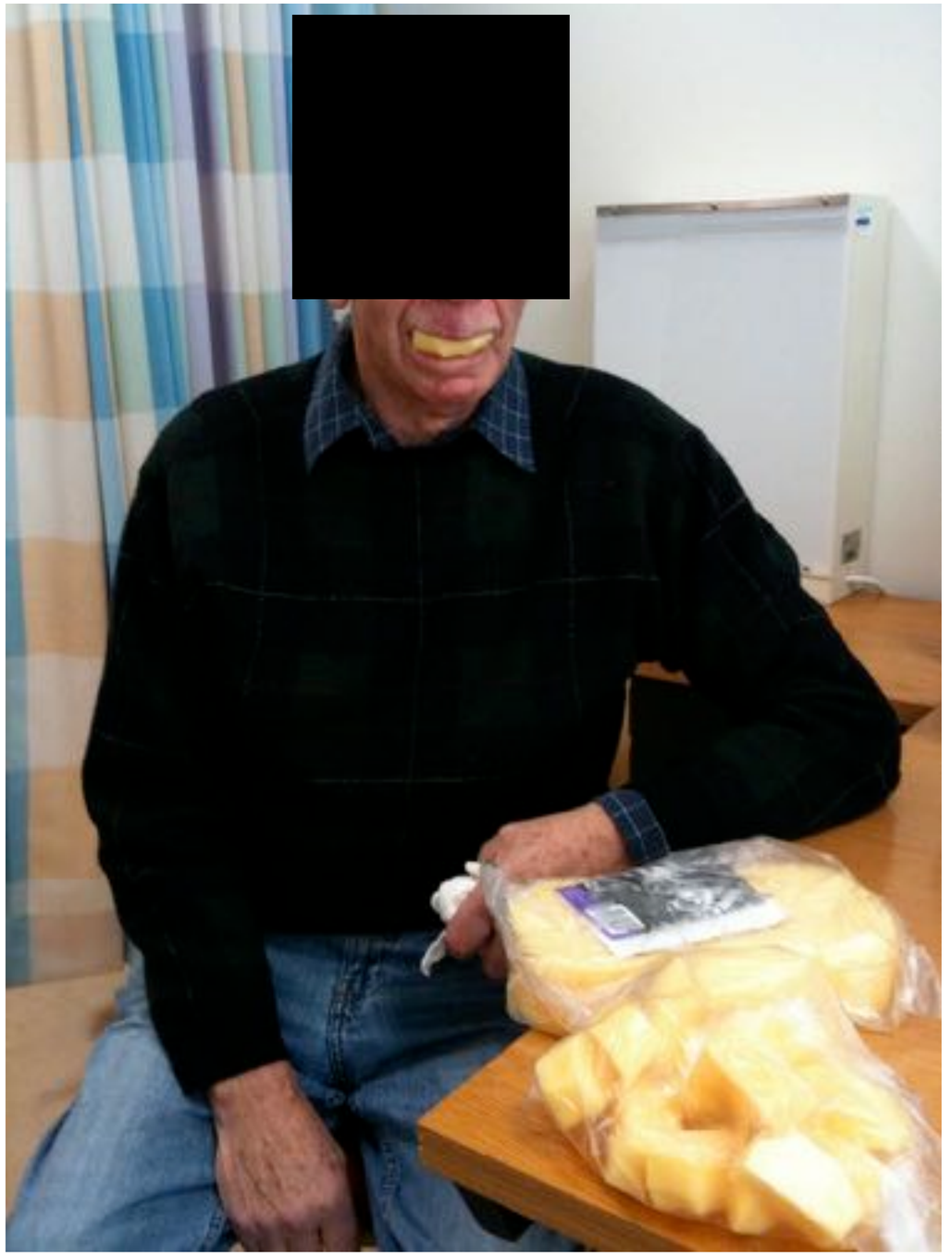
- The Cornerstone
- Specialist Nurse
- Sign-posting
- Liaison with community MDT

OT

- Physical aids
- Mobility review
- Wheelchair provision & optimisation
- Head support

Sialorrhoea

- Pooling of oral secretions
- Major source of morbidity
- Reduced swallowing frequency
  - Not over-production



Secretions

- Thin secretions
  - Hyoscine patches
    - skin allergy
    - 'dizziness'
  - Atropine eye drops 1%
    - may be hard to source
  - Amitriptyline
    - sedation
  - Glycopyrronium
    - Can be diluted and given via PEG
  - Botulinum toxin
    - transient
    - Unpredicatable
  - Radiotherapy
  - Suction device

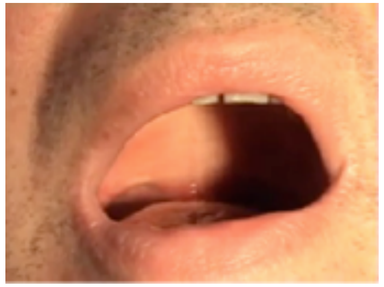
- Thick secretions
  - Peri-glottic (hard to clear)
  - Avoid anti-cholinergics
  - Pineapple/papaya
  - Nebulised saline
    - with suction device
  - Carbocisteine (Mucodyne)

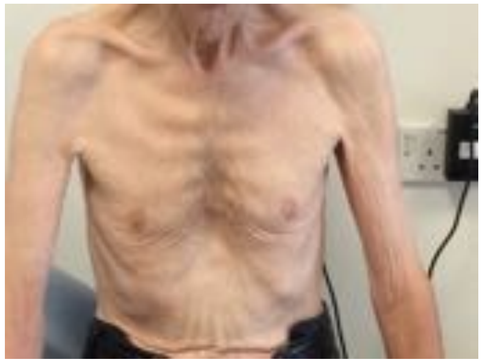
Emotionality

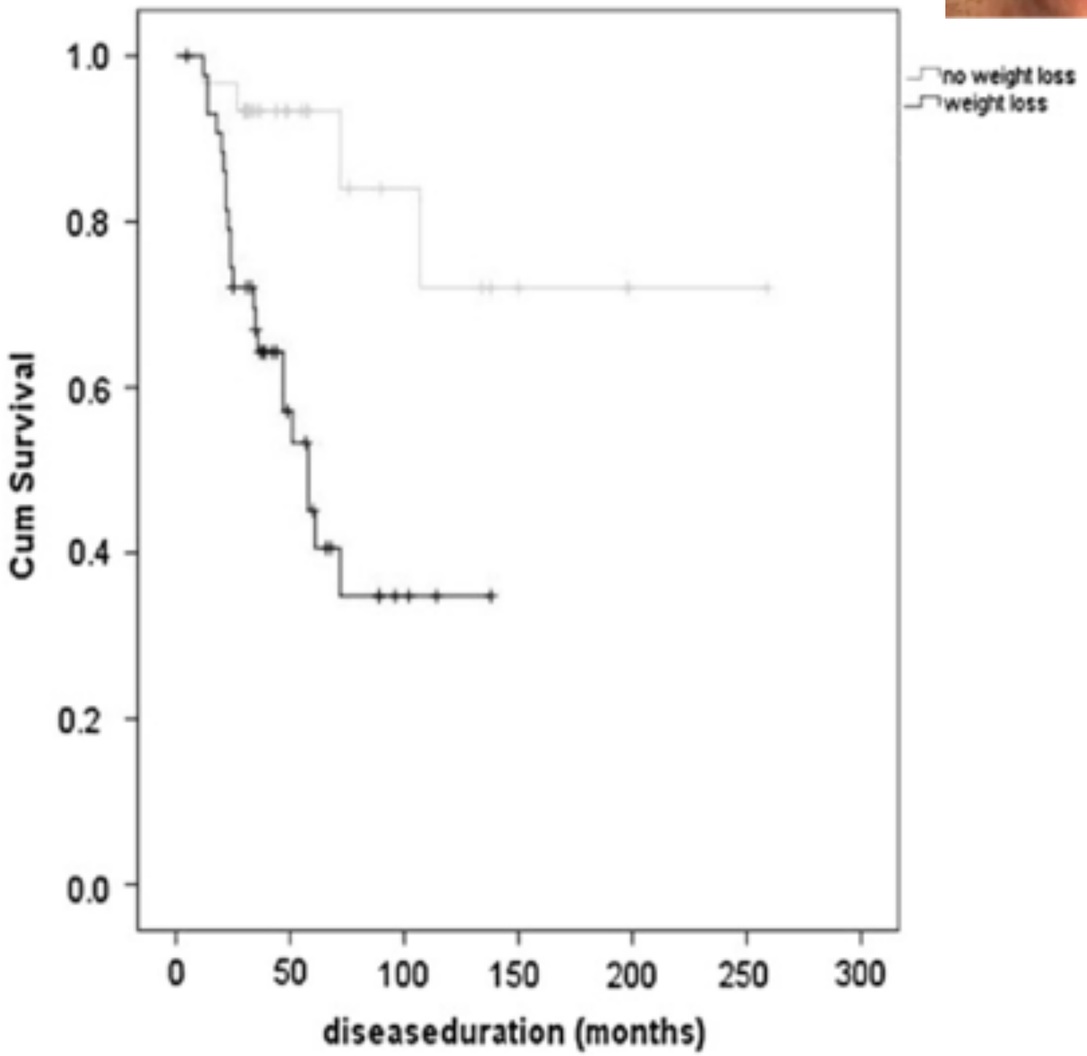
- ‘Pseudobulbar affect’
  – See in Alzheimer’s and PSP
- Corticobulbar pathway involvement
- Explosive, incongruous, short-lived burst of emotion
- Crying>>>laughing
- Dextromethorphan+quinidine (Neudexta)
- SSRI

Nutritional support in MND

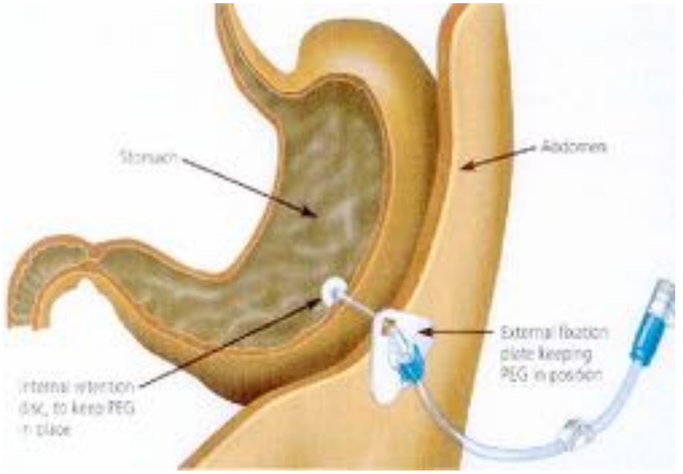
- Premorbid lower BMI
- Hypermetabolic state in disease
- Weight loss linked to survival
- Higher cholesterol linked to slower progression
- HighCALS trial starting 2020

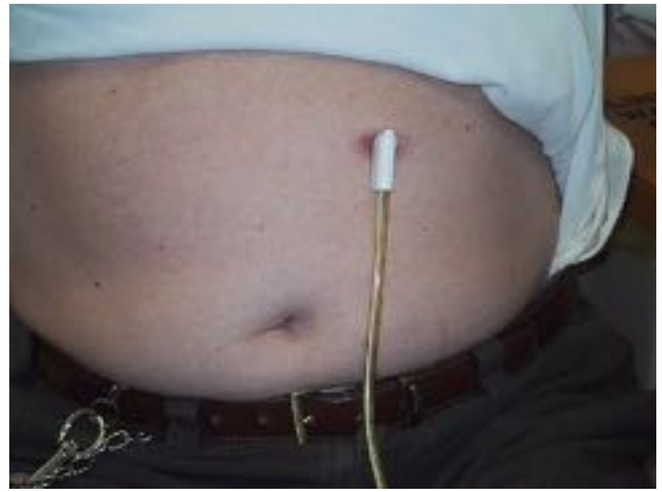






Koerner *et al.* BMC Neurology 2013





Dedicated MND Nutrition Clinic

- Recognition that gastrostomy decision is major issue for many
- Chance to discuss and allows 'cool off' period
  - May not use immediately or solely
- Specialist nurse, dietitian, enteral feeding nurses
- Spouse involvement encouraged
  - Reassure about physical management
- Explain what will happen in hospital
- (Reflect on whether PEG appropriate)

Traffic light system

Respiratory assessment

Data as yes/no responses

Traffic light category + actions

Gastrostomy placement risk assessment for patients with potential respiratory muscle weakness

Fax form to (2)22047 with gastrostomy request FAO specialist PEG nurse Clare Lawson

PATIENT DETAILS etc. TR

This form is intended to aid risk assessment and improve safety of patients considering a gastrostomy with potential respiratory muscle weakness.

Gastro contacts: Clare Lawson, specialist PEG nurse **tel. (7)40378**; Consultant interventional gastroenterologists – James East, Adam Bailey or Barbara Braden.

Respiratory contacts: Consultant specialists in ventilatory support John Stradling, Maxine Hardinge or Annabel Nickol **tel. (2)25230 or Fax (2)25221**

Respiratory assessments where information is available				
VC sitting/ standing	____ L ____ % pred		ABG/ CBG (delete as appropriate)	
VC lying (if done)	____ L		pH	
Fall in VC on lying	____ L ____ % fall		$PaCO_2$	____ kPa
Sniff nasal pressure	____ cmH_2O		PaO_2	____ kPa
SaO_2 on pulseox	____ %		Bicarbonate	____ mM/ L
			Base excess	____ mM/ L
			SaO_2	____ %

Please assess respiratory function as follows:

- Can the patient lie flat for 20 minutes? ..... Yes/ No
- Is their vital capacity greater than 50% predicted? ..... Yes/ No
- Does vital capacity fall by 15% or less on lying flat? ..... Yes/ No
- Is sniff nasal pressure 40cmH_2O or greater? ..... Yes/ No
- Are arterial oxygen saturations 94% or greater? ..... Yes/ No
- On a blood gas is $PaCO_2$ <6kPa and bicarbonate <27mM/ L ..... Yes/ No

Risk	Green light (Low risk)	Amber light (Moderate risk)	Red light (High risk)
Criteria	Answers 'yes' to all questions above	Answer to one or more questions above is 'no'	$PaCO_2$ or bicarbonate raised Patient is already on NIV Patient cannot lie flat
Action	PEG may be able go ahead on a routine list *(re-evaluate if delay between referral & procedure >1 month)*	PEG must go ahead on a Consultant list carried out by a team experienced in care of patients with potential respiratory compromise	As for 'amber' light, but NIV must be available for use peri- or during the procedure via a nasal mask

Please discuss request with consultant gastroenterologist if there is an absolute/ relative contraindication to PEG insertion such as:

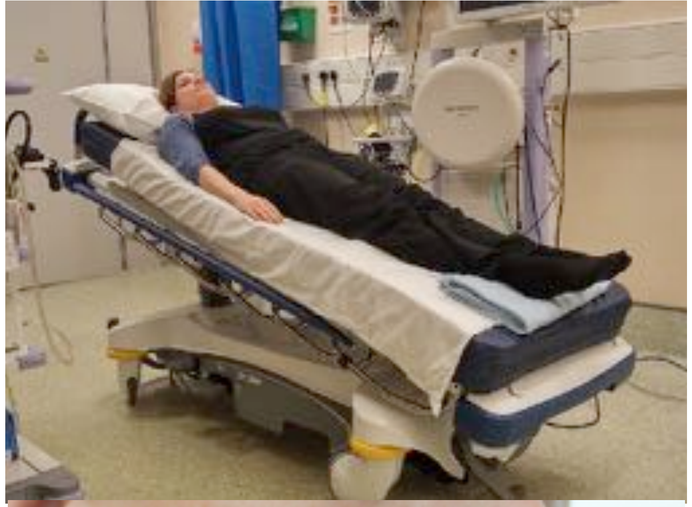
- Poor mouth opening (unable to put a 10ml syringe into mouth)
- Gastrectomy/ anatomical difficulty such as severe kyphoscoliosis
- Failed PEG
- Ascites
- Sepsis
- Anxiety/ refusal to have OGD
- VP shunt
- Patient dependent on NIV via a full facemask is unable/unwilling to switch to a nasal mask

REQUESTER NAME: _____ **CONTACT DETAILS:** _____

PATIENT'S CONSULTANT: _____

Procedural adaptations

- Experienced operator
- Minimal sedation
- Head up tilt 30°
- Paediatric mouthguard
- NIV available for those stratified red



Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2017; 18: 243–248

Taylor & Francis

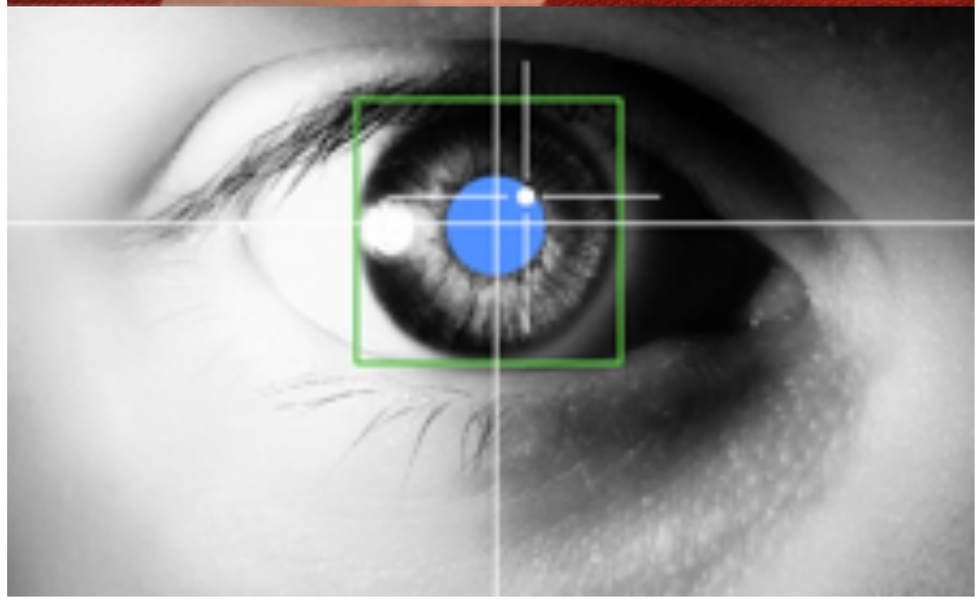
RESEARCH ARTICLE

A risk stratifying tool to facilitate safe late-stage percutaneous endoscopic gastrostomy in ALS

ALEXANDER G. THOMPSON[1]*, VICTORIA BLACKWELL[2]*, RACHAEL MARSDEN[1], EMMA MILLARD[3], CLARE LAWSON[2], ANNABEL H. NICKOL[4], JAMES E. EAST[2], KEVIN TALBOT[1], PHILIP J. ALLAN[2] & MARTIN R. TURNER[1]

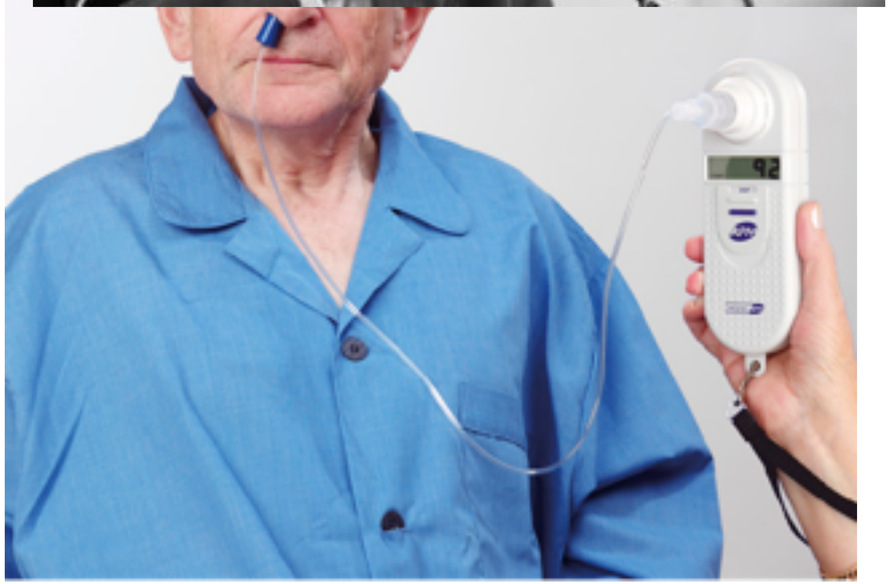
Communication

- Exceptional to lose all communication:
  - Lightwriter (iPad)
  - Point It!
  - Eye-tracking



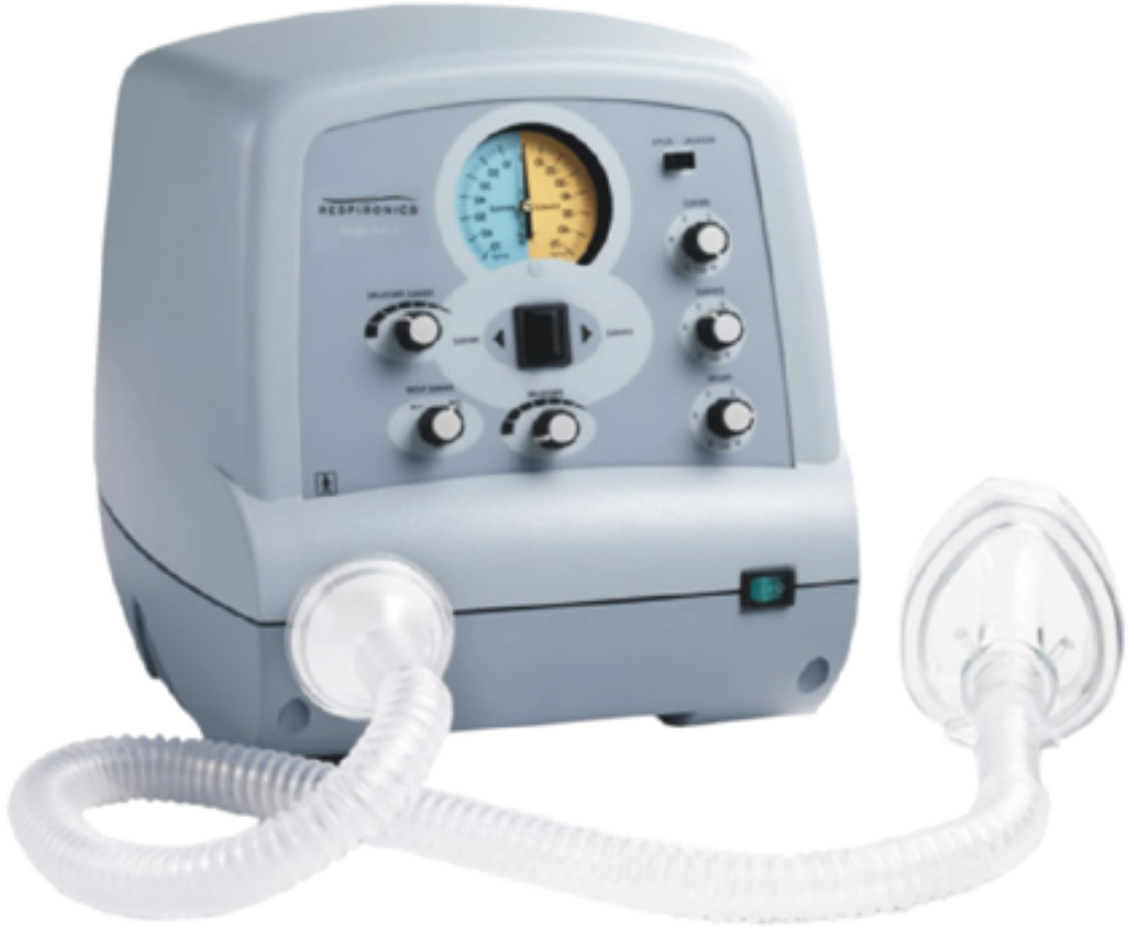
Respiratory care

- FVC
  - Sniff for those with bulbar symptoms
- Respiratory symptom questionnaire
- Overnight oximetry
- Respiratory physio
- Use of NIV



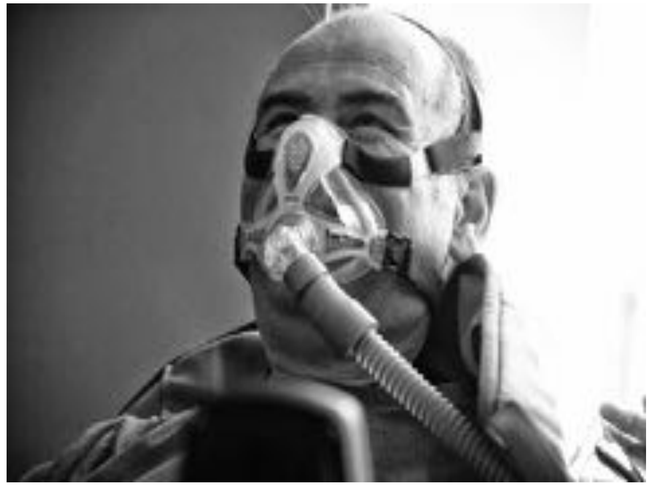
Cough Assist

- Clears secretions by gradually applying a positive pressure to the airway, then rapidly shifting to negative pressure
- Indication still uncertain
  - Trial planned
- Recurrent admissions for chest infection
- LMN-predominant, slowly-progressive

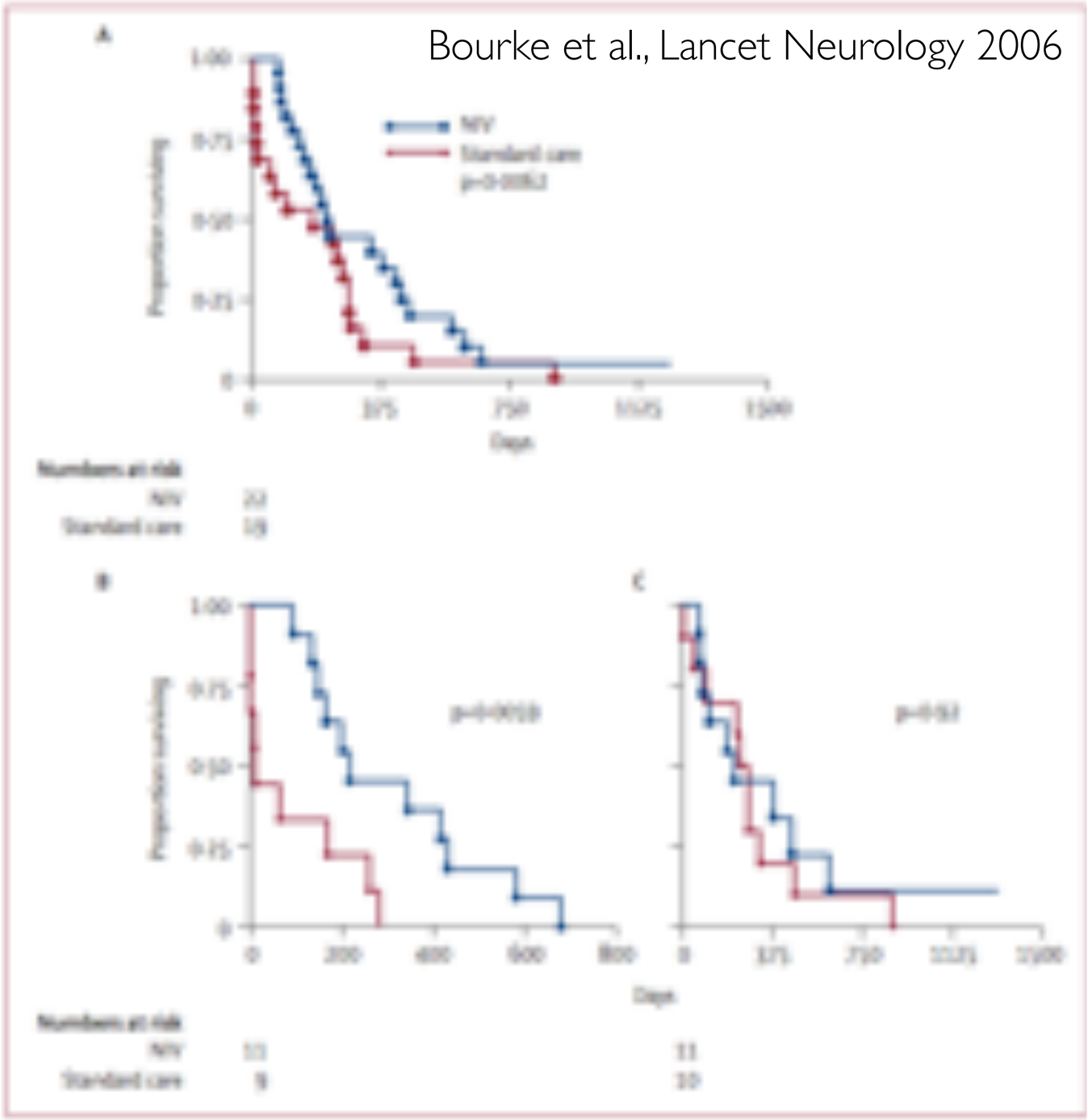


NIV effect on survival

Improves QoL



Bourke et al., Lancet Neurology 2006



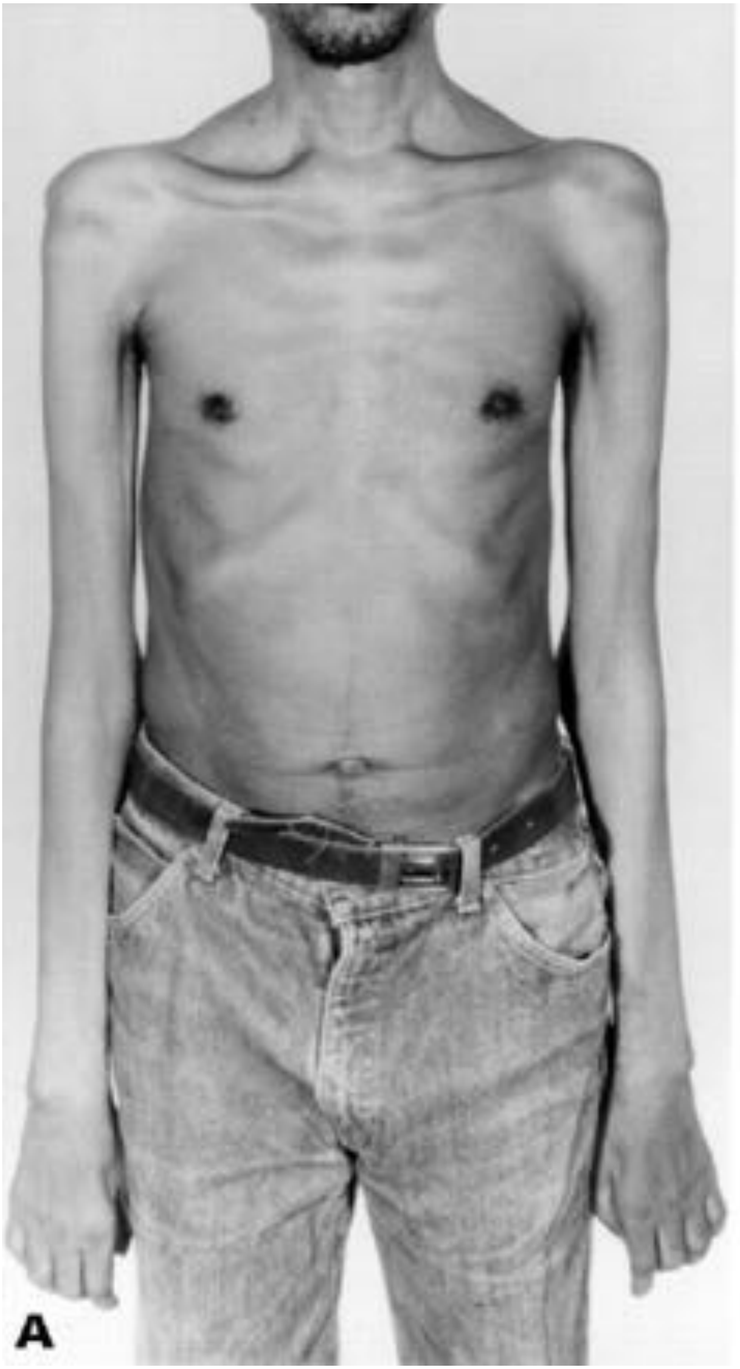
Tracheostomy

- 10% in recent Italian series (Chio *et al.* JNNP 2009):
  - Mean survival afterwards only 1 year
- 30% in Japan:
  - Frequently 'locked in'
- More open discussion:
  - What are patient's motives?
  - Avoiding sense of confrontation
  - Desire often dissipates
- For those that do:
  - Major resource challenge

Turner MR *et al.* Tracheostomy in MND. Practical Neurology 2019

Pain

- Multi-factorial, neglected area:
  - NSAIDs versus neuropathic pain agents
- Immobility:
  - Prolonged sitting (NB pressure sores RARE)
    - Posture and wheelchair management
  - Unable to turn in bed
- Muscle atrophy:
  - Altered joint dynamics
- Severe spasticity:
  - Uncommon, mainly PLS patients
  - Baclofen, Gabapentin



Distinct clinical and pathological characteristics of frontotemporal dementia associated with *C9ORF72* mutations

Brain 2012: 135; 693–708

Julie S. Snowden,[1,2] Sara Rollinson,[2] Jennifer C. Thompson,[1,2] Jennifer M. Harris,[1,2] Cheryl L. Stopford,[1,2] Anna M. T. Richardson,[1,2] Matthew Jones,[1,2] Alex Gerhard,[1,2] Yvonne S. Davidson,[2] Andrew Robinson,[2] Linda Gibbons,[2] Quan Hu,[2] Daniel DuPlessis,[3] David Neary,[1,2] David M. A. Mann[2] and Stuart M. Pickering-Brown[2]

Table 3 Behavioural changes in patients with C9ORF72 mutations

Behavioural domains	Symptoms	Patients															
		01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16
Psychotic symptoms	Delusions/paranoia	−	−	−	−	+	+	−	−	−	+	+	+	+	+	−	+
	Somatoform delusions	−	−	−	−	+	+	−	−	−	−	+	−	+	+	−	−
	Hallucinations	−	−	−	−	−	+	−	−	−	−	+	+	−	+	−	−
	Bizarre/irrational behaviour	−	−	−	−	+	+	+	+	+	+	+	+	+	+	+	+
Disinhibition	Socially inappropriate	−	+	+	+	+	−	−	+	+	−	+	+	−	+	+	+
	Loss of manners	+	+	+	+	+	−	−	+	+	+	+	+	−	+	+	+
	Impulsive (overspends)	−	−	+	−	−	−	+	−	−	−	+	+	−	+	+	+
Apathy	Apathy	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	Inertia	+	+	−	+	+	+	+	+	+	+	−	+	−	+	+	+
Loss sympathy and empathy	Neglects feelings	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
	Less interest/warmth	+	+	+	−	+	−	−	+	+	+	+	−	+	+	+	+
Repetitive behaviours, stereotypies and obsessionality	Simple mannerisms	−	−	−	−	+	−	−	−	−	−	−	−	+	−	−	−
	Complex routines/rituals	+	−	−	−	−	+	+	+	+	+	+	+	+	+	+	+
	Repetitive speech	+	−	+	−	+	−	+	+	−	+	+	+	+	+	+	−
	Clock watches	−	−	−	−	−	−	+	−	−	−	−	+	−	−	−	+
	Excess cleaning	−	−	−	−	−	−	+	−	−	−	−	+	−	−	−	−
Dietary change	Sweet food preference	−	−	+	−	−	−	−	−	+	−	−	−	−	−	−	−
	Food fads	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+
	Binge eating/cramming	+	−	−	−	−	+	+	−	+	+	−	−	+	−	+	+
	Mouths inedible objects	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
Loss of insight	Denial of illness	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+
	Unconcern	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+ = present at initial referral, − = absent at initial referral.

Pract Neurol
2017;**17**:128–129.

Sweet food preference in amyotrophic lateral sclerosis

Martin R Turner, Kevin Talbot

Aggregation of Neurologic and Neuropsychiatric Disease in Amyotrophic Lateral Sclerosis Kindreds: A Population-Based Case–Control Cohort Study of Familial and Sporadic Amyotrophic Lateral Sclerosis

ANN NEUROL 2013;74:699–708

Susan Byrne, PhD,[1,2] Mark Heverin, MSc,[1] Marwa Elamin, PhD,[2] Peter Bede, MD,[1,2] Catherine Lynch, MSc,[1] Kevin Kenna, BSc,[3] Russell MacLaughlin, PhD,[1] Cathal Walsh, PhD,[4] Ammar Al Chalabi, PhD,[5] and Orla Hardiman, FRCPI[1,2]

Clustering of Neuropsychiatric Disease in First-Degree and Second-Degree Relatives of Patients With Amyotrophic Lateral Sclerosis

JAMA Neurol. 2017;74(12):1425-1430.

Margaret O'Brien, PhD; Tom Burke, PhD; Mark Heverin, MSc; Alice Vajda, PhD; Russell McLaughlin, PhD; John Gibbons; Susan Byrne, PhD; Marta Pinto-Grau, MSc; Marwa Elamin, PhD; Niall Pender, PhD; Orla Hardiman, FRCPI

Table 2. Prevalence and Relative Risk of Neuropsychiatric Conditions in First- and Second-Degree Relatives of Patients With ALS Compared With Controls

Condition	Relatives, No.		RR	*P* Value
	Of Cases (n = 2116)	Of Controls (n = 2139)		
Suicide	13	4	3.30	.04
Schizophrenia and psychotic illness	17	5	3.40	.02
Autism	10	1	10.10	.03
Depression	35	31	1.14	.59
Alcoholism	63	43	1.48	.045
Obsessive-compulsive disorder and rigid personality disorders	11	2	5.60	.02

Psychiatric disorders in *C9orf72* kindreds

Study of 1,414 family members

Emma M. Devenney, MBBChBAO, Rebekah M. Ahmed, MBBS, Glenda Halliday, PhD, Olivier Piguet, PhD, Matthew C. Kiernan, DSc, FRACP, and John R. Hodges, MD

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Dr. Devenney
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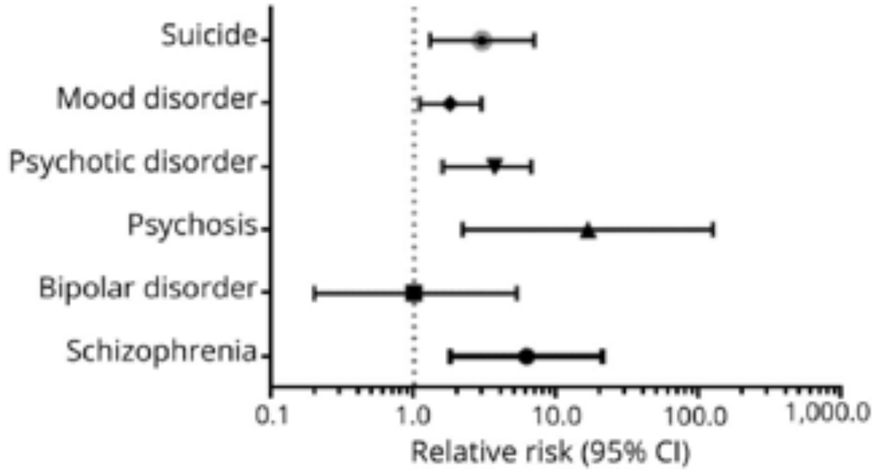
Neurology® 2018;91:e1498-e1507. doi:10.1212/WNL.0000000000006344



Neuropsychiatric changes precede classic motor symptoms in ALS and do not affect survival

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Jashelle Caga, MPsyHealth
Patricia Lillo, PhD
Sharpley Hsieh, PhD
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ABSTRACT

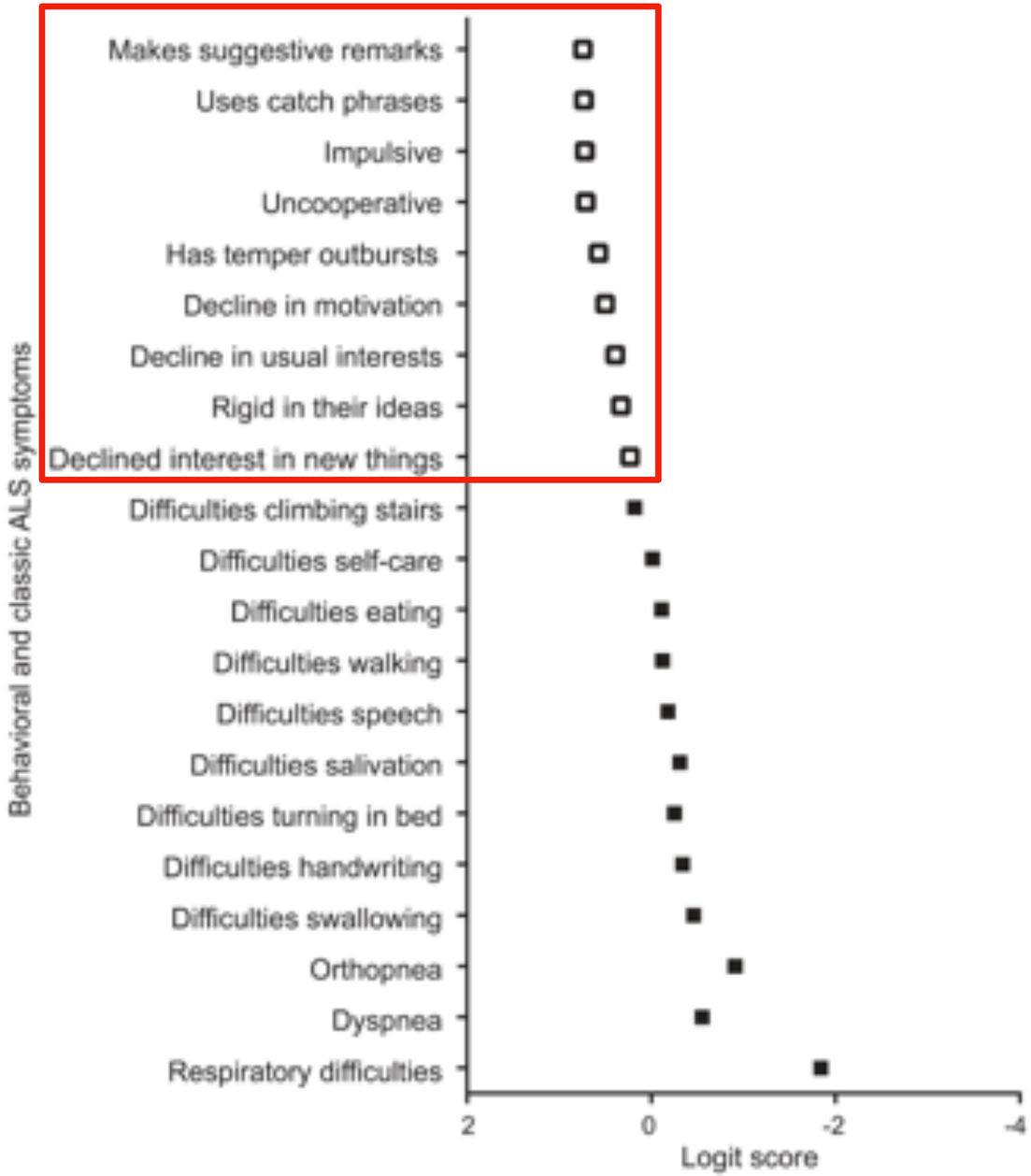
Objectives: To investigate patient susceptibility to neuropsychiatric symptoms in the context of progression of more classic motor symptoms in amyotrophic lateral sclerosis (ALS) and to examine the impact of neuropsychiatric symptoms on survival.

Methods: The study cohort consisted of 219 patients with ALS (limb onset = 159; bulbar onset = 60), with neuropsychiatric symptoms measured using the Motor Neuron Disease Behavioural Scale and more classic ALS symptoms assessed by the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised. For detection of symptom susceptibility (neuropsychiatric vs classic motor), a Rasch analysis was applied (n = 219). Cox proportional hazard regression models were used for the survival analysis (n = 115 patients), which incorporated neuropsychiatric and classic motor symptoms.

Results: Rasch analysis demonstrated that neuropsychiatric symptoms appeared earlier than classic motor features of ALS. However, differences in neuropsychiatric scores did not affect survival: patients with abnormalities in neuropsychiatric domains did not exhibit a different rate of survival than those without (χ^2, 3.447, p = 0.328, −2 log-likelihood 377.341).

Conclusions: Neuropsychiatric symptoms appear before classic motor features in ALS, which corroborates the notion that ALS and frontotemporal dementia lie on a disease continuum. The early detection of neuropsychiatric symptoms will be critical to inform clinical decisions and alleviate carer burden. Importantly, subtle neuropsychiatric symptoms alone do not affect survival in ALS, which in turn confirms their pervasive nature in ALS. **Neurology® 2014;82:149-155**

Logit scores of each individual question from the MiND-B and ALSFRS-R in a combined Rasch analysis



Frontotemporal involvement

- Frank dementia rare (10%)
  - Precedes the onset of motor problems
  - Faster progression of motor disease
- Clinical features:
  - Apathy or disinhibition (personal neglect)
  - Poor insight
  - Altered food preference, narrowed and favouring sweet foods
  - Food cramming (can precipitate choking)
- Involve extended family
  - Minimize risk-taking behaviour
- Ask about subtle behavioural change
  - Source of carer morbidity

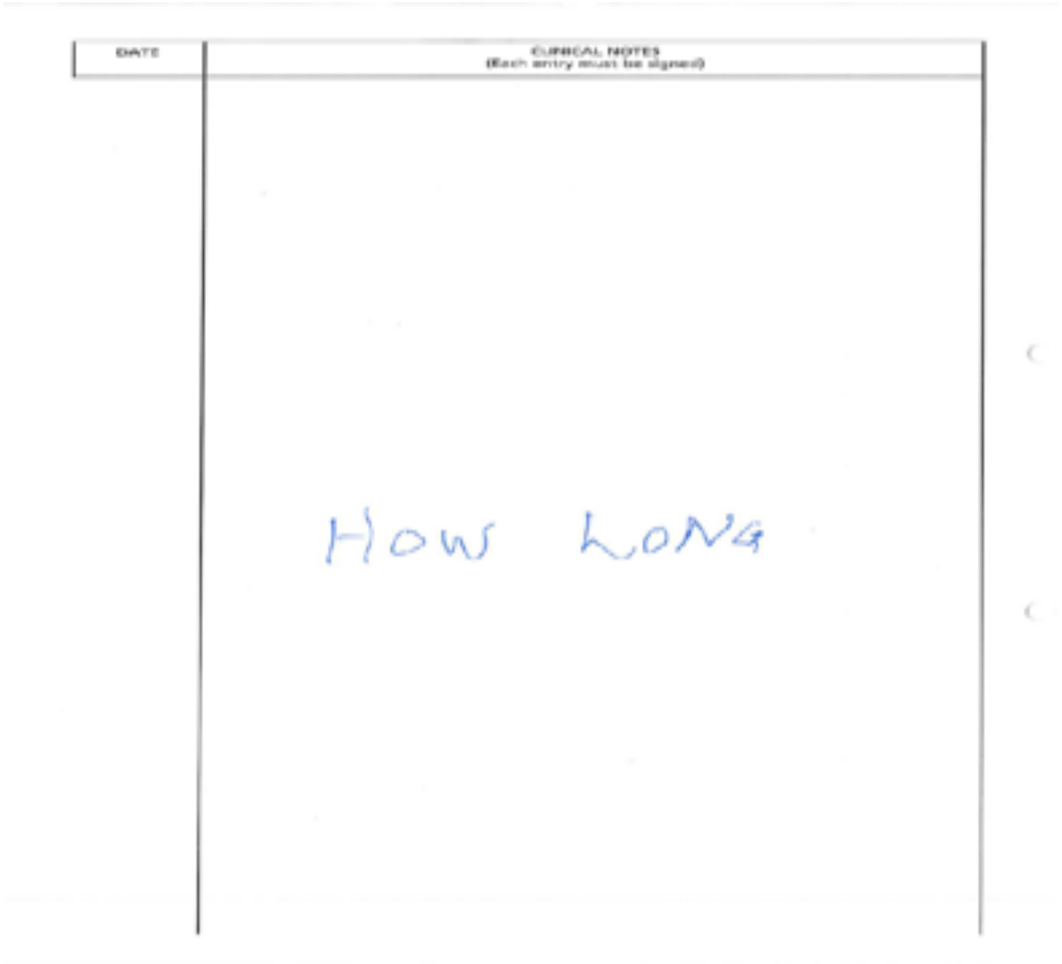
Carers

- Very high morbidity
- Depression rates high
  - cf MND patient low
- Benefit hugely from periods of Hospice-based respite
- Community palliative care involvement strongly linked to later perception of 'good death'

Opinions vary upon what the affected patient should be told. There is no doubt that a responsible relative should be told the truth, even if one stresses the variability of the clinical course of the condition, emphasizing that some cases are more benign. It has been my custom to tell the affected individual first that the condition is one which is well-recognized, if of unknown cause, and to explain something of research now in progress. In order not to destroy all hope, I believe that it is best to say also that the condition progresses slowly up to a point but then usually becomes arrested, and may even subsequently improve spontaneously, while making it clear that no-one can predict when and if arrest will occur. Comparatively few patients seem to be aware of the deception, even to the end.

From Brain's Diseases of the Nervous System, Ed. Walton 1977

Compassionate honesty



RESEARCH PAPER

A multidisciplinary clinic approach improves survival in ALS: a comparative study of ALS in Ireland and Northern Ireland

James Rooney,[1] Susan Byrne,[1] Mark Heverin,[1] Katy Tobin,[1] Alison Dick,[2] Colette Donaghy,[2] Orla Hardiman[1]

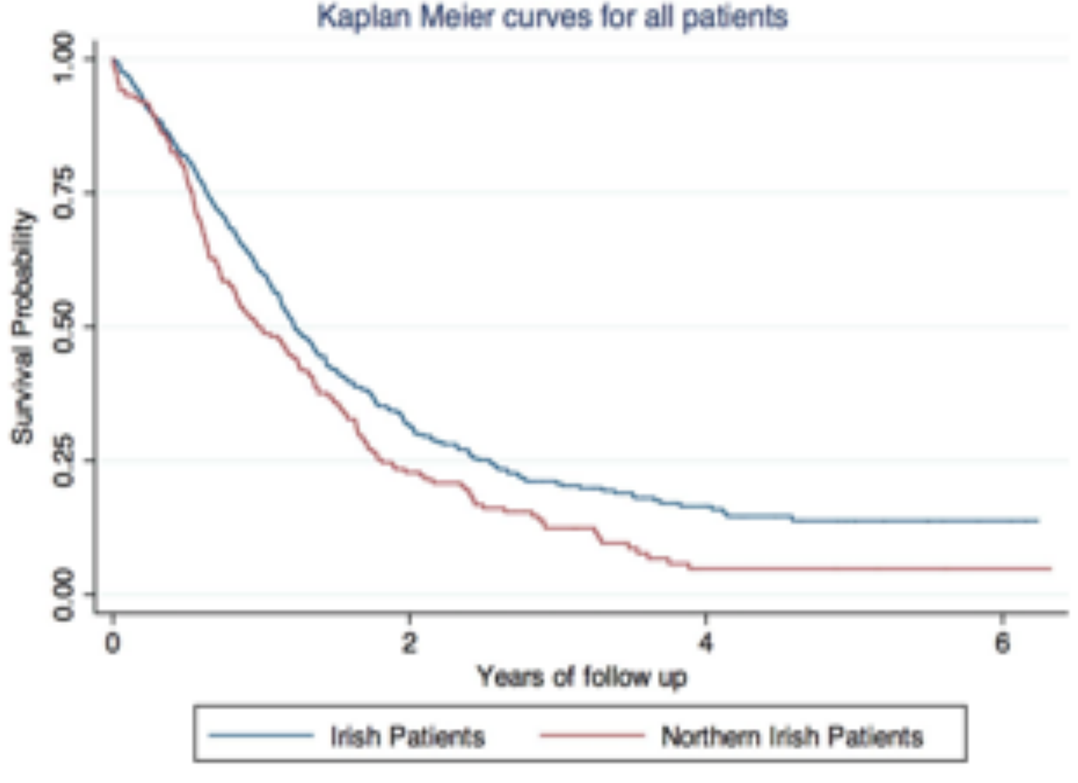
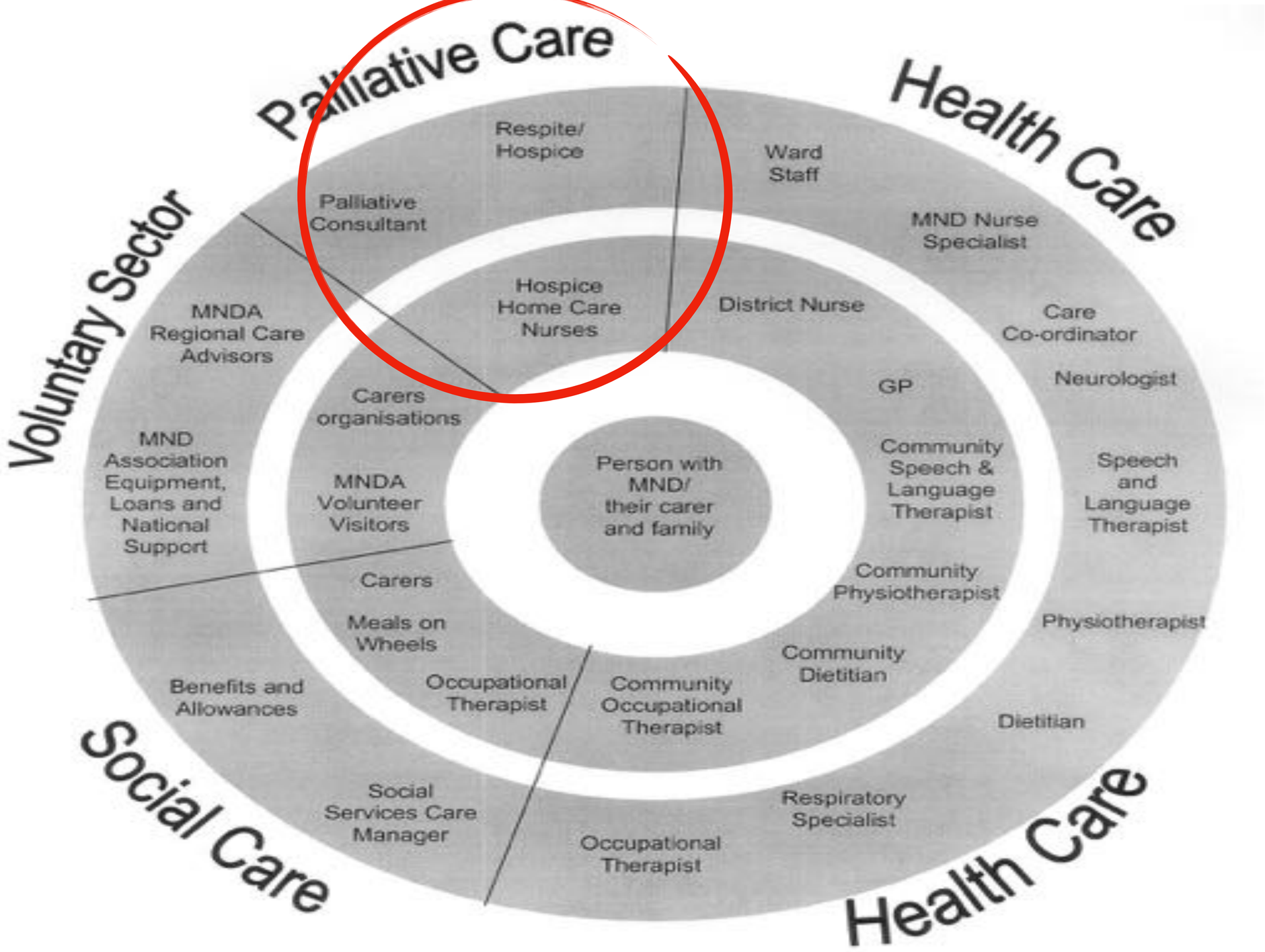
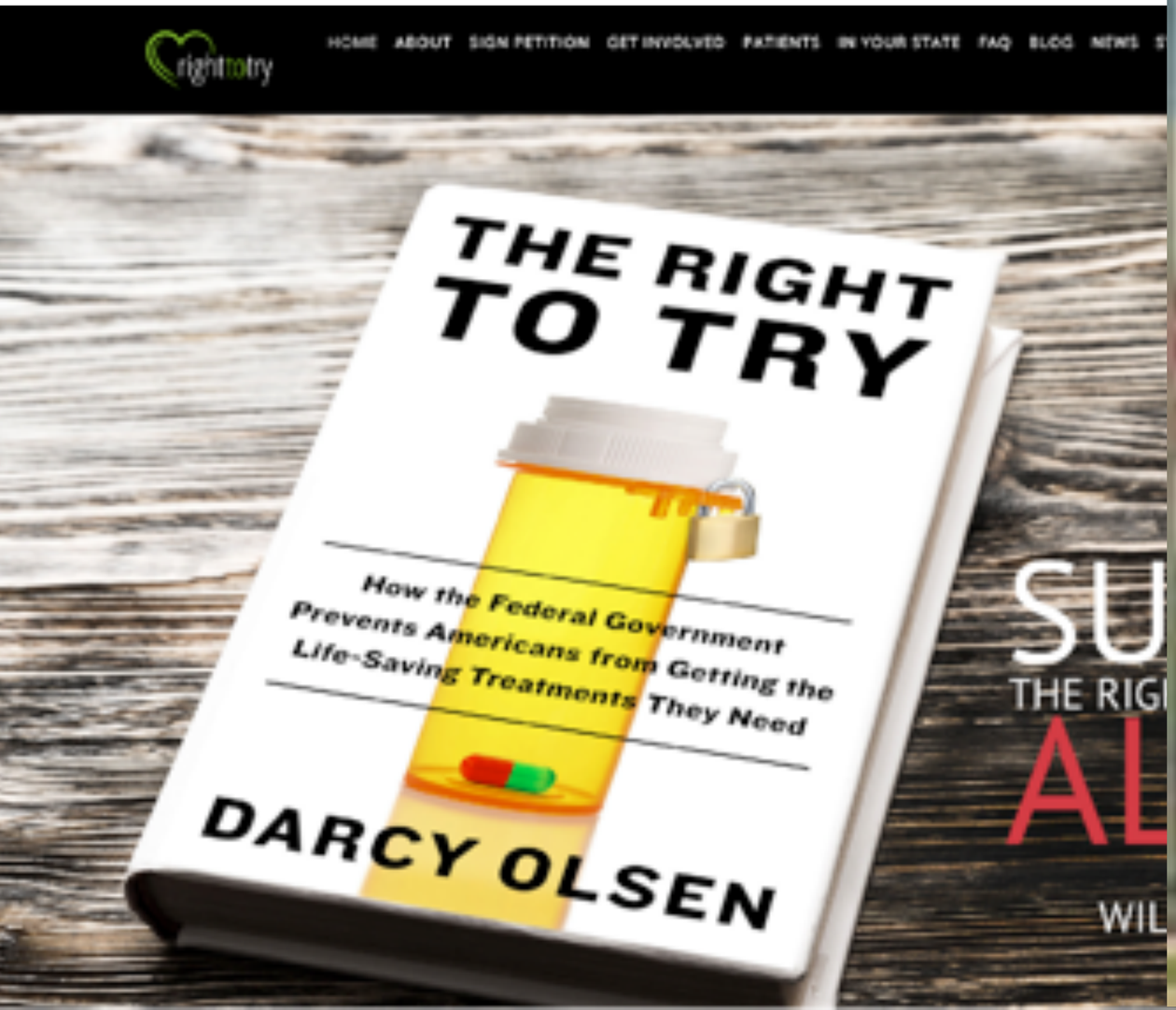


Figure 2 Survival difference between Ireland and Northern Ireland.

Multivariate regression of MDT care vs general care				
Age at diagnosis	Per 10 year increase	1.40	1.28 to 1.53	<0.001
Diagnostic delay	<31 weeks	1		
	31–55 weeks	0.96	0.77 to 1.19	0.685
	>55 weeks	0.67	0.53 to 0.84	0.001
MDT	No	1		
	Yes	0.59	0.49 to 0.71	<0.001
Sex	Female	1		
	Male	1.02	0.84 to 1.24	0.829
Site of onset	Limb	1		
	Bulbar	1.04	0.84 to 1.29	0.701
	Both	1.80	0.66 to 4.89	0.249
Riluzole use	No	1		
	Yes	0.68	0.54 to 0.87	0.002
Gastrostomy	No	1		
	Yes	0.90	0.71 to 1.13	0.355
NIV	No	1		
	Yes	1.38	1.12 to 1.69	0.003


Palliative Care
Health Care
Voluntary Sector
Social Care
Health Care
Respite/
Hospice
Palliative
Consultant
Ward
Staff
MND Nurse
Specialist
Hospice
Home Care
Nurses
District Nurse
Care
Co-ordinator
MNDA
Regional Care
Advisors
Carers
organisations
GP
Neurologist
MND
Association
Equipment,
Loans and
National
Support
MNDA
Volunteer
Visitors
Person with
MND/
their carer
and family
Community
Speech &
Language
Therapist
Speech
and
Language
Therapist
Carers
Community
Physiotherapist
Meals on
Wheels
Physiotherapist
Community
Dietitian
Benefits and
Allowances
Occupational
Therapist
Community
Occupational
Therapist
Dietitian
Social
Services Care
Manager
Respiratory
Specialist
Occupational
Therapist

Do something rather than nothing?



I want to try drug X

- Examples (not complete):

- Edaravone – Mitsubishi Tanabe Pharma
  - TW001 (Oral Edaravone) – Treeway
- NurOwn - Brainstorm
- Masitinib – AB Science
- Ibudilast – MidicNova
- GM604 - Genervon
- Cu-ATSM…

Neurofilament light chain

A prognostic biomarker in amyotrophic lateral sclerosis

OPEN ▲ *Neurology*® 2015;84:2247-2257

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Liz Gray

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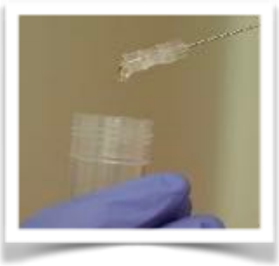
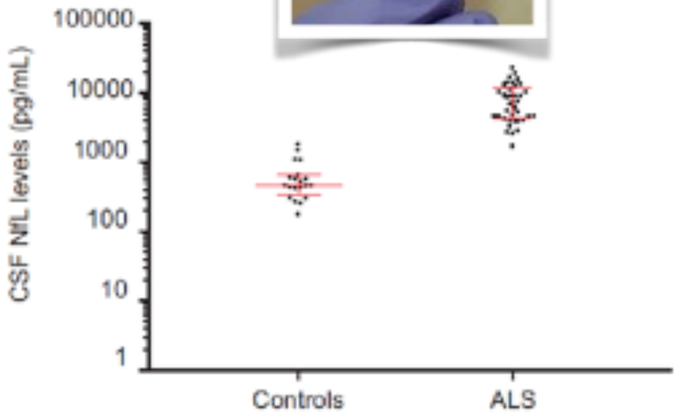
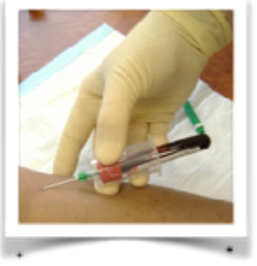
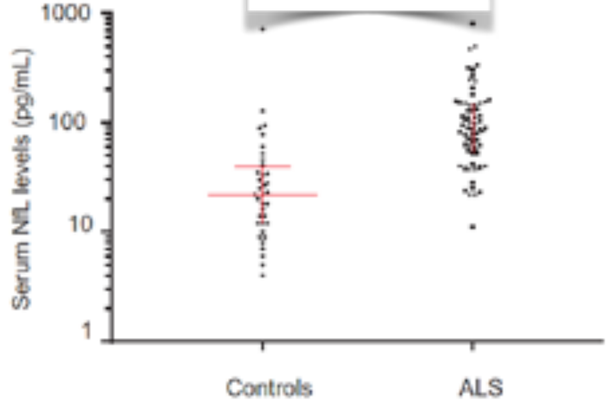
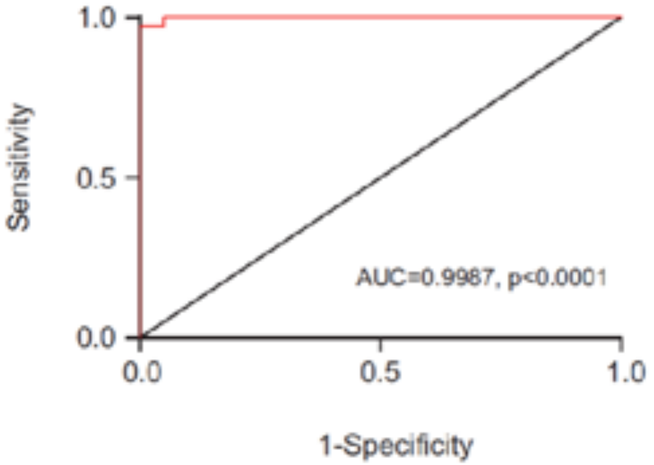
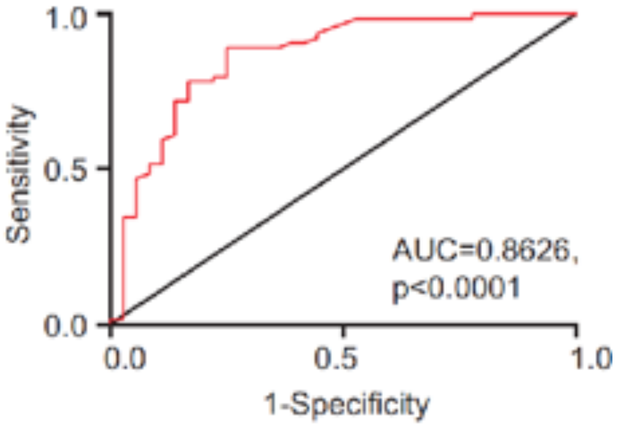


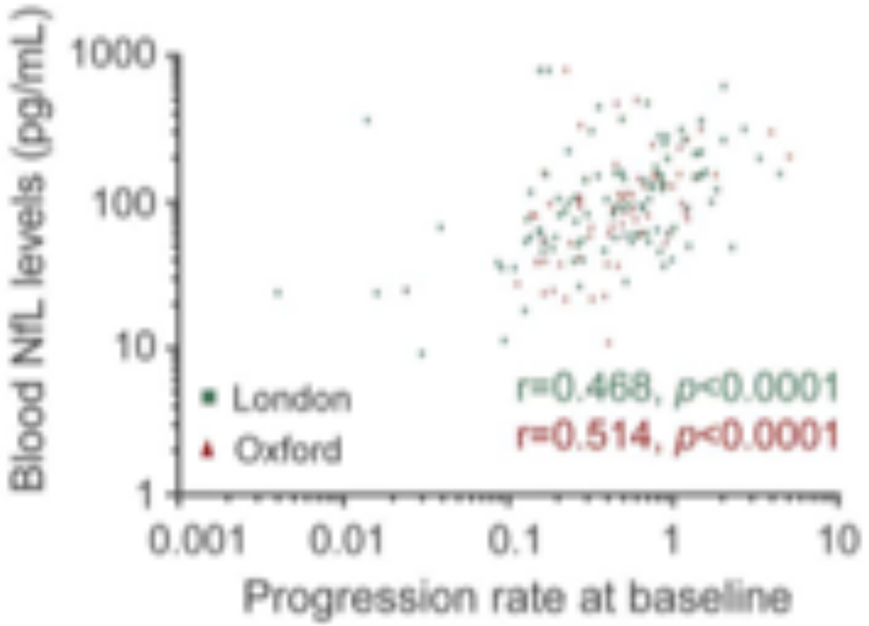




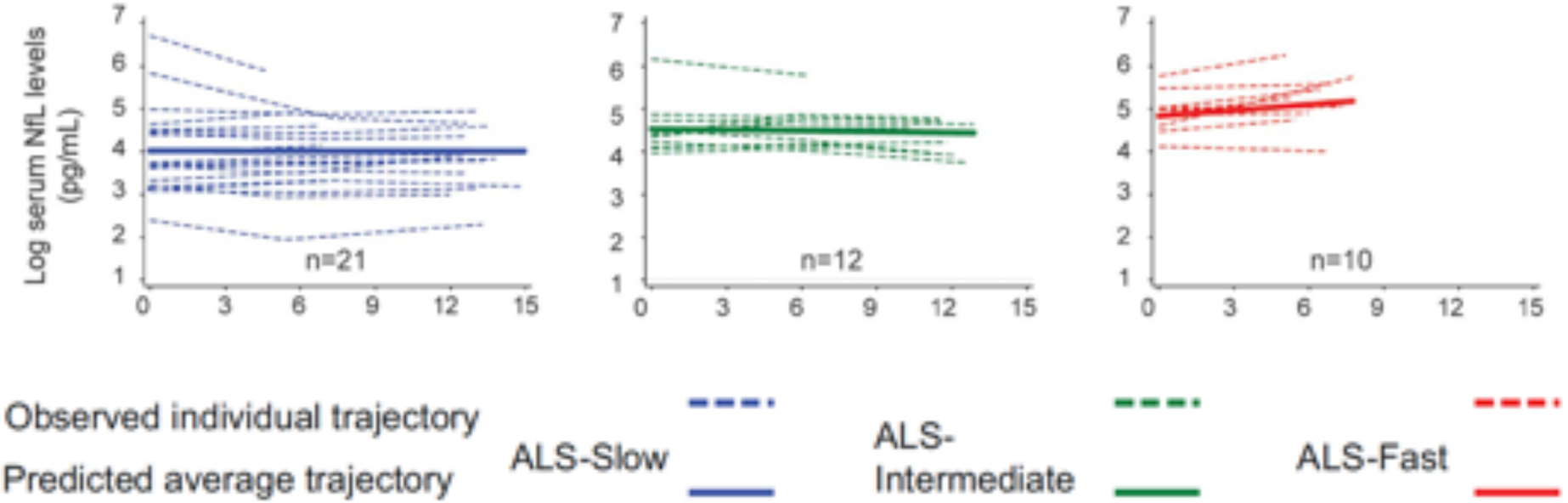


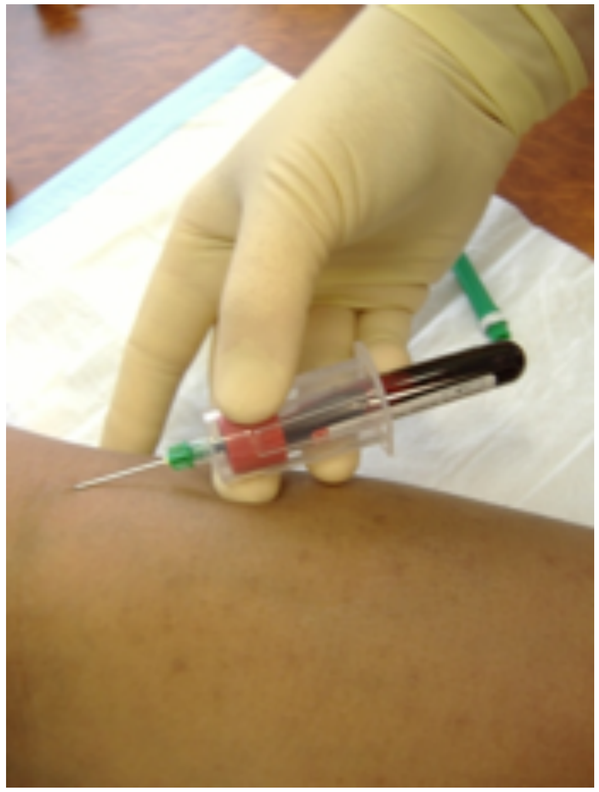






Levels reflect rate of progression and the individual stability over time is ideal for assessing therapy





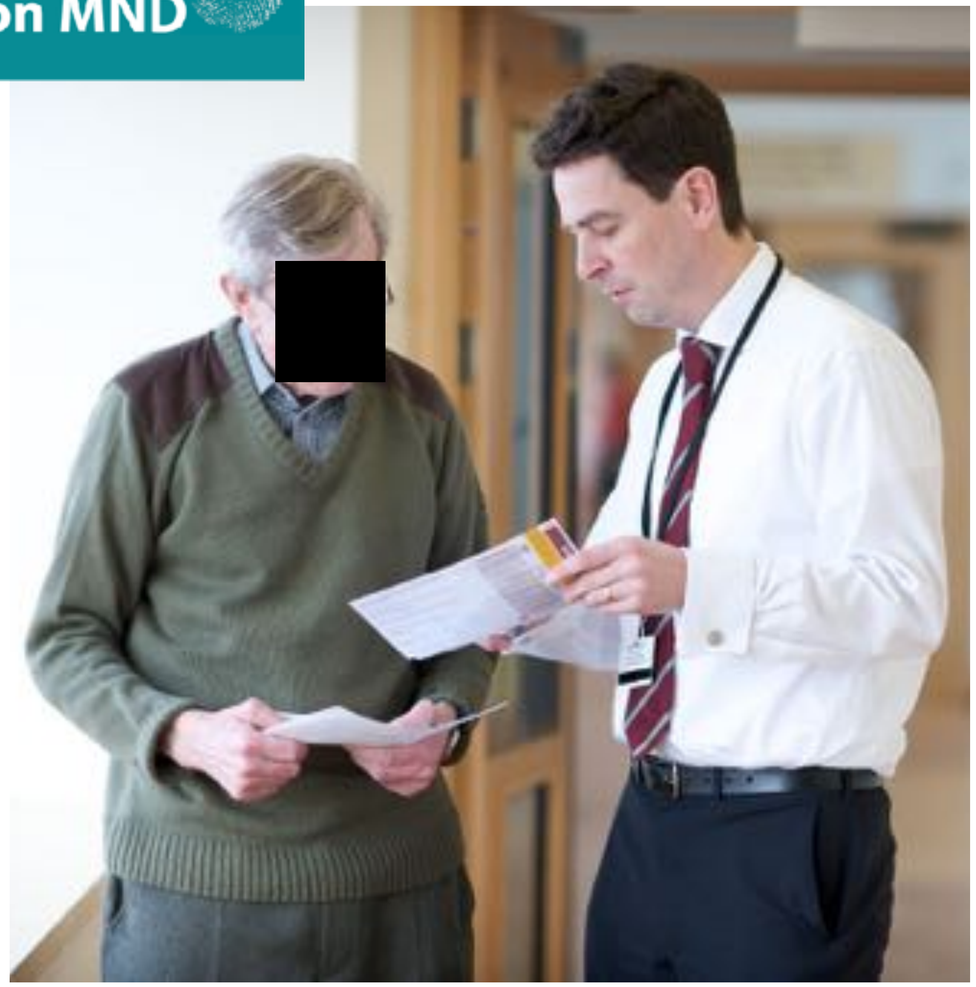
Compare where MS is

Hauser S *et al.* ANN NEUROL 2013;74:317–327

AMBRoSIA

A Multicentre Biomarker Resource Strategy In ALS

MAKE YOUR MARK on MND



An opportunity for every patient: Integrating research with care

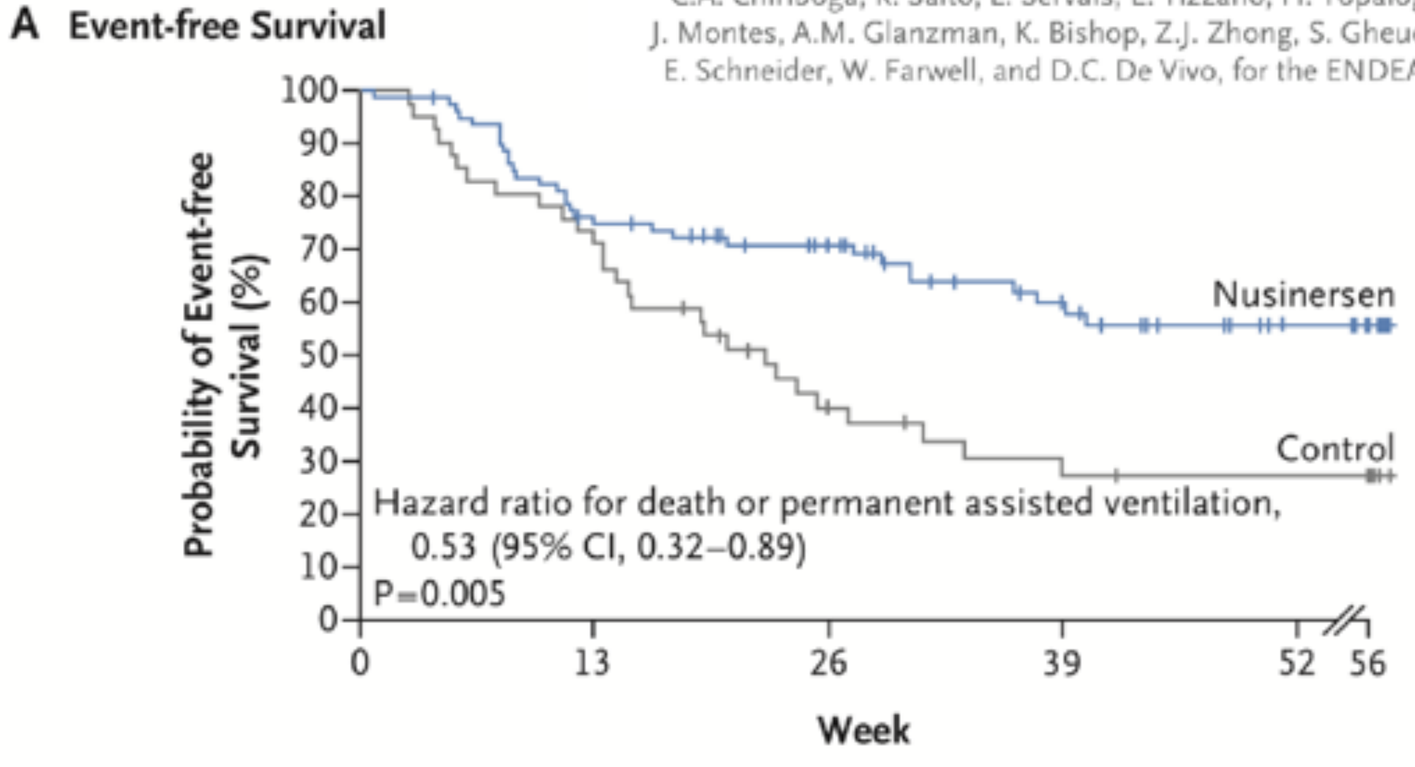
A genetic therapy revolution has arrived

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy

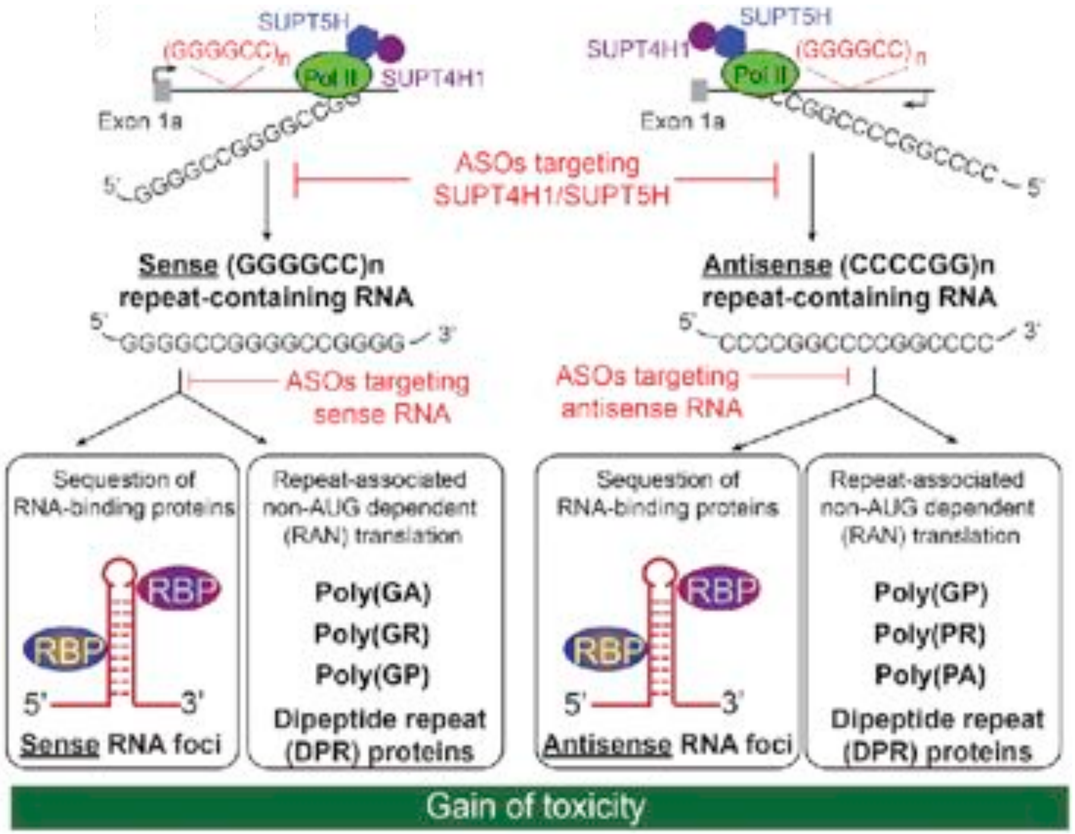
R.S. Finkel, E. Mercuri, B.T. Darras, A.M. Connolly, N.L. Kuntz, J. Kirschner, C.A. Chiriboga, K. Saito, L. Servais, E. Tizzano, H. Topaloglu, M. Tulinius, J. Montes, A.M. Glanzman, K. Bishop, Z.J. Zhong, S. Gheuens, C.F. Bennett, E. Schneider, W. Farwell, and D.C. De Vivo, for the ENDEAR Study Group*

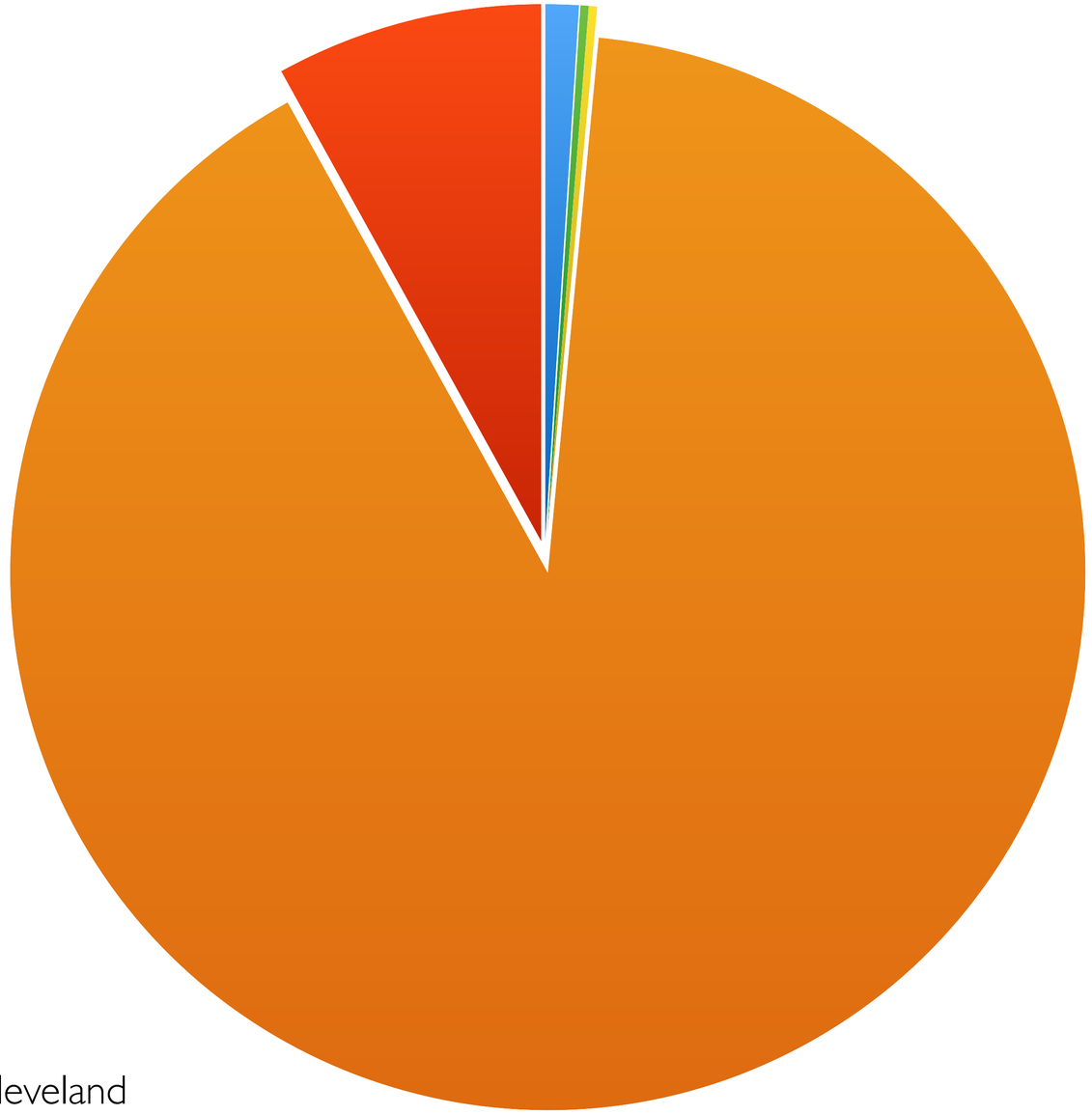


10% of <u>all</u> MND is now potentially treatable

Oligonucleotides:

1. *SOD1* in trial
2. *C9orf72* imminent…





Jiang & Cleveland
Neuron 2016

NUFFIELD DEPARTMENT OF
CLINICAL NEUROSCIENCES
Medical Sciences Division

UNIVERSITY OF
OXFORD

Families for the Treatment of Hereditary MND

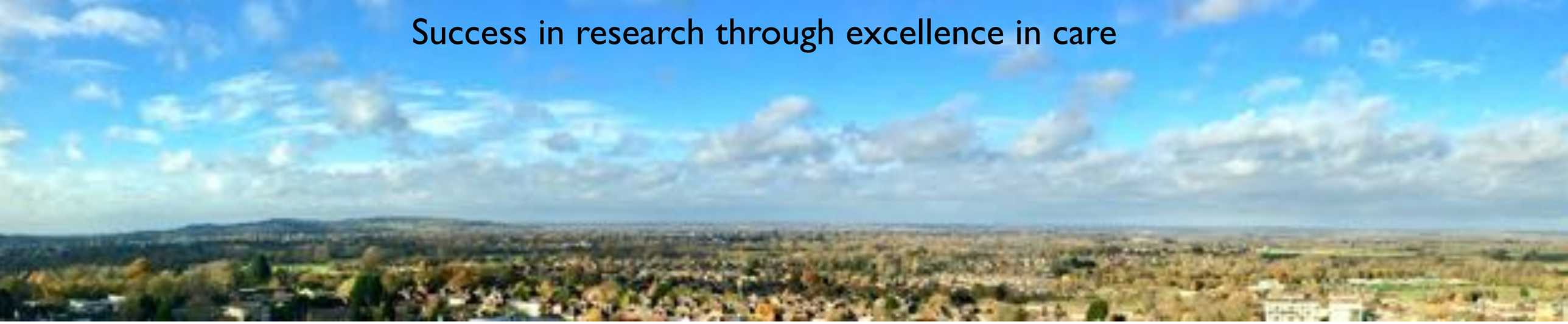
FaTHoM

mnda
motor neurone disease
association

Take home points

- Multi-disciplinary care anticipates problems, reduces hospital admissions, maximises quality of life and improves survival
- Early Community Palliative Care referral is extremely valuable
- MND & FTD overlap, with a common molecular background
- Behavioural change in MND has been underestimated and is a major burden for carers
- Genetic screening is becoming more routine and requires wider MDT training
- A therapeutic era for MND is imminent but may increase community support needs

Success in research through excellence in care



THE OXFORD MND CENTRE

Kevin Talbot
Neurologist

Rachael Marsden
Nurse Consultant
Clinic Coordinator

Jenny Rolfe
Occupational
Therapist

BioMOx

Lynn Ossher
Research
Coordinator

Liz Gray
Post-doctoral
scientist

Emily
Feneberg
Neurologist

Evan Edmond
Neurology
trainee

Lucy Farrimond
Neurology
trainee

Thanuja
Dharmadasa
Neurology
post-doctoral
trainee
(Sydney)

mnda

motor neurone disease
association