CRITICAL DECISIONS IN MND

Tim Williams
Consultant Neurologist & MND Care Centre Director, RVI

PROGNOSIS

- Average survival:
  30-36 months from symptom onset.
  18-24 months from diagnosis, av. diagnostic delay 12 months).
- 50% dead at 30 months
- 10-20% live ≥ 5yrs
- 5-10% live ≥ 10yrs
- V. occasional patients live 20 yrs (or more)

WHAT I TELL PATIENTS, THEIR FAMILIES AND CARERS

- I confirm the diagnosis of MND
- No alternative inflammatory, infective, structural or metabolic cause
- MND is a neurodegenerative disorder – similar but much less common than Alzheimer's or Parkinson's disease
- **MND is invariably fatal**

WHY SAY CLEARLY THAT MND IS FATAL?

Not usually relevant or of vital immediate importance at first appointment, but:

- no elephants in the room (death and taxes)
- tempers or influences the decisions we will make together in the future regarding disease management

DISEASE PROGRESSION

- Typical onset mid 50’s to mid 70’s (av. 63yrs)
- Patients typically fit and with little co-morbidity
- Progress from fit and active to high levels of dependency over 2-3yrs
- Houses converted into mini-hospitals, families and partners into carers/nurses
- High proportion (~50%) have cognitive impairment, with resultant emotional blunting, further eroding loving relationships

PHILOSOPHY OF MANAGEMENT

The management of MND is palliative from diagnosis

MANAGING RELENTLESSLY PROGRESSIVE DISEASE

- The mainstay of management is the timely provision of help and support to maintain independence
- Most patients/families want to remain independent in their own homes – not much to ask!
- The MND centre will help to coordinate care with the multiple disciplines and agencies likely to be involved

MANAGING RELENTLESSLY PROGRESSIVE DISEASE

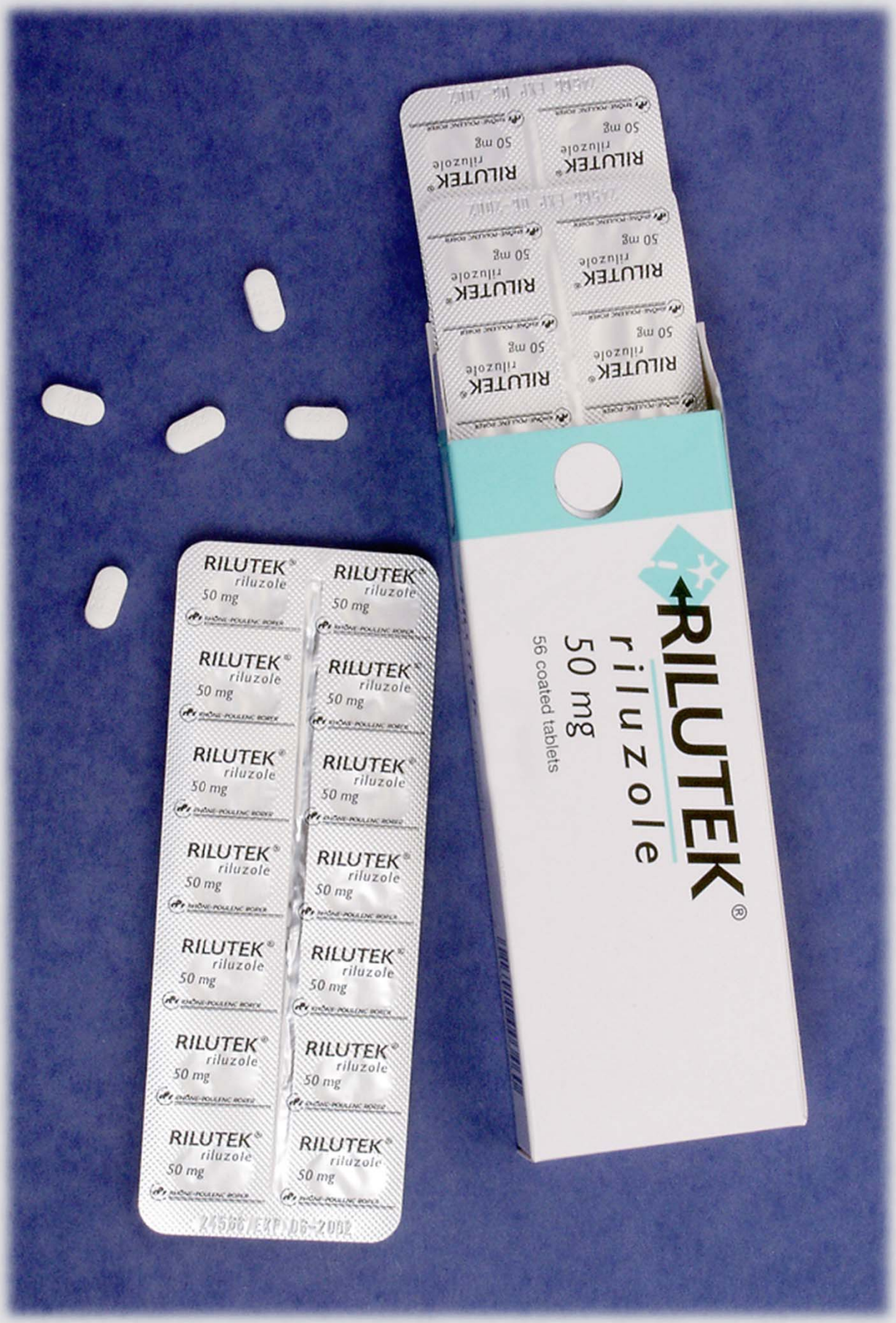
- We will consider and discuss appropriate and timely interventions

But……

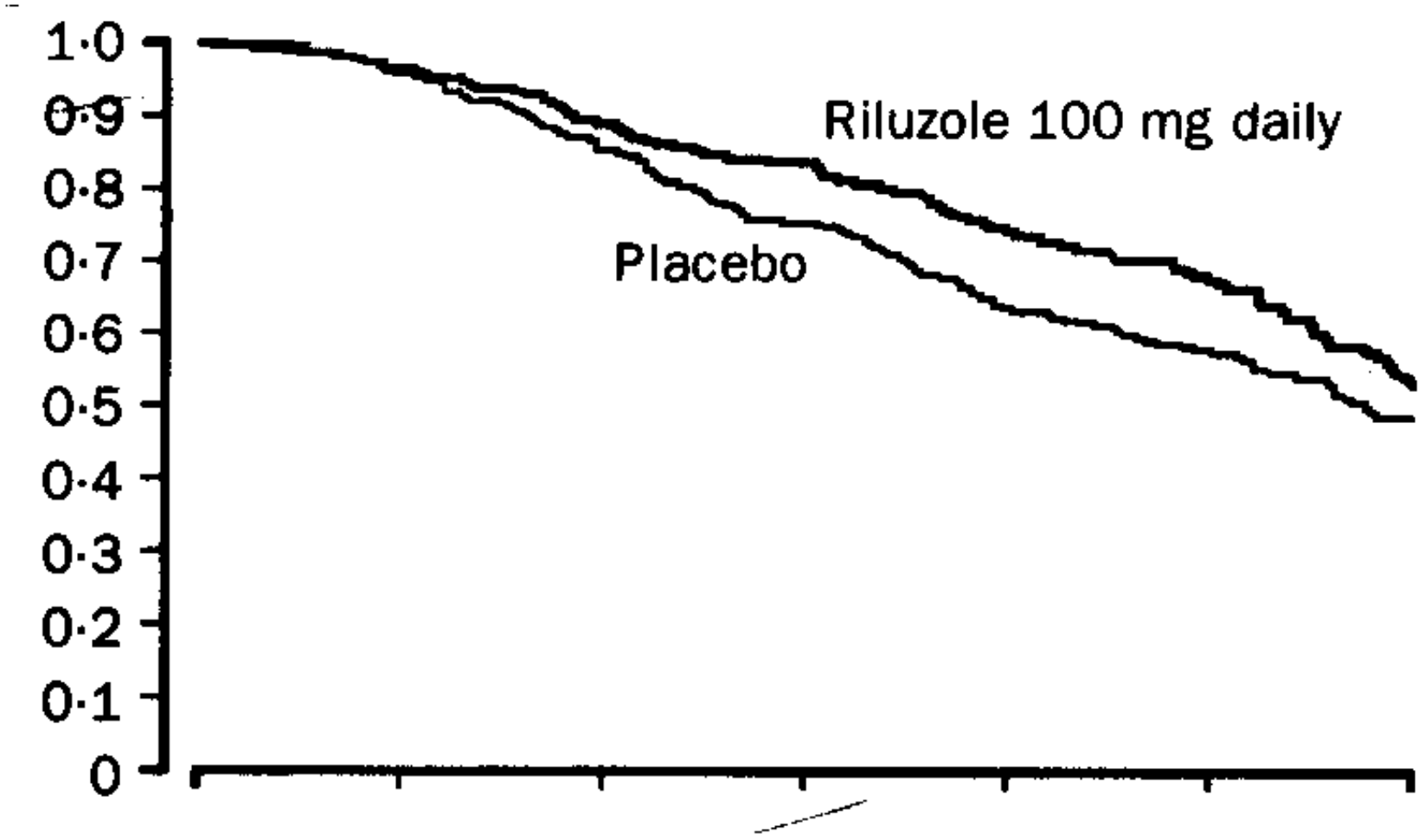
- the ultimately fatal nature of MND should temper management decisions

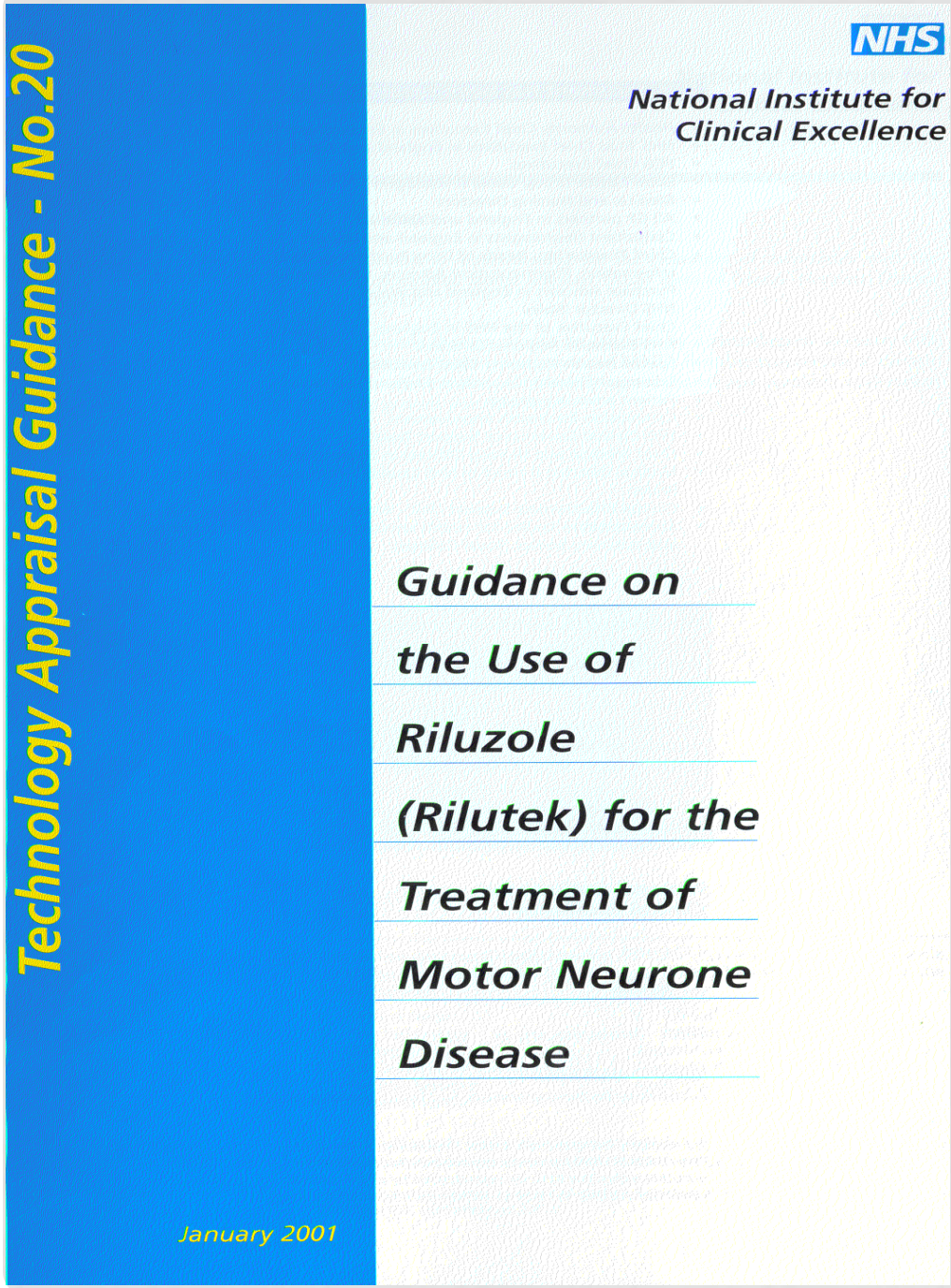
TREATMENTS (DRUGS, PILLS & POTIONS)

- Limited and the last aspect of management I discuss.
- Riluzole is the only licensed therapy


RILUTEK®
riluzole
50 mg
56 coated tablets
RILUTEK®
riluzole
50 mg
RHÔNE-POULENC RORER

RILUZOLE DATA





Local practice:

- ~45% patients on riluzole

Less likely if:

- >70yrs
- advanced disease
- poor resp function
- dementia
- other medical problems
- low threshold to stop treatment

CRITICAL DECISIONS IN MND

1. Respiratory support

2. Non-oral (gastrostomy) feeding

3. Use, timing & site of antibiotic administration

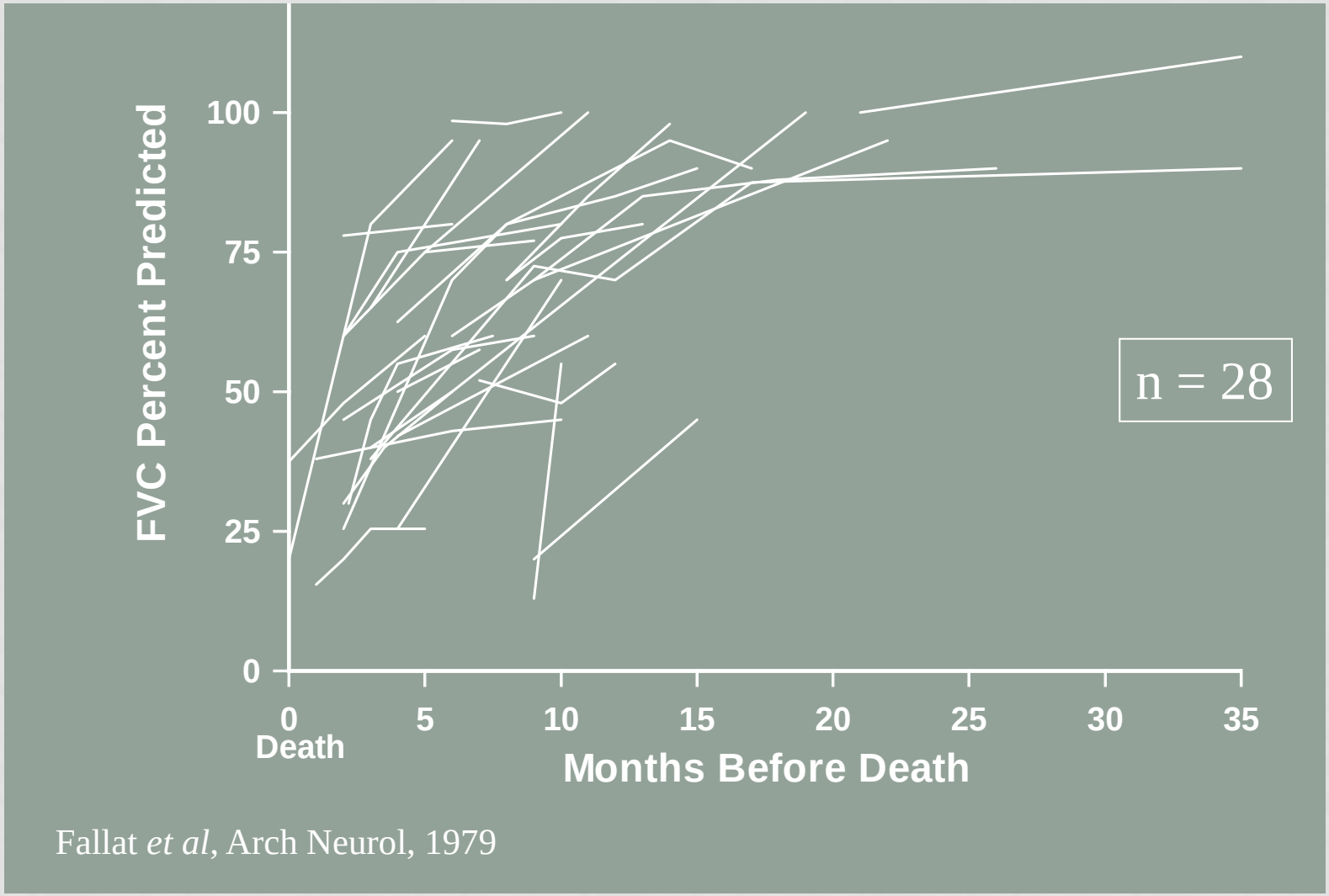
CRITICAL DECISIONS IN MND

1. Respiratory support

RESPIRATORY FAILURE IN MND

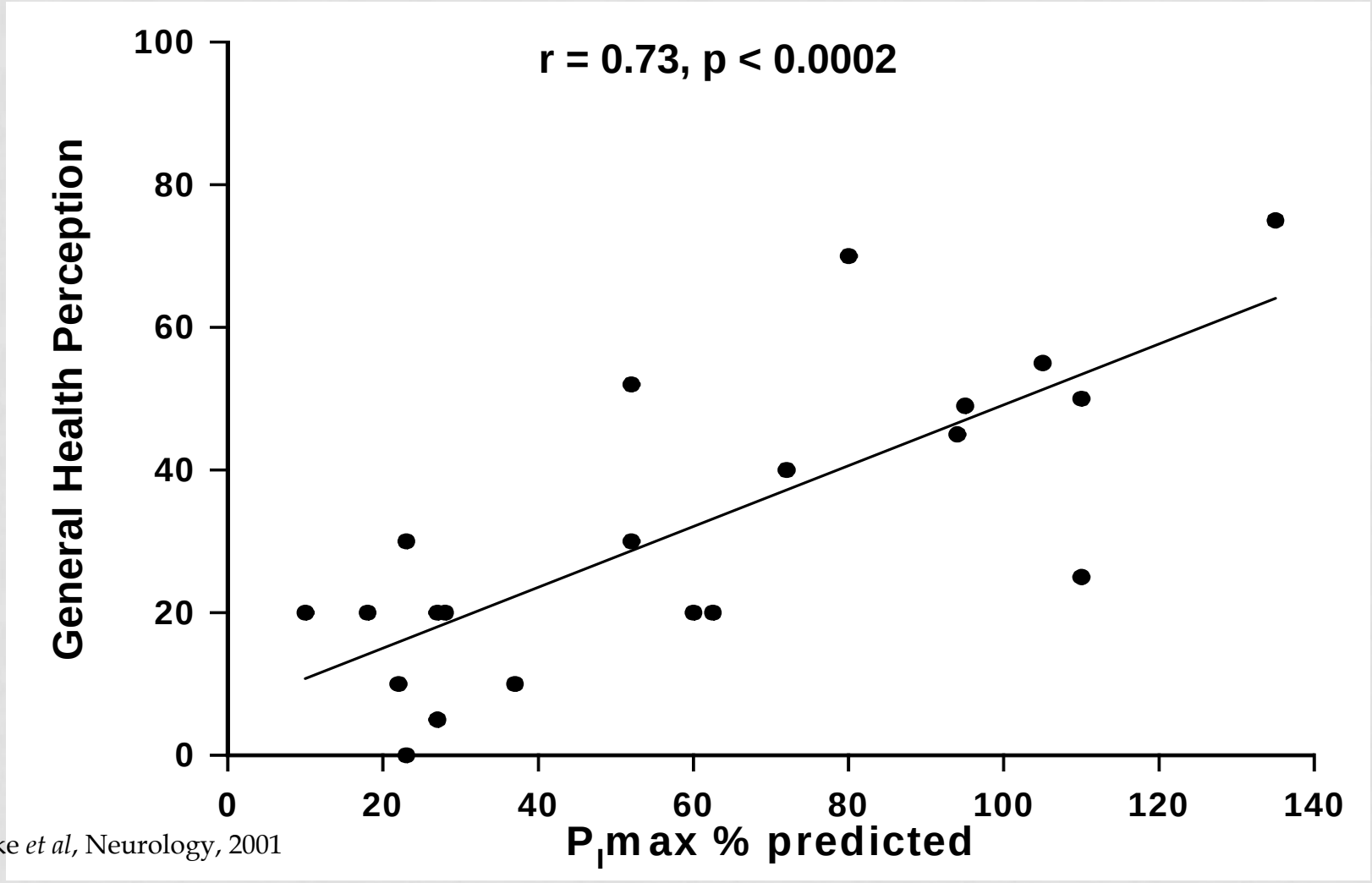
- Respiratory muscle weakness universal, with resp failure all but invariable mode of death in MND
- Mediates an effect not just on survival but also on quality of life
- Appropriate to consider “active” or “conservative” management

FVC AND SURVIVAL



Fallat *et al*, Arch Neurol, 1979

QOL VRS RESPIRATORY FUNCTION



Bourke *et al*, Neurology, 2001

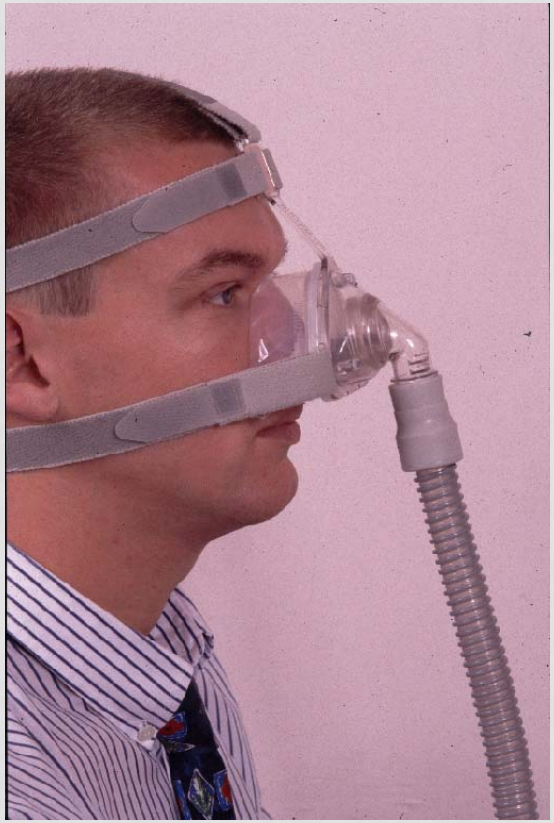
RESPIRATORY FAILURE IN MND

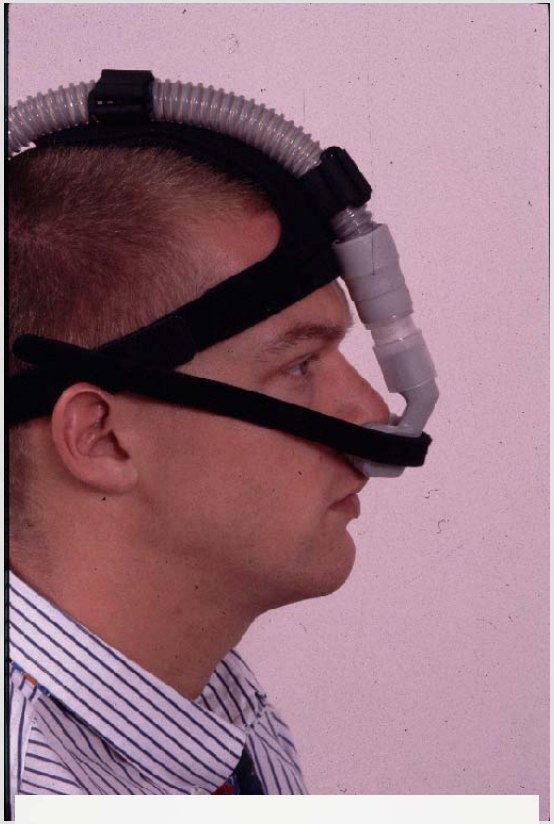
Conservative:

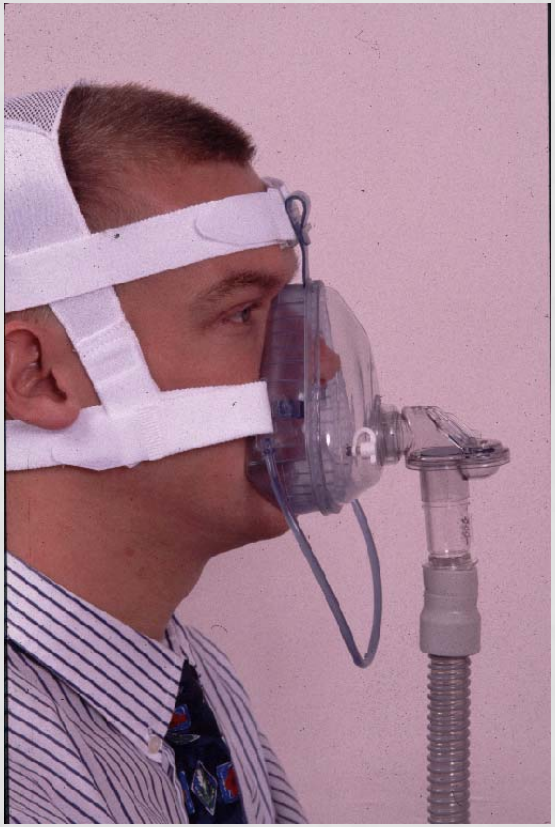
- posture, sedative (symptom relieving) medication, O_2.
- may hasten decline

Active

- Consider ventilatory support alongside more conservative measures as outlined above

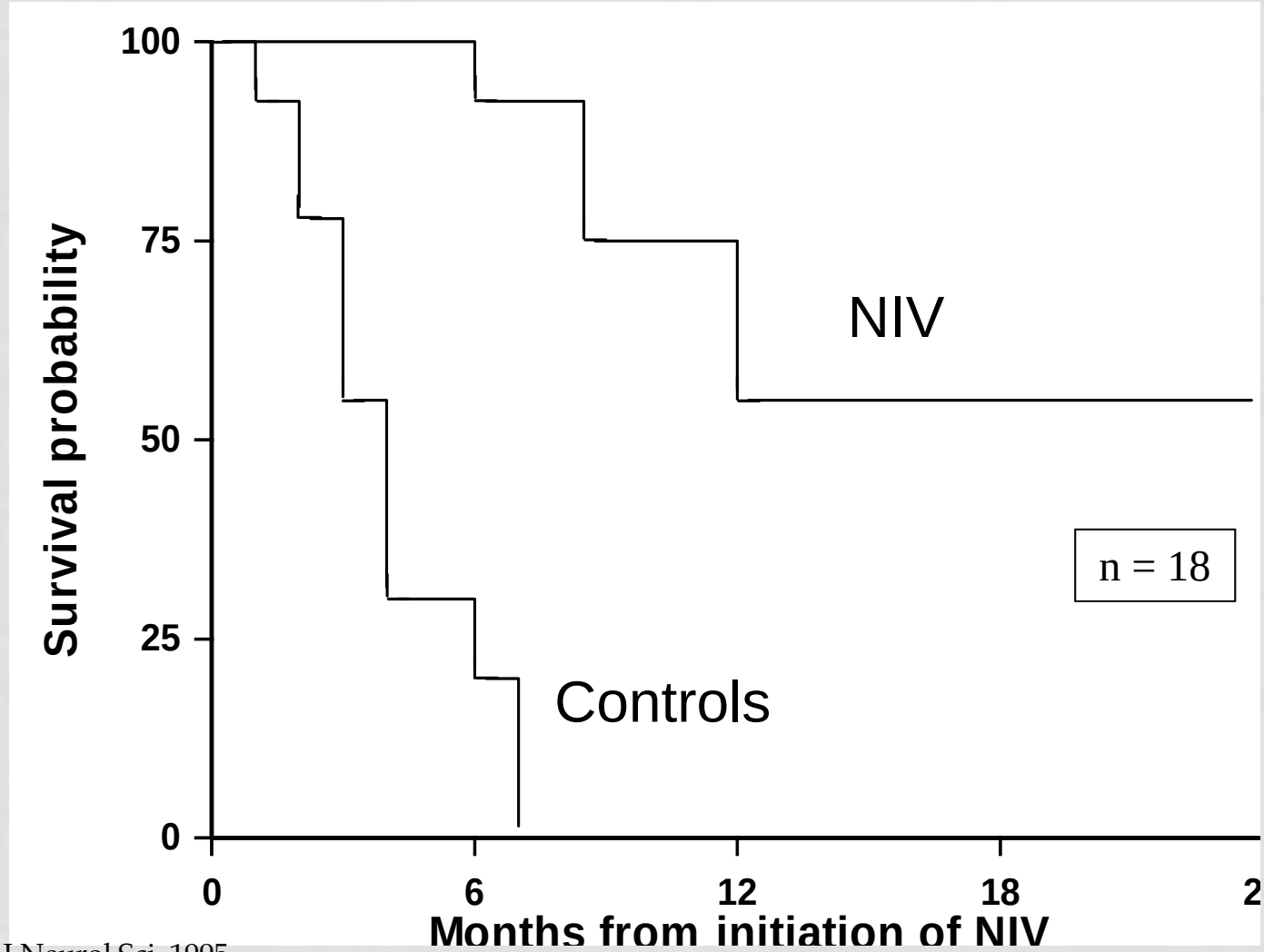






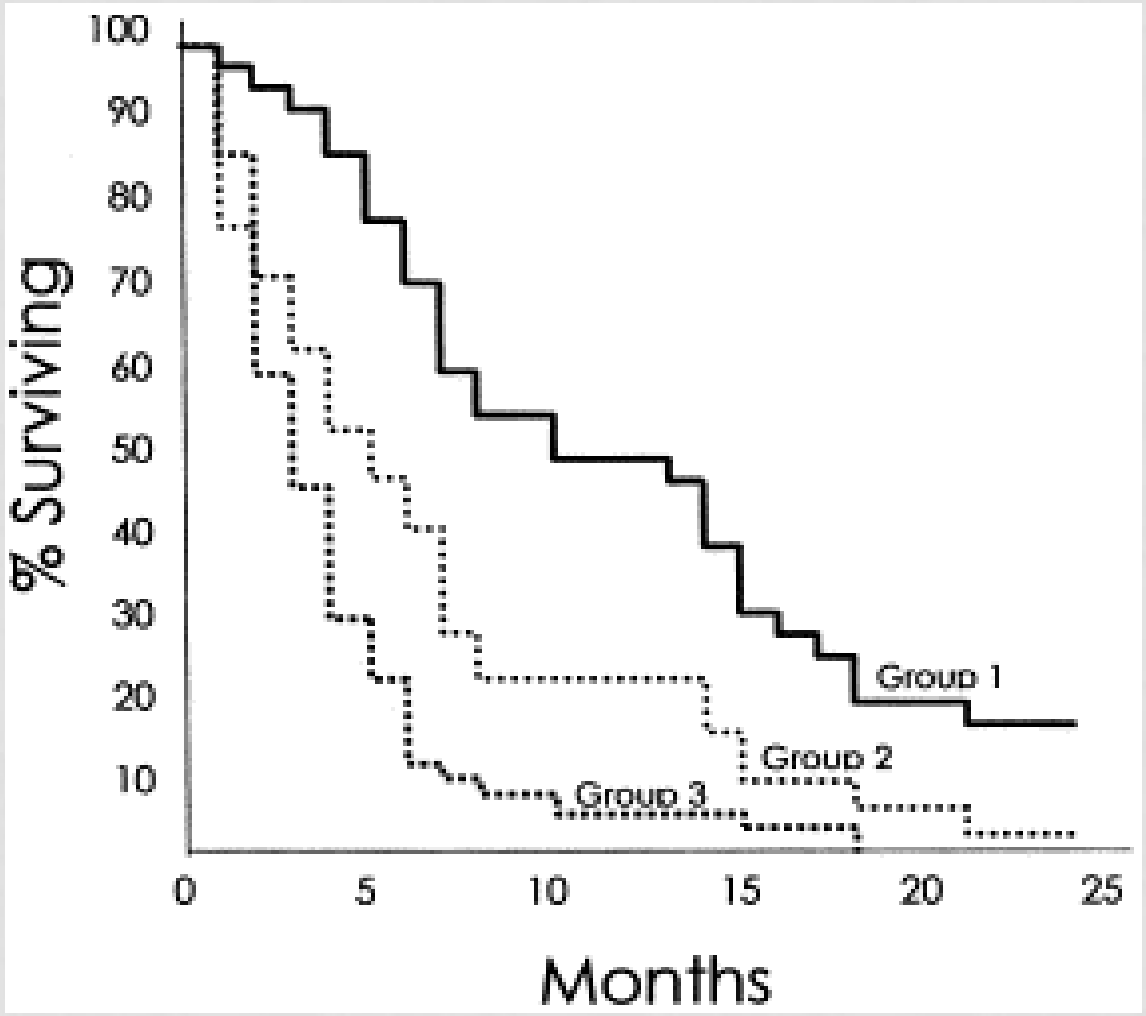

IPAP
EPAP
Ti
Back Up
Mode
Hi Alarm
Lo Alarm
Help
Menu Clear
Battery
Power
NIPPY 3+
Set

SURVIVAL: NIV VS NO NIV



Pinto *et al*, J Neurol Sci, 1995

SURVIVAL AND COMPLIANCE WITH NIV



Group 1 > 4 hr/d (n = 38)

Group 2 < 4 hr/d (n = 32)

Group 3 declined or intolerant of NIV (n = 52)

Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial

Stephen C Bourke, Mark Tomlinson, Tim L Williams, Robert E Bullock, Pamela J Shaw, G John Gibson

Lancet Neurol 2006; 5: 140–47

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Summary

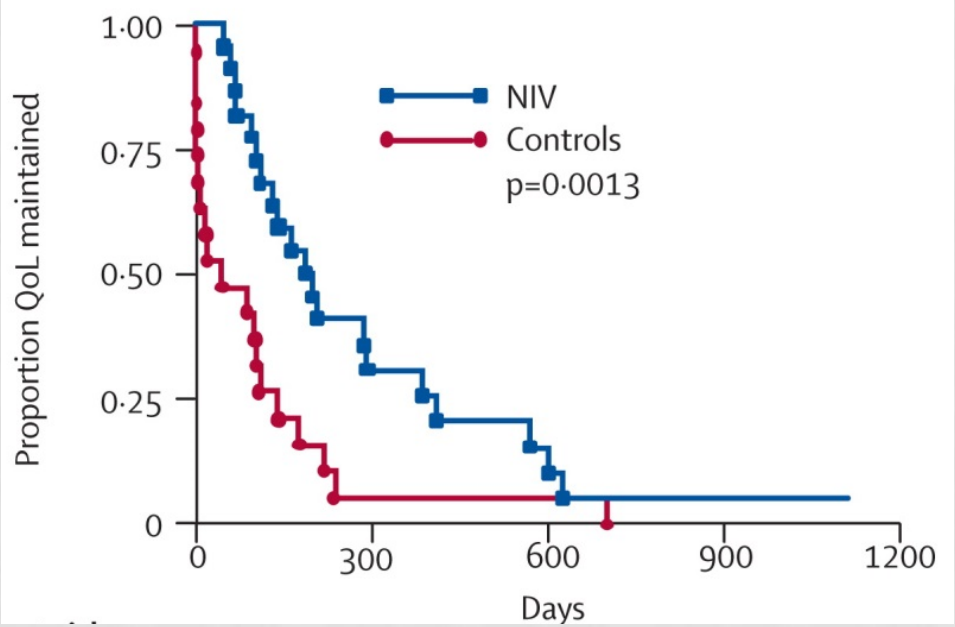
Background Few patients with amyotrophic lateral sclerosis currently receive non-invasive ventilation (NIV), reflecting clinical uncertainty about the role of this intervention. We aimed to assess the effect of NIV on quality of life and survival in amyotrophic lateral sclerosis in a randomised controlled trial.

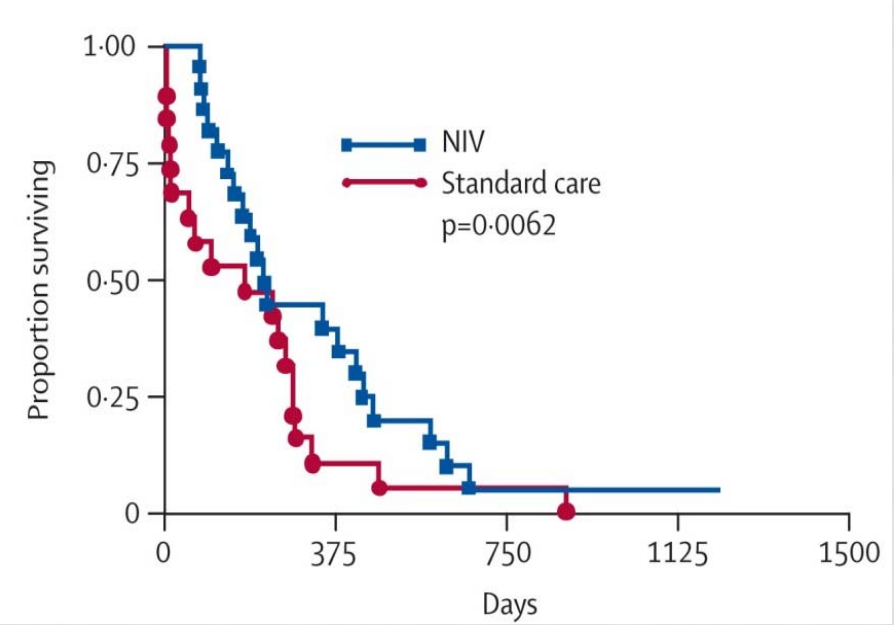
Methods 92 of 102 eligible patients participated. They were assessed every 2 months and randomly assigned to NIV (n=22) or standard care (n=19) when they developed either orthopnoea with maximum inspiratory pressure less than 60% of that predicted or symptomatic hypercapnia. Primary validated quality-of-life outcome measures were the short form 36 mental component summary (MCS) and the sleep apnoea quality-of-life index symptoms domain (*sym*). Both time maintained above 75% of baseline (T_MCS and T_*sym*) and mean improvement (μMCS and μ*sym*) were measured.

Findings NIV improved T_MCS, T_*sym*, μMCS, μ*sym*, and survival in all patients and in the subgroup with better bulbar function (n=20). This subgroup showed improvement in several measures of quality of life and a median survival benefit of 205 days (p=0·006) with maintained quality of life for most of this period. NIV improved some quality-of-life indices in those with poor bulbar function, including μ*sym* (p=0·018), but conferred no survival benefit.

Interpretation In patients with amyotrophic lateral sclerosis without severe bulbar dysfunction, NIV improves survival with maintenance of, and improvement in, quality of life. The survival benefit from NIV in this group is much greater than that from currently available neuroprotective therapy. In patients with severe bulbar impairment, NIV improves sleep-related symptoms, but is unlikely to confer a large survival advantage.

SURVIVAL AND QOL FROM RANDOMISATION





NIV AND MND?

- NIV is for symptoms not survival (or poor tests of respiratory function)
- Not for simply for those with advanced physical disability at the end of their disease
- NIV is not for all
- Pros and cons discussed in detail
- NIV should, as a minimum, improve or maintain QoL – if it doesn't patients should be supported in stopping treatment!

CRITICAL DECISIONS IN MND

2. Non-oral (gastrostomy) feeding

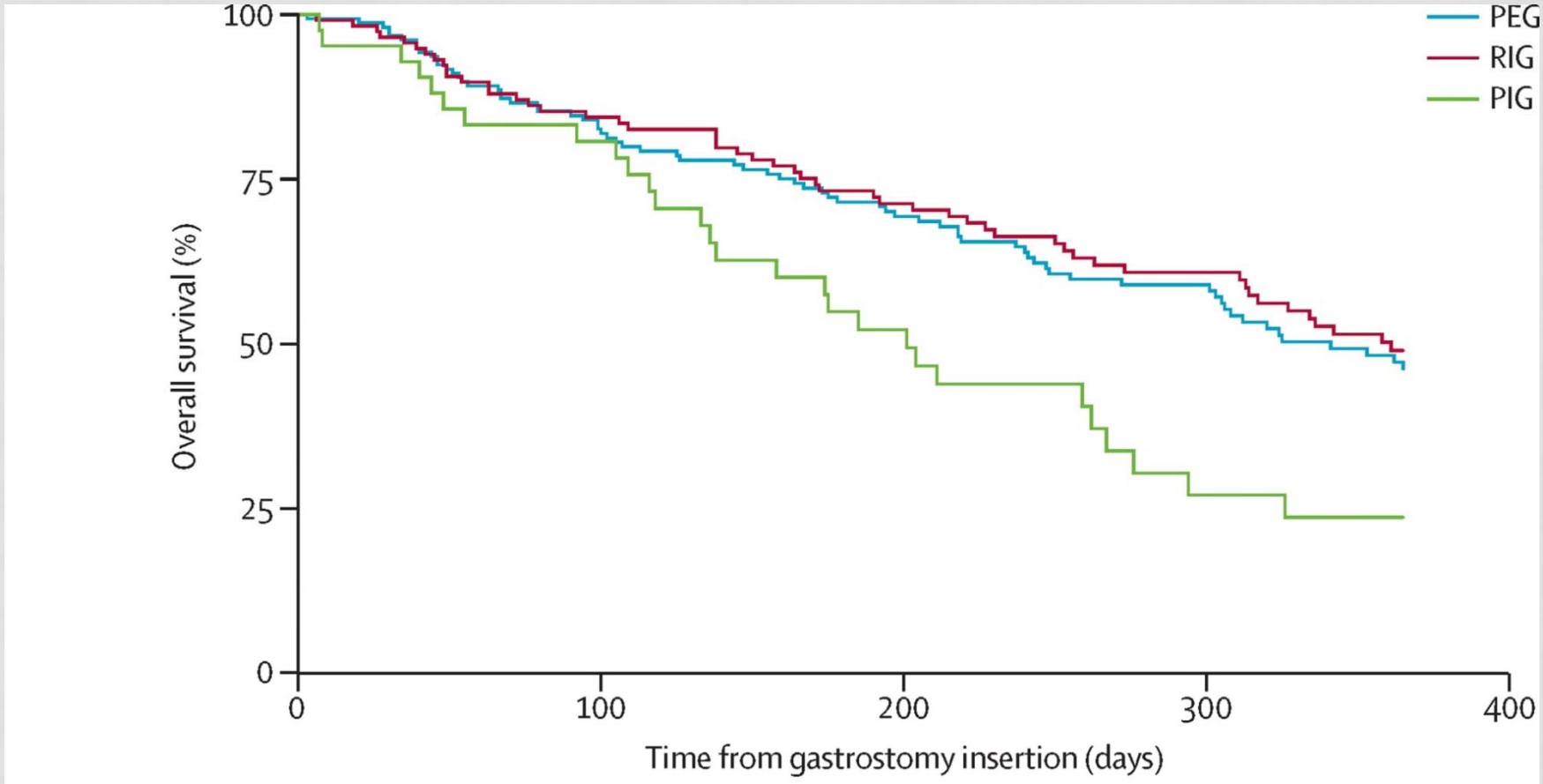
GASTROSTOMY

- Nutritional failure & difficulties maintaining hydration and medication intake common
- Issues abound regarding timing and type of procedure
- Gastrostomy feeding, fluid & medication administration feels like it should be of significant benefit for QoL

PROGAS

Prospective study of gastrostomy in MND:

SURVIVAL BY GASTROSTOMY TECHNIQUE

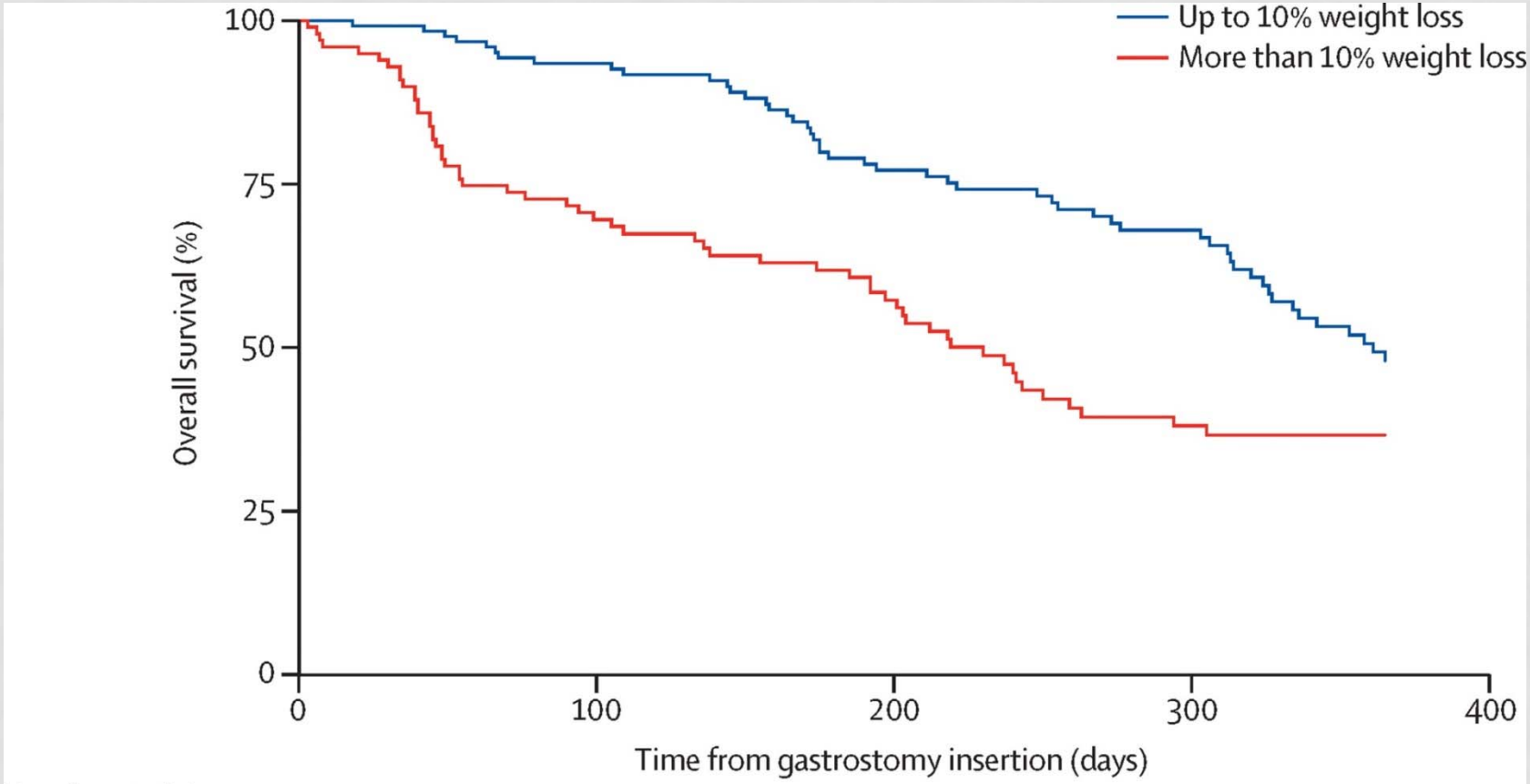


Number at risk				
PEG	159	122	92	64
RIG	117	94	74	53
PIG	42	32	19	8

PROGAS

- Technique – PEG, RIG, PIG did not affect outcome/survival, but suggestion RIG less good and greater number of complications

SURVIVAL BY WEIGHT LOSS



Number at risk				
Up to 10% weight loss	124	107	82	58
More than 10% weight loss	99	66	48	28

PROGAS

- Pre-procedural wt loss key to survival, 10% the key figure
- No benefit in terms of weight gain, but continued loss poor prognostic indicator

GASTROSTOMY POST-PROGAS

Issues abound regarding timing and type of procedure but:

- Technique – PEG, RIG, PIG dod not affect outcome/survival, but suggestion RIG less good and greater number of complications
- Pre-procedural wt loss key to survival, 10% the key figure
- No benefit in terms of weight gain, but continued loss poor prognostic indicator
- No significant effect on QoL, but caregive strain higher!
- 30 day mortality 4%

WHAT DO I SAY?

- That I believe gastrostomy does improve QoL.
- That better done early in disease course.
- That there is a risk of procedural failure but can usually be managed during admission (RVI).
- Is risk of death but small and less now with close collaboration of home vent team

- But that there is no evidence of major benefit and that I am very comfortable managing bulbar failure with out gastrostomy

CRITICAL DECISIONS IN MND

3. Use, timing & site of antibiotic administration

PROGNOSIS

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WHAT I TELL PATIENTS, THEIR FAMILIES AND CARERS

- blah
- blah
- blah
- **MND is invariably fatal**

PHILOSOPHY OF MANAGEMENT

The management of MND is palliative from diagnosis

It’s about quality not quantity

CONCLUSIONS

MND is/remains:

- A rapidly progressive neurodegenerative disease without effective modifying treatments with a poor prognosis
- A palliative approach is appropriate
- All interventions, in the face of such a physically destructive condition should be viewed with caution
- A good evidence base is necessary to consider interventional treatments

CRITICAL DECISIONS IN MND

3. Use, timing & site of antibiotic administration

USE, TIMING & SITE OF ANTIBIOTIC ADMINISTRATION

- Little controversy in appropriate and at times aggressive treatment of infection (usually respiratory) early in disease or on first occasion.

But remember:

- Respiratory muscle weakness is universal, with resp failure all but invariable mode of death in MND

Postponing (perhaps appropriately) an inevitable process.

USE, TIMING & SITE OF ANTIBIOTIC ADMINISTRATION

- Typically discussion in clinic or with care coordinator on home support visit.
- Often linked to discussion of other intervention(s) as before.
  - How was hospital/dependent stay?
  - Would you want to consider such an episode in the future?
- Consider options:
  - no antibiotics?
  - antiobiotics at home or in palliative care setting?

USE, TIMING & SITE OF ANTIBIOTIC ADMINISTRATION

- No right or wrong answers
- Responses or decisions not fixed in stone
- Often undertaken around generation or discussion of ADRT, EHCP and DNACPR
- ADRT’s etc a useful framework around which to consider overall disease management