# NeuroPalliative Care

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**Potential Conflicts of Interest:**

Up to Date Royalty for Functional Movement Disorders

Patient Centered Outcomes Research Institute (NIH) 2015-2018

University Hospital Foundation 2016-25

Merz educational grant 2018 march

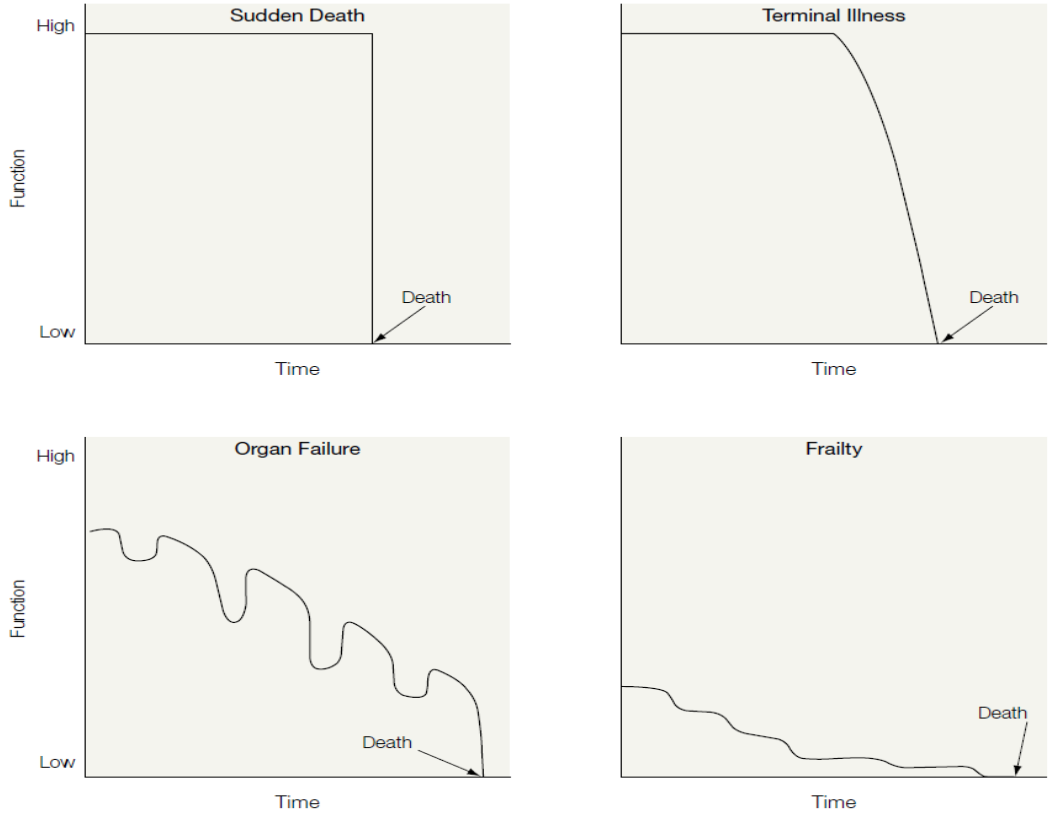
Associate Editor, *Parkinsonism and Related Disorders*

## Objectives

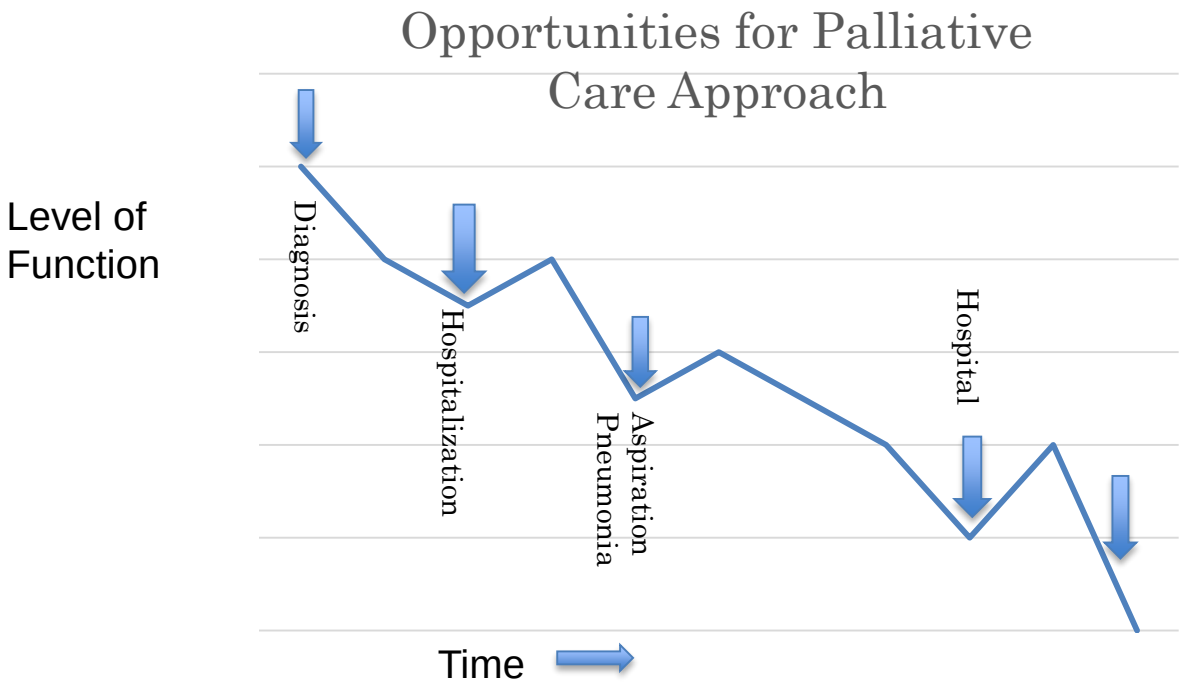
1. Prevalence, natural history, pathophysiology, end of life trajectory, symptoms relevant to palliative care, treatments of the symptoms of:

2. PD and related disorders and dementia

# Theoretical Trajectories of Dying




Lunney, JR et al. Patterns of Functional Decline at End of Life. JAMA, 289(18): 2387-2392.


Opportunities for Palliative Care Approach
Level of Function
Diagnosis
Hospitalization
Aspiration Pneumonia
Hospital
Time

# Overarching Theme of Neurologic Illness and Palliation

Illnesses have Motor and Non-motor symptoms

Undetected pain is often reason behind MAID requests

Cognitive decline occurs in many illnesses thought of as purely motor

Find a motivated neurologist in an academic setting to partner with you

Consider attending clinics with advanced illness patients to learn common scenarios and treatment tips

## Medications to Avoid with Neurologic Patients

Typical neuroleptics

Atypical neuroleptics – except quetiapine or clozapine

Metoclopramide, nozinan

Nearly all neurologic patients will have dementia at the end of life – therefore, delirium may not be avoidable if good pain control is also required

# Behavioral Pain Scale

| Item | Description | Score |
|---|---|---|
| Facial expression | Relaxed | 1 |
| | Partially tightened (e.g. brow lowering) | 2 |
| | Fully tightened (e.g. eyelid closing) | 3 |
| | Grimacing | 4 |
| Upper limbs | No movement | 1 |
| | Partially bent | 2 |
| | Fully bent with finger flexion | 3 |
| | Permanently retracted | 4 |
| Compliance with ventilation | Tolerating movement | 1 |
| | Coughing but tolerating ventilation for most of the time | 2 |
| | Fighting ventilator | 3 |
| | Unable to control ventilation | 4 |

From Payen et al. [11], Table 1 with permission of Wolters Kluwer Health, Inc.

# Triggers for Conversations about Goals

| General |
| --- |
| Age >80 years and hospitalized |
| Metastatic cancer, advanced dementia or other serious comorbidity |
| Patient or family asks to discuss these issues |
| Would you be surprised if patient died during this hospitalization? |
| Would you be surprised if patient died in the next year? |

# Triggers for Conversations

| **Emergent ('Very Early' – hours to 1 day)**[a] |
|---|
| Intubation and mechanical ventilation |
| Nasogastric tube if needed for urgent medication[b] |
| Emergent brain surgery (for example external ventricular drain placement, decompressive craniotomy, clot evacuation) |
| **Early (days to weeks)** |
| >3 days of intubation |
| Starting artificial nutrition[b] |
| Considering transition from nasogastric feeding to percutaneous gastrostomy |
| Considering transition from endotracheal tube to tracheostomy |
| Any unexpected change or decline (for example new infection, need to re-intubate, reinsert feeing tube or readmit to ICU) |

| Late (months and years) |
| --- |
| Scheduled: every patient who was discharged to a nursing or long-term care facility, or who was discharged with artificial support (feeding or breathing tube), should have a scheduled appointment for a serious illness conversation 3–6 months after admission |
| Event-driven: any unexpected change or decline (for example new infection, need to re-intubate, reinsert feeing tube or readmission to the hospital) |

## Consider LTC and Community Pall or Inpatient Palliative Care if:

Inability to maintain hydration and caloric intake + One of:

Palliative Performance Scale < 40%

Weight loss >10%/6mo or >7.5%/3mo

Serum albumin low

Dysphagia severe enough to prevent receiving sufficient food and fluid to sustain life and patient does not receive artificial nutrition and hydration

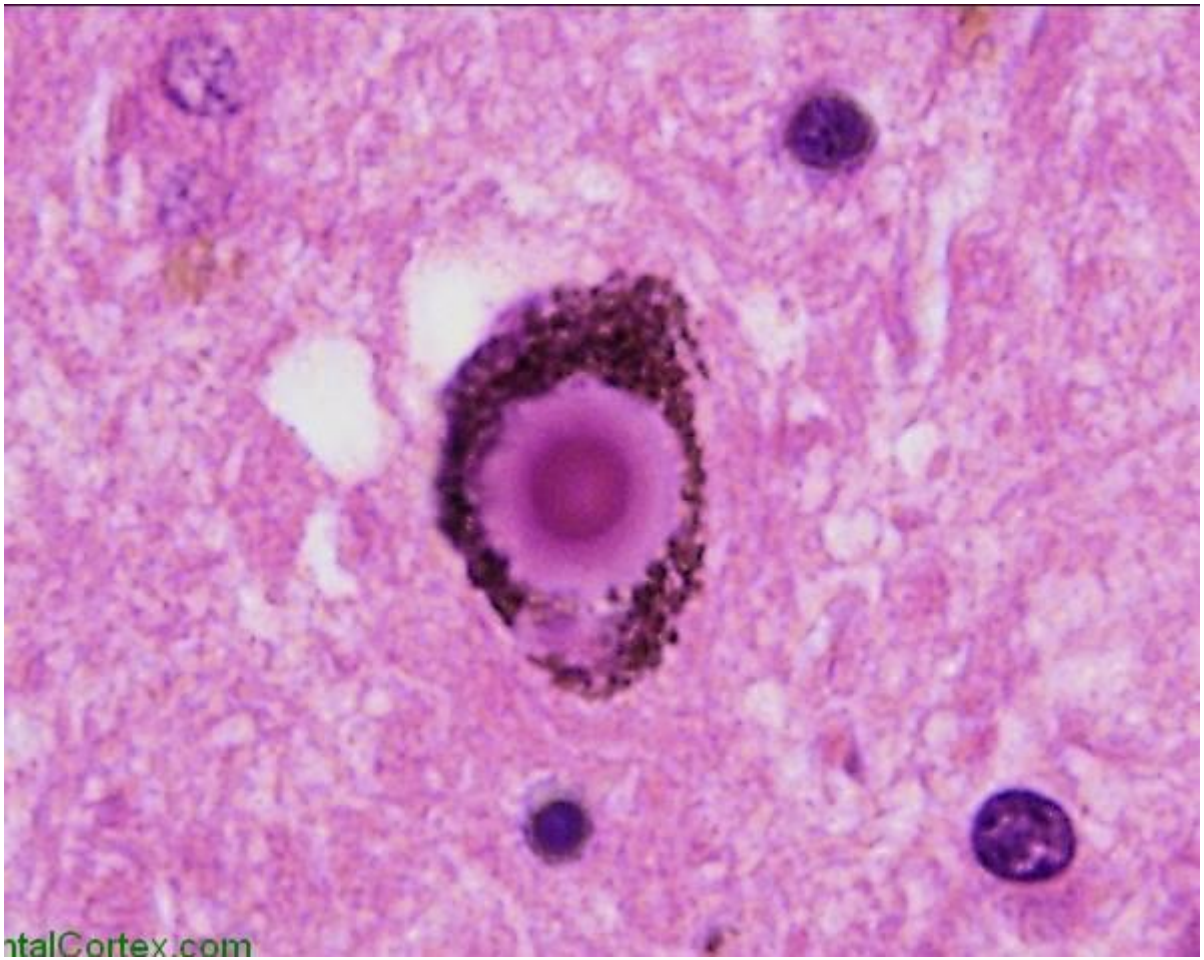
# Parkinson disease

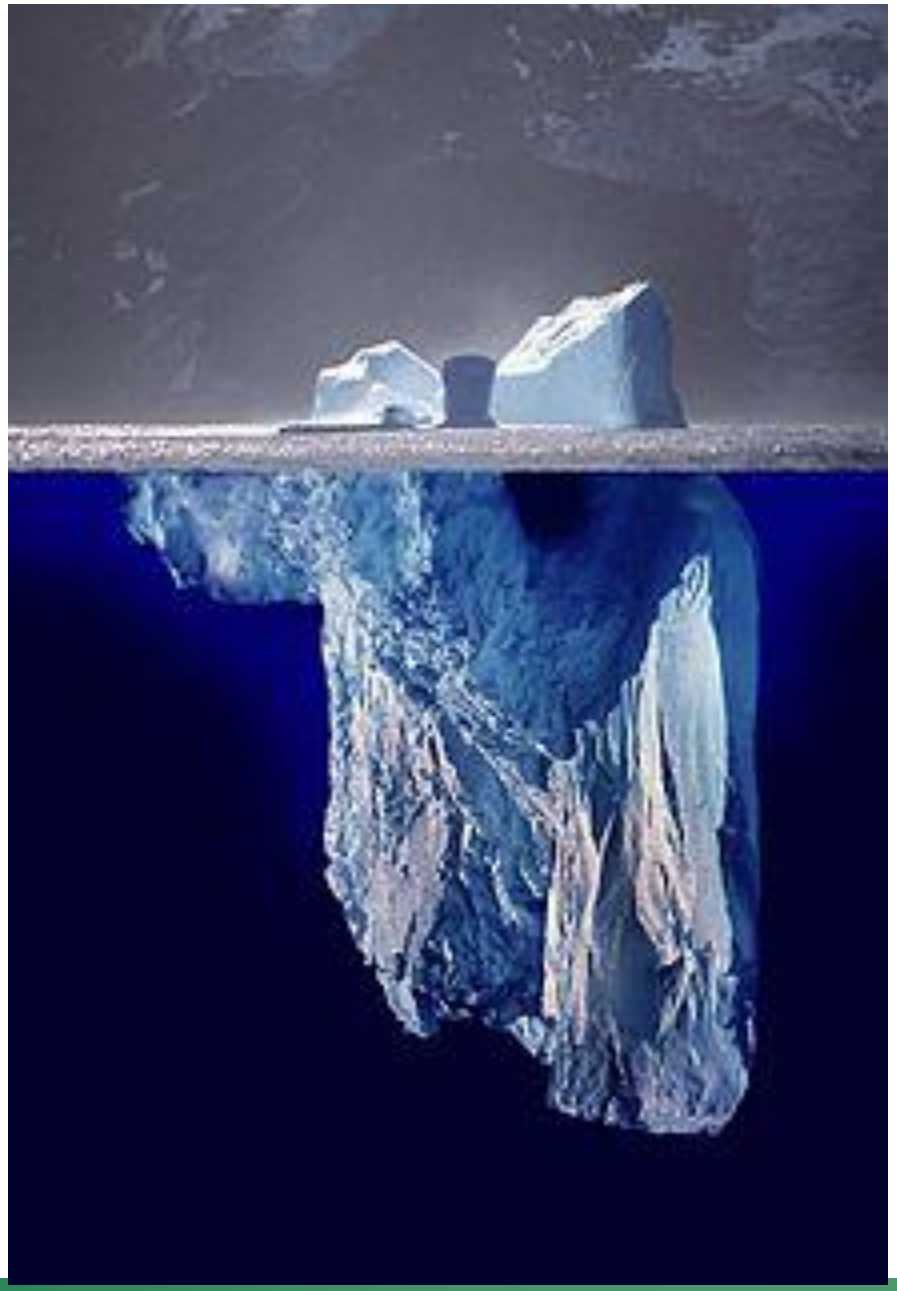
275-500/100,000 prevalence

Average age of onset 55 years

Mean survival: 15 years

Pathophysiology: progressive neurodegenerative disorder with unknown etiology


ntalCortex.com

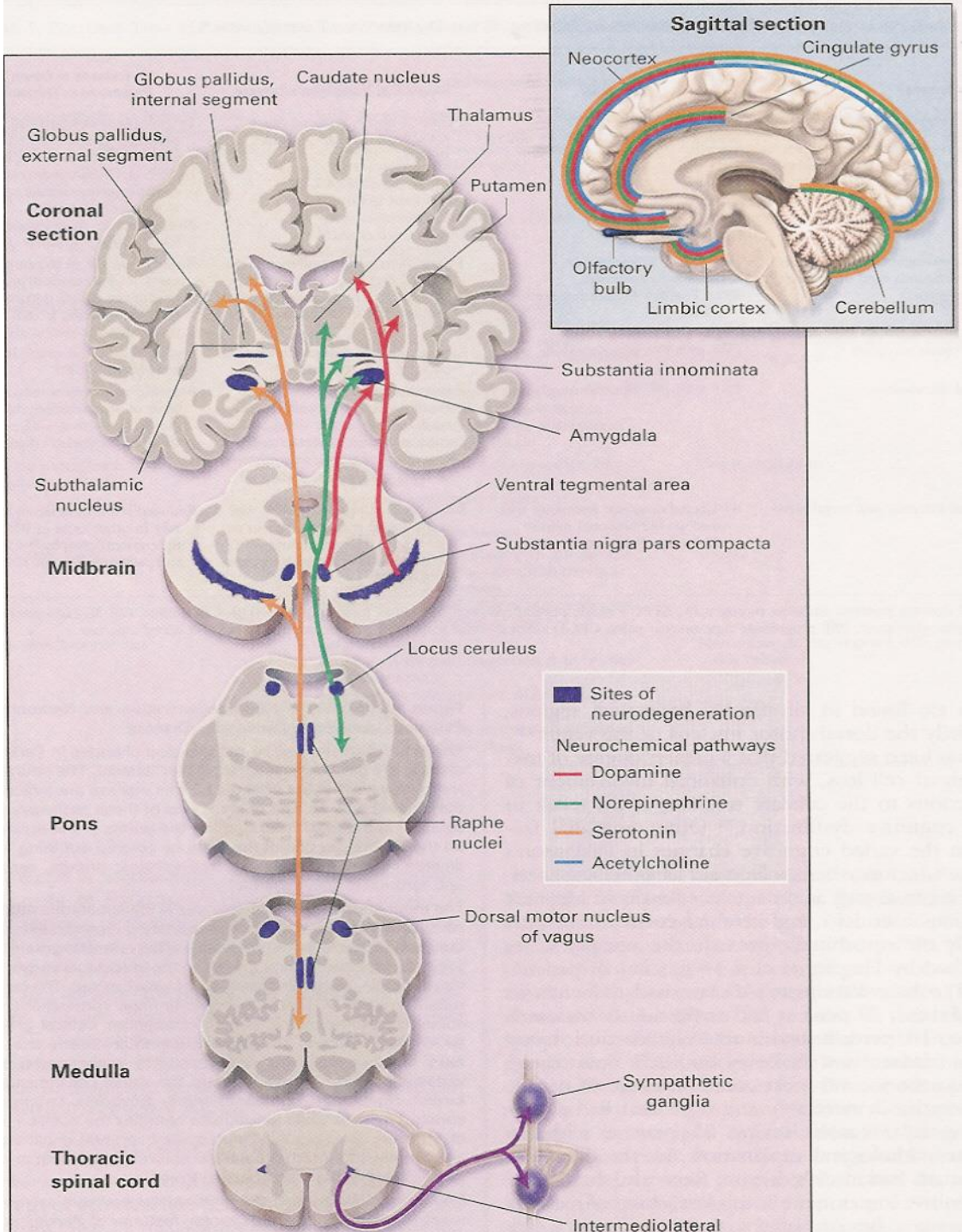


## Synucleinopathies

Parkinson's disease – "slow" progression

Lewy body dementia – cognitive change precedes or within 1 y of motor, cognitive fluctuations, hallucinations

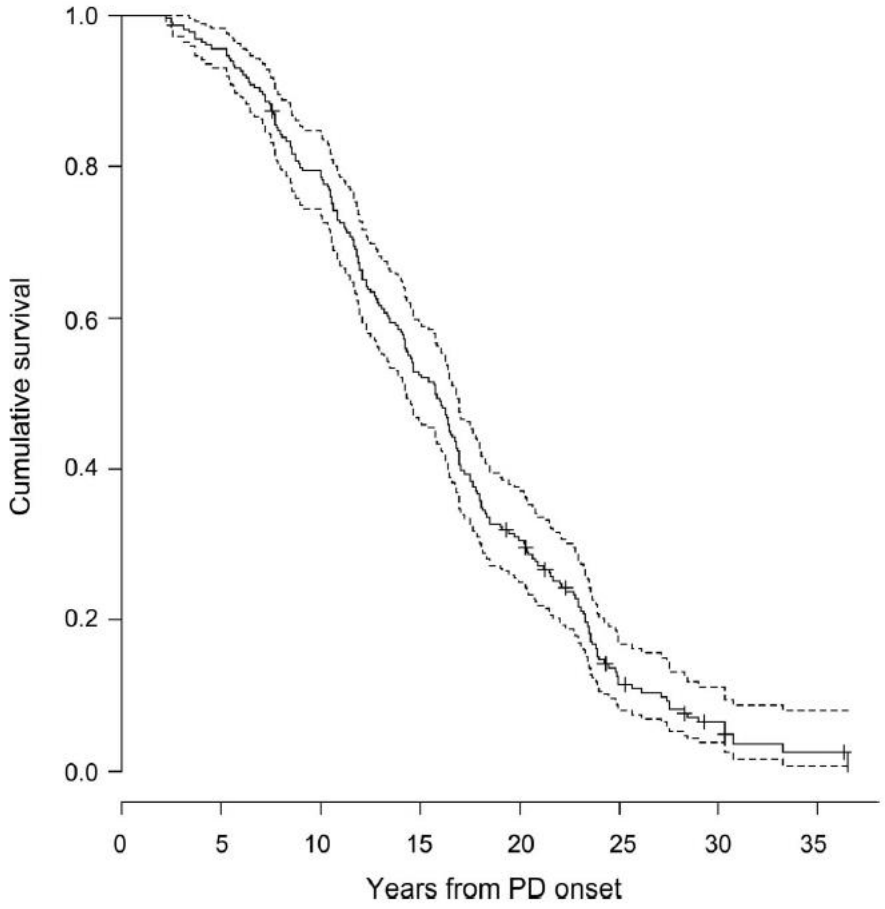
Multiple system atrophy- dysautonomia + parkinsonism or ataxia



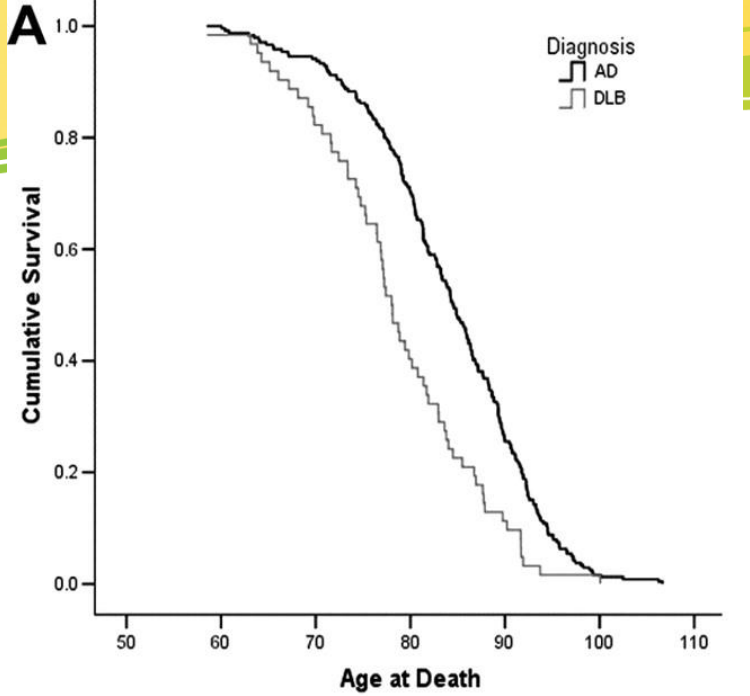

With permission from Lang and Lozano, NEJM, 1998

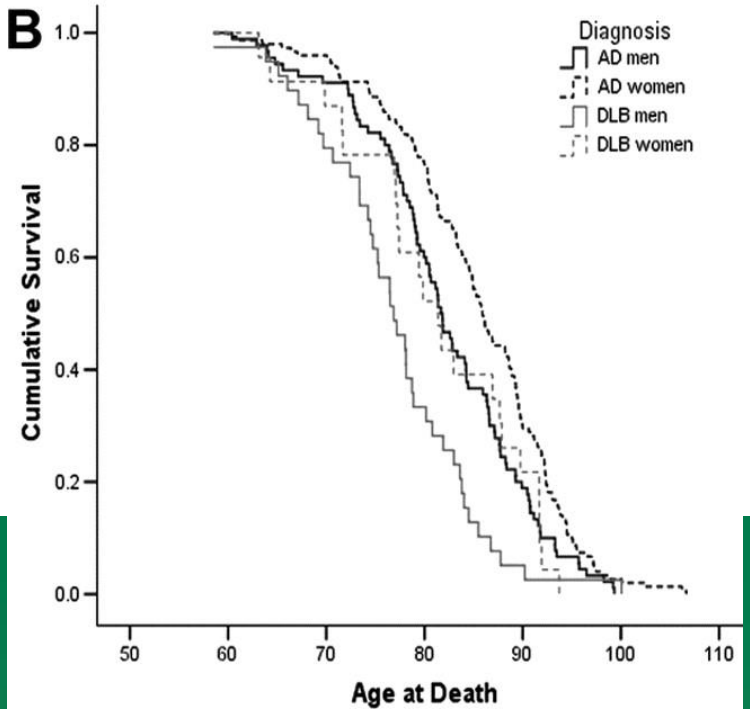
# What predicts mortality in Parkinson's disease

Figure 1 Survival in 230 community-based patients with Parkinson disease (PD)




Neurology 2010;75:1270

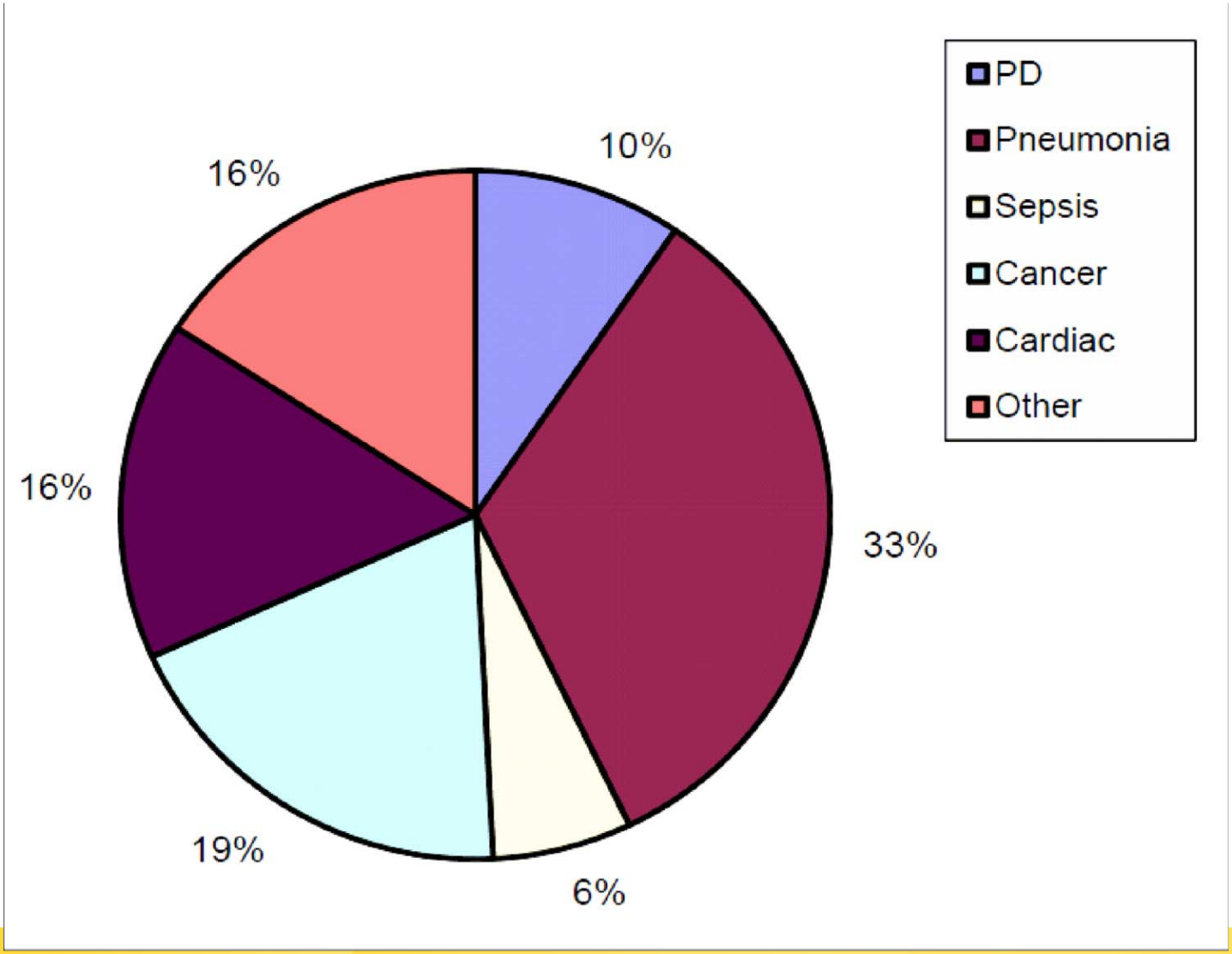



Williams, Neurology 2006

# Cause of Death Over 10 y

Williams-Gray JNNP 2013



# Potential Triggers for Palliative Conversations

Bothersome or disabling pain not responsive to PD medication management

Behavioural complications requiring reduced motor control

Caregiver distress or burnout

Recent or repeated hospitalizations

Loss of ability to drive

Falls or need for gait assistance

Cognitive impairment

# Triggers

Behavioural issues:  hallucinations, delusions, wandering

Significant dysphagia

Hospitalization from aspiration pneumonia

Weight loss

Existential distress

Acceleration in changes in functional status

| Symptom | Treatment | Dose range |
|---|---|---|
| Dementia | Donepezil | 10 mg daily |
| | Rivastigmine | 3–12 mg daily |
| | Memantine | 10–20 mg daily |
| Psychosis | Quetiapine | 12.5–100 mg daily |
| | Clozapine | 12.5–150 mg daily |
| RBD | Melatonin | 3–15 mg |
| | Quetiapine | 12.5–50 mg |
| Parasomnia nonREM | Clonazepam | 0.25–2 mg qhs |
| Insomnia | Melatonin | 3–15 mg |
| | Yang-Xue-Qing -Nao granules | 4 g tid |

| | | |
|---|---|---|
| Restless Leg syndrome | Levodopa | Varies |
| Sialorrhea | Candies, gum | |
| | Atropine drops | 0.1% |
| | Botulinum toxin injection | 15–40 units/side |
| Constipation | PEG 3350 | 14 mg 1–4 times daily |
| | Senokot | 8.5–34 mg qhs |
| Orthostatic hypotension | Fludrocortisone | 0.1 mg qam |
| | Midodrine | 10 mg Morning, noon, dinner |
| | Droxidopa | 100–600 mg daily |
| Urinary frequency | Pelvic floor exercises | |
| | Mirabegron | 25–50 mg once daily |
| | Botulinum toxin injection | Refer to urologist |
| Pain | Range of motion exercises | |
| | Acetaminophen | 250–300 mg tid |
| | Oxycodone/ naloxone | 5/2.5 mg bid |
| | Botulinum toxin injection | Varies |

## Unable to Swallow

Rotigotine 3 mg (patch) = 100 mg Levodopa

Beware confusion, somnolence, psychosis

Rectal Levodopa:

Crush 10 tabs 100/25

Add to 10 ml 50% H2O, 50% glycerol + 1 g citric acid

100 ml/ml

Shake well before use

## Alternatives to Oral Levodopa

Rotigitine patch (beware psychosis/confusion, orthostatic hypotension)

Rectal levodopa

Give regular levodopa by PEG if in place – be aware duration of action will be approx. 30-60 min/dose

**Edmonton Symptom Assessment System**
**Revised: Parkinson's Disease (ESAS-R: PD)**

**Please circle the number that best describes how you feel NOW:**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No Pain | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Pain |
| No Tiredness *(Tiredness = lack of energy)* | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Tiredness |
| No Drowsiness *(Drowsiness = feeling sleepy)* | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Drowsiness |
| No Nausea | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Nausea |
| No Lack of Appetite | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Lack of Appetite |
| No Shortness of Breath | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Shortness of Breath |
| No Depression *(Depression = feeling sad)* | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Depression |
| No Anxiety *(Anxiety = feeling nervous)* | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Anxiety |
| Best Wellbeing *(Wellbeing = how you feel overall)* | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst Possible Wellbeing |
| No _____ Other Problem *(for example constipation)* | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | Worst possible _____ |

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**Edmonton Symptom Assessment System Revised: Parkinson's Disease (ESAS-R: PD)**

**Please circle the number that best describes how you feel NOW:**

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No Stiffness | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst Possible Stiffness |
| No Constipation | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst Possible Constipation |
| No Swallowing Difficulties | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst Possible Swallowing Difficulties |
| No Confusion | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst Possible Confusion |

## Outcomes

ESAS-PD improved significantly (56 to 40)and to similar extent as those with endstage metastatic cancer (48 to 39) $p < 0.0001$ (95% CI 10,21)

Symptoms responding most to interventions: Dysphagia, constipation, anxiety, pain, drowsiness and other

Zarit Caregiver Burden Scale (modified) improved from mean V1 43.5 to V2 36 ($p < 0.0001$, 95% CI 6, 9) (max score 96)

## Cause of death in clinic

130 patients: 33 deaths
Place of death: LTC 4
Home 29 (community palliative care)
Palliative inpt unit 4
Acute care hospital 6 (no hospice bed 1)
Cause of death: aspiration pneumonia 26
died in sleep 5
other 2

## Practical Tips

NO metoclopramide, nozinan, any typical or atypical neuroleptic

EXCEPT quetiapine and clozapine

Do NOT stop Parkinson medications unless imminently dying

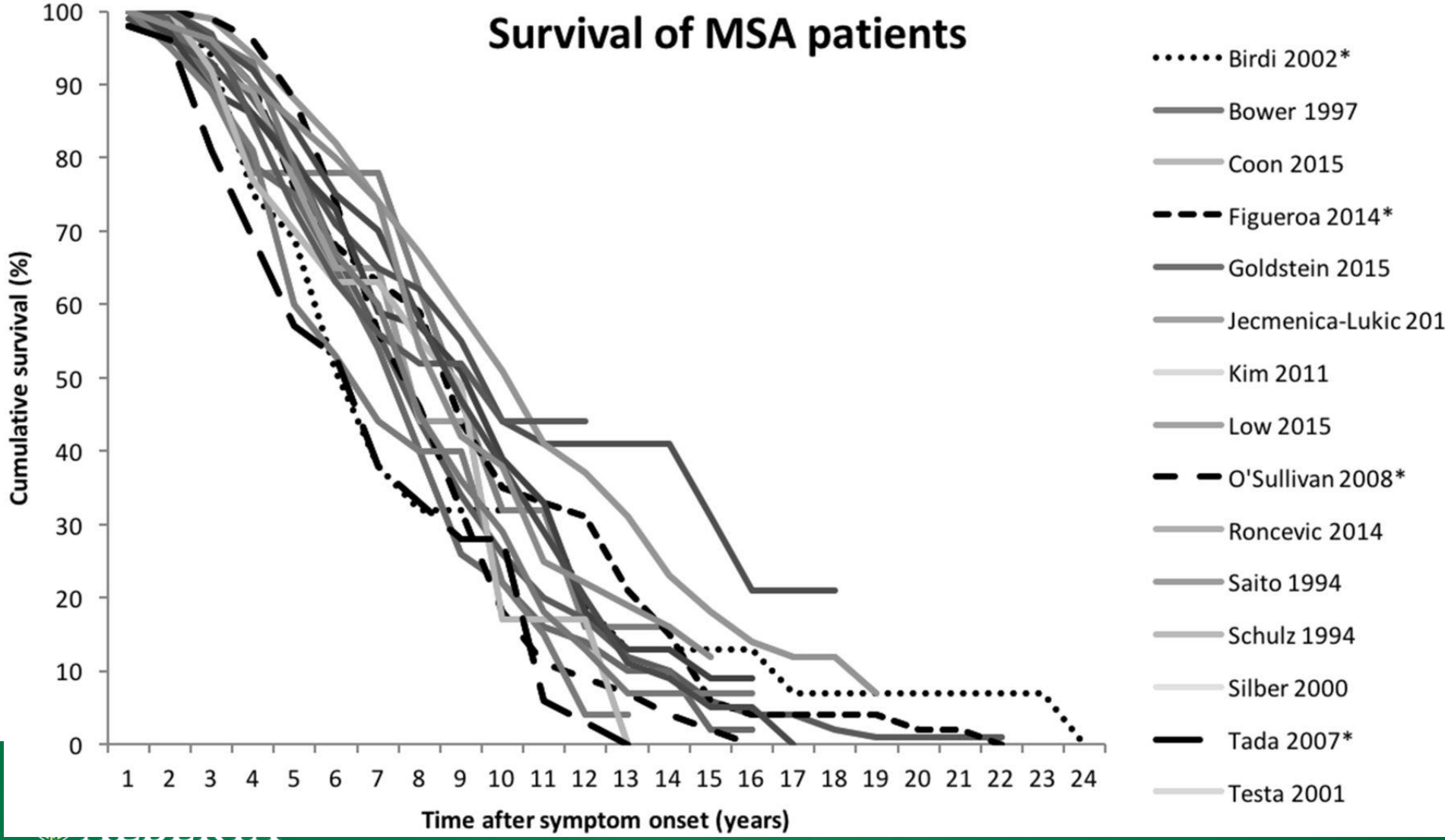
# Multiple System Atrophy

Prevalence: 10-20/100,000

Life expectancy: 5 years (range 2 years-20)

Pathophysiology: synucleinopathy

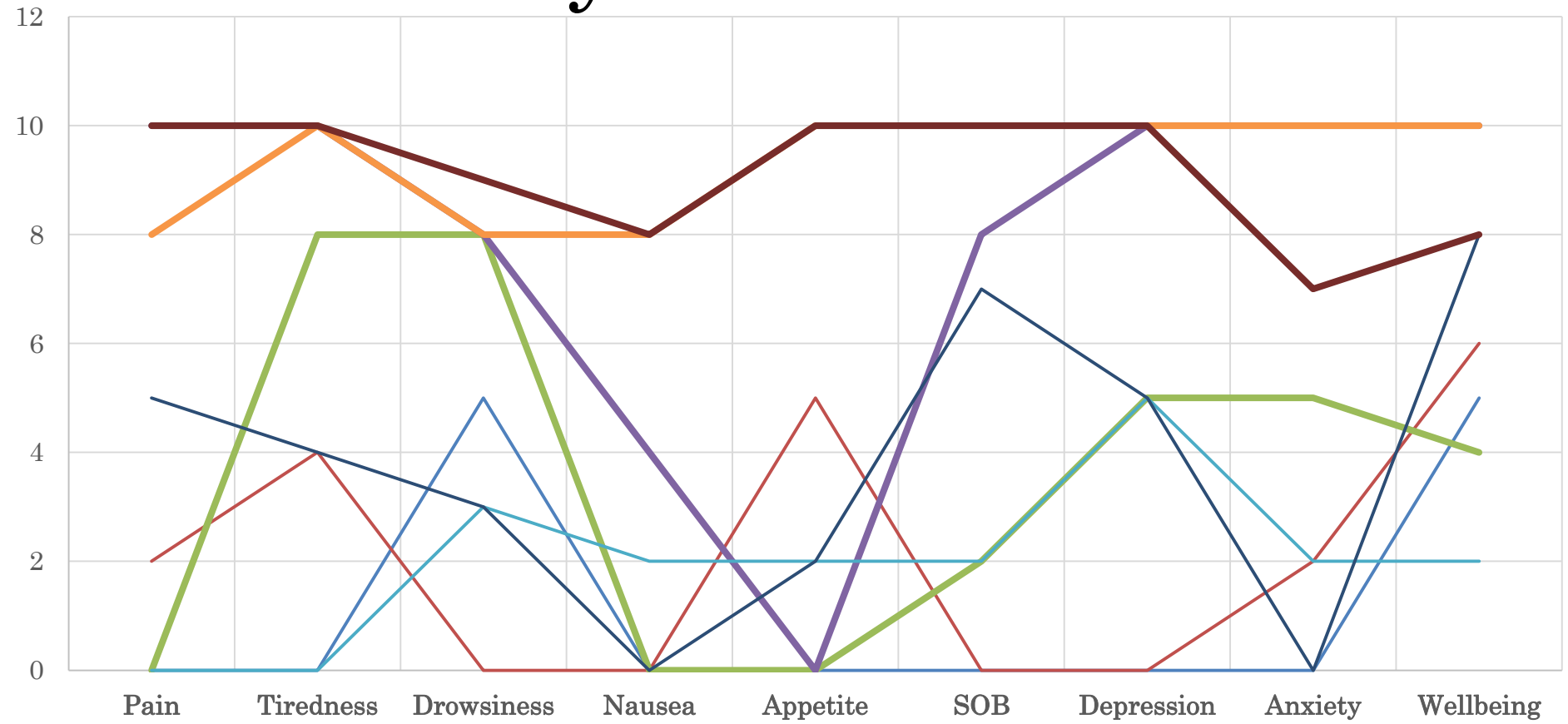
Many symptoms overlap with PD, but compressed in time course – always changing, relentless, more pain


Survival of MSA patients
Cumulative survival (%)
100
90
80
70
60
50
40
30
20
10
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time after symptom onset (years)
Birdi 2002*
Bower 1997
Coon 2015
Figueroa 2014*
Goldstein 2015
Jecmenica-Lukic 201
Kim 2011
Low 2015
O'Sullivan 2008*
Roncevic 2014
Saito 1994
Schulz 1994
Silber 2000
Tada 2007*
Testa 2001

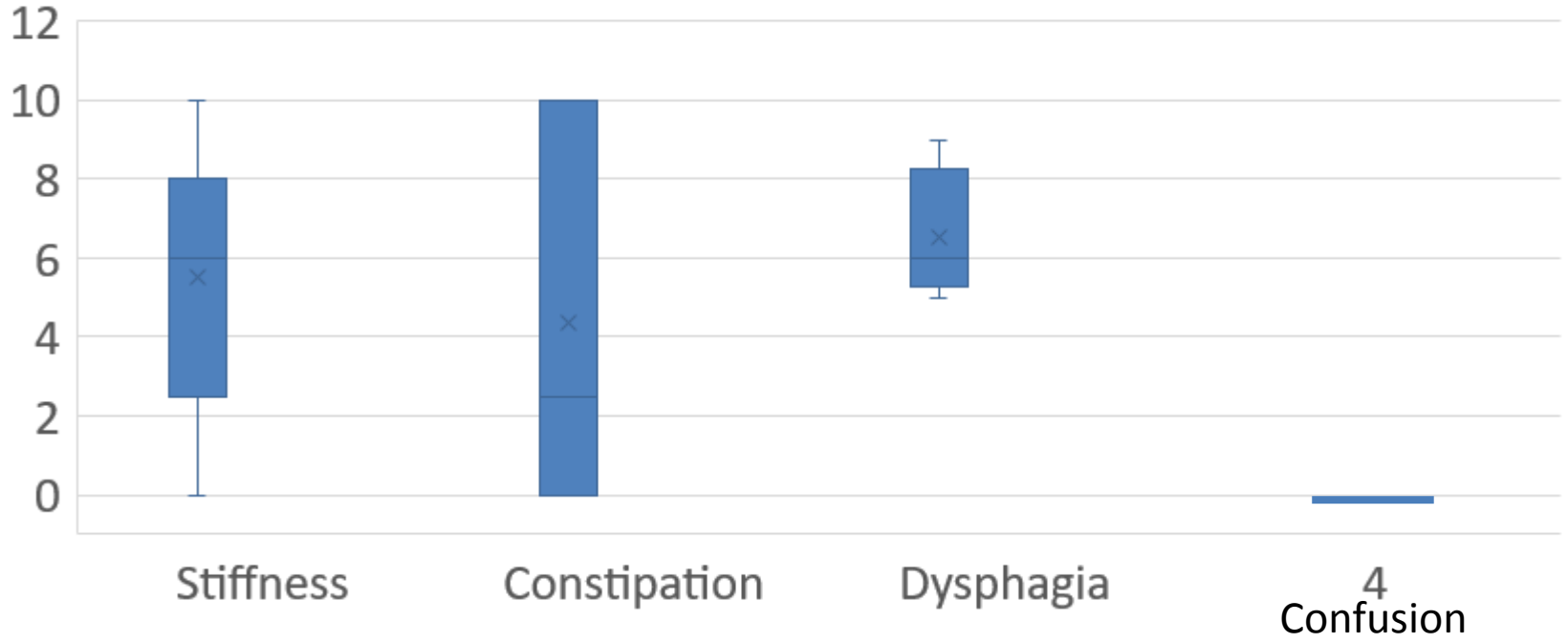
# What predicts mortality in MSA

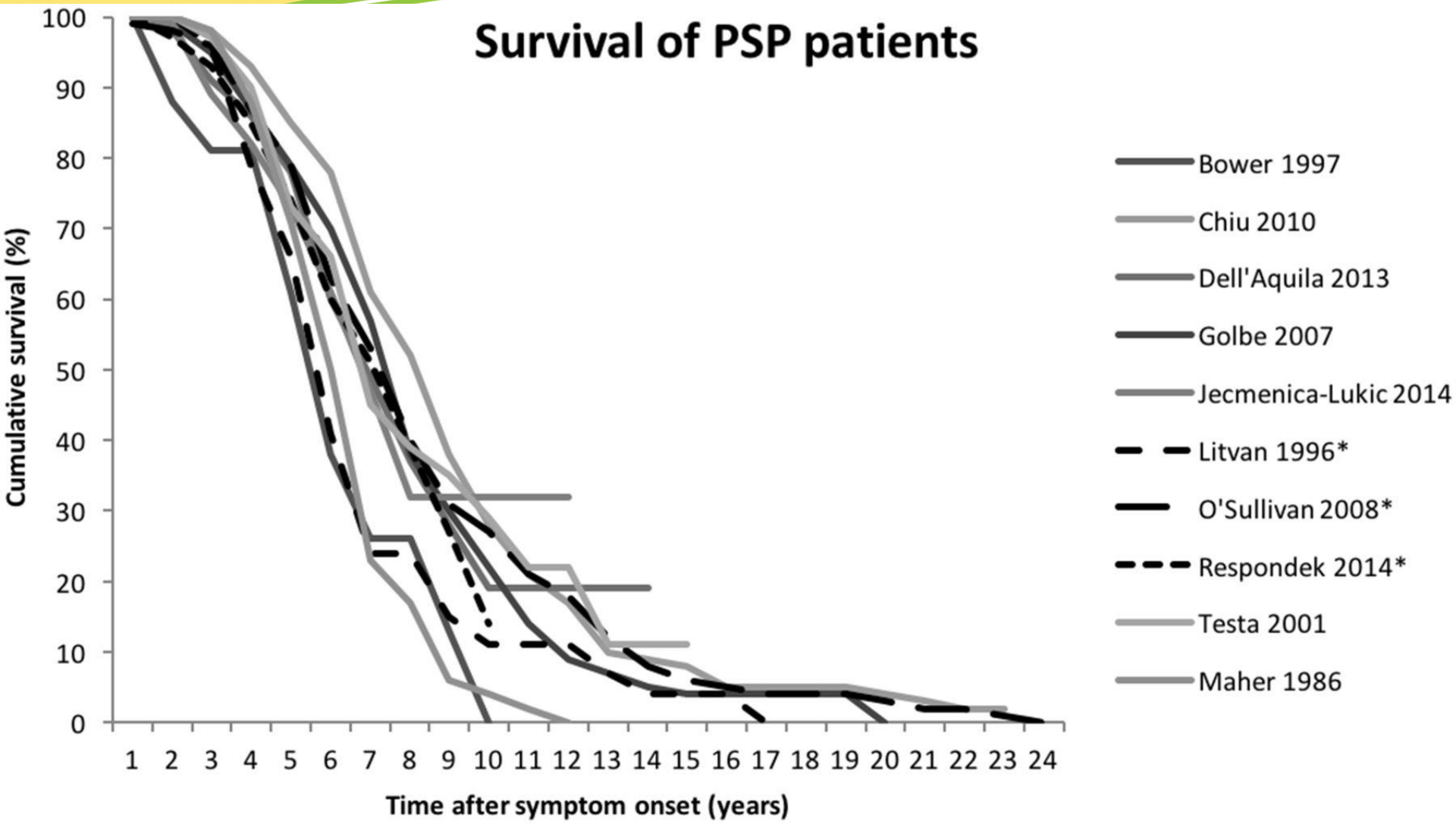
| | |
|---|---|
| MSA-P (vs MSA-C phenotype) | |
| Severe dysautonomia:<br>-Mild vs severe (2 studies)<br>-CGI dysautonomia score (1 study)<br>-CASS (2 studies) | 2.3-year difference median survival<br>3.5-year difference median survival<br>MV: 1.41 (1.19 to 1.67)<br>MV: 1.07 (1.02 to 1.11)<br>MV: 2.8 (1.01 to 9.26) |
| Development of dysautonomia within 1, 2 and 2.5 years of MSA onset | UV: 1.24 (1.04 to 1.49)<br>MV: 6.0 (3.1 to 11.7)<br>MV: 3.4 (1.61 to 7.15) |
| Combined motor and autonomic symptoms within 3 years of MSA onset | UV: 2.65 (1.42 to 4.93)<br>3-year difference median survival |
| Orthostatic hypotension | |
| Dysautonomia present at MSA onset | NA |
| Bladder symptoms | ous definitions of prognostic factor |
| Stridor | MV comparing untreated stridor with no stridor: 3.0 (1.63 to 5.53)<br>Reduced survival after 6 years as evident from the Kaplan Meier curve |

# Edmonton Symptom Assessment System:MSA



# MSA: Other Important Symptoms




Survival of PSP patients
Cumulative survival (%)
100
90
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30
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10
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time after symptom onset (years)
Bower 1997
Chiu 2010
Dell'Aquila 2013
Golbe 2007
Jecmenica-Lukic 2014
Litvan 1996*
O'Sullivan 2008*
Respondek 2014*
Testa 2001
Maher 1986

# What predicts mortality in Progressive Supranuclear Palsy?

| | |
|---|---|
| PSP-RS (vs PSP-P phenotype) | |
| Early development of dysphagia | MV: 3.91 (1.39 to 11.0)<br>MV: 2.84 (1.51 to 5.34)<br>MV: 2.3 (1 to 5.3)<br>1.9 year difference median survival |
| Early development of cognitive symptoms | MV: 3.6 (1.6 to 8.2)<br>MV: 1.99 (1.17 to 3.38) |
| Vertical supranuclear gaze palsy | MV: 2.74 (1.52 to 4.94)<br>UV: 1.12 (1.10 to 1.31) |

What specific dementia diagnoses do you know?

Alzheimer disease: 4.4% of the population 65+

19/1000 population

Vascular dementia: 26% of all dementias

Prevalence 0.6-2% of those over 65 y

# Dementia

**AD** accounts for 60-80% of all cases

Amnestic – short then immediate, last remote

Socially appropriate

**Vascular dementia** 10-28%

Stepwise progression

**Lewy body dementia** 5-20%

Cognitive fluctuations, hallucinations, dysautonomia

Exactly like Park dis dementia except within 1 y of motor symptoms

## Frontotemporal Dementia

5-10%

Onset 45-64 (younger than AD)

Executive dysfunction:  poor decision-making, lack of empathy, impulsiveness

Can occur with ALS

May be inherited as autosomal dominant

| | Mild | Moderate | Severe |
|---|---|---|---|
| Cognitive | Short term memory loss- difficulty learning new information, trouble remembering names, misplacing objects | Disorientation, development of cognitive decline in other domains; visuospatial ability, executive function, verbal abilities | Significant impairment in most or all domains of cognition, decreased verbal fluency, long term memory loss |
| Functional | Impaired performance of complex tasks (IADLS[a]) -work, finances, event planning | Requiring assistance with some daily tasks (ADLS[b])- picking out clothing, taking medications | Impaired mobility and require significant assistance with all ADLS[b] (feeding, dressing, bathing). |
| Mood/ behavioral | Apathy, social withdrawal | Disinhibition, poor judgment, agitation, wandering, hallucinations, delusions | Variable- may continue to have behavioral disturbances, but may fade away with time |

From Neuropalliative Care, 2018

# Functional Assessment Staging

| Stage | Assessment |
|---|---|
| 1 | No difficulties, either subjectively or objectively |
| 2 | Complains of forgetting location of objects; subjective work difficulties |
| 3 | Decreased job function evident to coworkers; difficulty in traveling to new locations. Decreased organizational capacity[a] |
| 4 | Decreased ability to perform complex tasks (e.g., planning dinner for guests), handling personal finances (such as forgetting to pay bills), difficulty marketing, etc. |
| 5 | Requires assistance in choosing proper clothing to wear for the day, season, or occasion, e.g. patient may wear the same clothing repeatedly unless supervised[a] |
| 6 | 6a – Improperly putting on clothes without assistance or cuing (e.g. may put street clothes on overnight clothes, or put shoes on wrong feet, or have difficulty buttoning clothing) occasionally or more frequently over the past weeks[a] |
| | 6b – Unable to bathe (shower) properly (e.g., difficulty adjusting bath-water temperature) occasionally or more frequently over the past weeks[a] |
| | 6c – Inability to handle mechanics of toileting (e.g., forgets to flush the toilet, does not wipe properly or properly dispose of toilet tissue) occasionally or more frequently over the past weeks[a] |
| | 6d – Urinary incontinence (occasional or more frequently over the past weeks)[a] |
| | 6e – Fecal incontinence (occasional or more frequently over the past week)[a] |

| |
|---|
| 7a – Ability to speak limited to approximately a half dozen intelligible different words or fewer, in the course of an average day or in the course of an intensive interview |
| 7b – Speech ability limited to the use of a single intelligible word in an average day or in the course of an interview (the person may repeat the word over and over) |
| 7c – Ambulatory ability lost (cannot walk without personal assistance) |
| 7d – Cannot sit up without assistance (e.g., the individual will fall over if there are no lateral rests [arms] on the chair) |
| 7e – Loss of the ability to smile |
| 7f – Loss of ability to hold head up independently |

At FAST 7 25% 6 month mortality, median survival 1.3 years

# Steps for Dementia Palliation

| Stage/Trigger | Palliative Care Interventions |
|---|---|
| Time of Dx<br>New behavioural symptoms | GOC<br>PD, POA<br>Rx depression, cognitive symptoms<br>Caregiver support |
| Moderate: new or inc agitation<br>Inc dependency | Screen and treat Psychiatric Sx<br>Safety screening: finances, driving, abuse<br>Caregiver support<br>Assess care needs |
| Severe: incontinence<br>Dec ambulation, frequent falls<br>Dec ability to have a conversation<br>Choking dysphagia<br>Pneumonia, Weight loss, Hospitalizations | Symptom management<br>GOC reassessment<br>De-prescribe medications of limited benefit<br>Consider hospice or LTC referral |

# Pain Assessment in Advanced Dementia (PAINAD)

| Observation | 0 | 1 | 2 |
|---|---|---|---|
| Breathing | Normal | Occ laboured breathing, short hyperventilation | Noisy laboured, longer period of hypervent or CS |
| Negative Vocalization | None | Occ moan/groan Low level neg | Repeated calling out, loud moaning, groaning, crying |
| Facial Expression | Smiling or inexpressive | Sad, Frightened, Frown | Grimacing |
| Body Language | Relaxed | Tense, distressed pacing, fidgeting | Rigid, fisting, pulled up, striking |
| Consolability | No need to console | Distressed or reassured by voice or touch | Unable to console, distract |
| | | | |



Warden, 2003

## Unmet Physical or Emotional Needs

Screen for hunger, thirst, need to urinate, defecate/constipation, inability to communicate

Strained staff/caregiver

Past history of physical or sexual trauma may make even good nursing care traumatic

## Practice Tips

Leading cause of institutionalization and death in older population

Severe functional limitation occurs

Explore GOC early while patients still capable

Behavioural management is challenging

## Dyspnea Treatment

Lung recruitment strategies:  partner with respirologist early in course of illness

Bronchodilators

Glycopyrrolate for sialorrhea:  1-2 mg qid (delirium)

Morphine in low dose for dyspnea

# MAID

Early requests often due to fear or unaddressed symptoms

Oregon review:  ALS second most common condition

- Loss of autonomy
- Inability to engage in activities

## Medications to Avoid with Neurologic Patients

Typical neuroleptics

Atypical neuroleptics – except quetiapine or clozapine

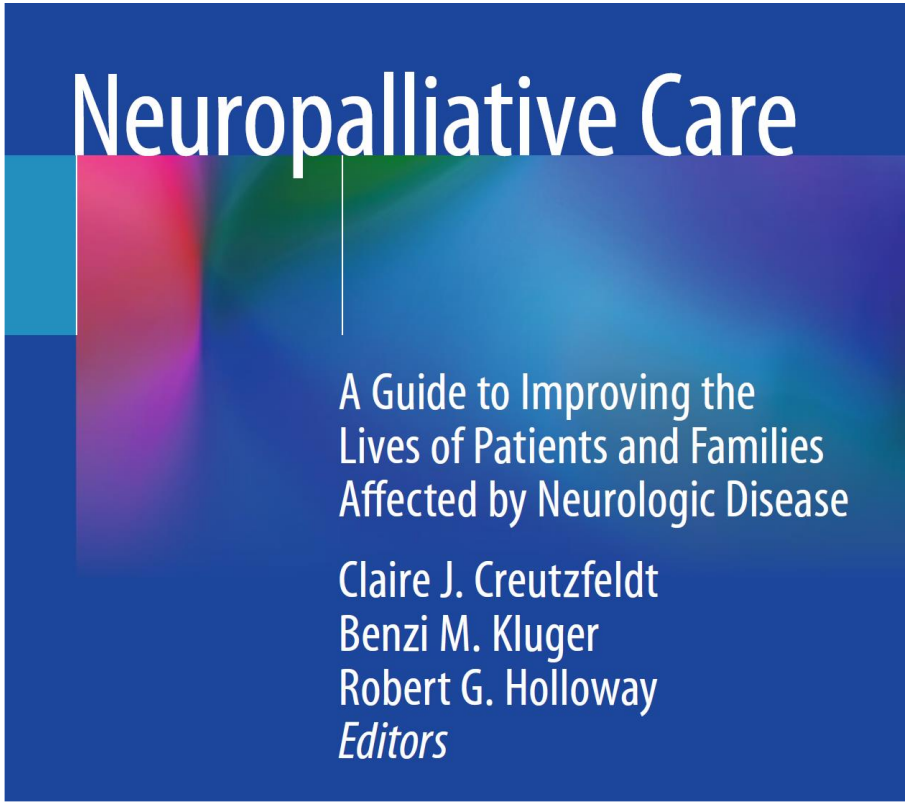
Metoclopramide, nozinan

Nearly all neurologic patients will have dementia at the end of life – therefore, delirium may not be avoidable if good pain control is also required

## Conclusions

1. People DO die of neurologic illness
2. Symptom burden is high and often over y – decades
3. Symptoms typically include motor and non-motor
4. Treatments may not be compatible with optimal motor function
5. Treatment may not be typical of the palliative care toolkit
6. Medications can worsen mental status

# References


Neuropalliative Care
A Guide to Improving the Lives of Patients and Families Affected by Neurologic Disease
Claire J. Creutzfeldt
Benzi M. Kluger
Robert G. Holloway
Editors