Prescribing for the different stages of dementia

Jenny Lee
Geriatrician

Adjunct Assistant Professor,
The S H Ho Centre for Gerontology and Geriatrics, Dept of Med and Therapeutics, CUHK
Associate Consultant, Alice Ho Miu Ling Nethersole Hospital

Dementia symptoms by stages

- Early stage –
  - cognition, mood, +/- behaviour psychological symptoms of dementia (BPSD)
- Moderate stage –
  - BPSD, cognition, activities of daily living (ADL) preservation
- Late stage –
  - competing co-morbidities, complications (appetite, aspirations)

Choice of medications in demented patient

- For dementia
- For co-existing chronic medical conditions
- For acute condition

- Multi-system frailty:
  - CNS, renal, underweight
- Prone to side-effect esp. CNS side effects

Medications

- Drugs affecting cognition
  - either improve or worsen

- Drugs without direct effect on brain but affects patient symptoms/ behaviour
  - BPSD (Behavioural Psychological Symptoms of Dementia) drugs

Symptoms

- Cognition
- BPSD
- “Confusion”

Cognition Drugs

- Anti-dementia drugs
  - Cholinesterase inhibitors
  - NMDA receptor antagonist (Memantin)
- Vitamins & supplements
  - Ginko Biloba, Vit E
- Neurotropics
- Anti-depressants
- BPSD drugs
- Risk factor control drugs

Pharmacotherapy in Dementia: Goals of treatment

- Slow down clinical progression
- Maintain independent functioning for as long as possible
- Stabilise rather than cure:
  - Cognitive function
  - Behaviour
- Secondary aim: relieve caregiver burden and delay institutionalisation

AChEIs

- Donepezil (5, 10 mg daily; tablet or efferescent)
- Rivastigmine (1.5 mg BD to 6 mg BD capsule; patch 4.5 mg, 9.5 mg daily)
- Galantamine (8 mg to 24 mg daily, capsule)
- s/e profile: similar, mostly GI, dizziness, anorexia
- Infrequent: agitation
- Patch less GI s/e but ~30% skin problem

AChEI choice

- Depends on:
  - Subtype of dementia
  - Stage
  - Drug compliance supervision
  - GI tolerance
  - Appetite / weight (50kg cut-off)
  - Skin condition
  - Patient/ carer preference

First-line Alzheimer's Disease Treatment Approaches with Cholinesterase Inhibitors (ChEIs)[1-3]

- First line therapy for newly diagnosed patients (EFNS, AAN, NICE)[1-3]: **ChEIs (donepezil, rivastigmine, galantamine)**

	Rivastigmine	**Donepezil**	**Galantamine**
Common brand name	**Exelon®** **Exelon® Patch**	**Aricept®**	**Razadyne®** **Reminyl®**
Approved indications	AD PDD (Exelon®)	AD	AD
Indicated AD patients	Mild to moderate	Mild to severe	Mild to moderate
Available formulations	Capsules Oral solution **Transdermal patch**	Capsules ODT*	Capsules
Dosing schedule	Capsules and liquid – b.i.d. Patch – q.d.	q.d.	q.d.

1. Hort J, et al. *Eur J Neurol* 2010;17:1236–48; 2. Doody RS, et al. *Neurology* 2001;56:1154–66; 3. NICE Technology Appraisal Guidance 217.

*ODT, orally disintegrating tablets

First-line Alzheimer's Disease Treatment Approaches with Cholinesterase Inhibitors (ChEIs)[1-3]

- First line therapy for newly diagnosed patients (EFNS, AAN, NICE)[1-3]: **ChEIs (donepezil, rivastigmine, galantamine)**

	Rivastigmine	**Donepezil**	**Galantamine**
Common brand name	**Exelon®** **Exelon® Patch**	**Aricept®**	**Reminyl®**
Approved indications	AD PDD (Exelon®)	AD	AD
Indicated AD patients	Mild to moderate	Mild to severe	Mild to moderate
Available formulations	Capsules Oral solution **Transdermal patch**	Capsules ODT*	Capsules
Dosing schedule	Capsules and liquid – b.i.d. Patch – q.d.	q.d.	q.d.

1. Hort J, et al. *Eur J Neurol* 2010;17:1236–48; 2. Doody RS, et al. *Neurology* 2001;56:1154–66; 3. NICE Technology Appraisal Guidance 217.

*ODT, orally disintegrating tablets

Starting / escalating anti-dementia drugs

- 1/3 to ¼ may have side effect on starting
  - GI
  - Agitation or not sleeping
- “Start low” for GI:
  - donepezil 2.5 mg daily AFTER meals
  - rivastigmine patch
- “Go slow”: 2.5 -> 5 -> 7.5 -> 10 mg, increase by 4-12 wks
- Watch out for s/e and allow step-down
- Bradycardia

Compliance and supervision

- Drug supervision:
  - Important for safety
  - Cases of cardiac deaths due to ChEI overdose (including patch)
- No effect if not taken
- Waste of resources

Caregiver / patient education

- Along side with starting dementia treatment
- Expectation management
- Harm / side effect reduction
- Non-pharmacological management at same time

“Prescribing” non-pharmacological treatment

- Patient:
  - Cognitive stimulation
  - Social stimulation

http://www.jccpa.org.hk/tc/facts_on_dementia/what_is_dementia/about_dement
Gmail | hkjc positive aging centr... | 賽智園 - 關於腦退化症
檔案(F) 編輯(E) 檢視(V) 我的最愛(A) 工具(T) 說明(H)

腦退化症資訊

甚麼是腦退化症
- 關於腦退化症
- 十個腦退化症徵兆

評估診斷
照顧錦囊
照顧者系列
十個給照顧者的實用提示
家居安全重要提示
家傭照顧技巧
護腦貼士
他們的故事
媒體報導
常見問題
相關連結

主頁 / 腦退化症資訊 / 甚麼是腦退化症 / 關於腦退化症

關於腦退化症(前稱：痴呆症)

1. 甚麼是腦退化症？
2. 腦退化症有甚麼種類？
3. 腦退化症有甚麼具體症狀？
4. 甚麼人較容易患上腦退化症？
5. 如何治療腦退化症？

下載「甚麼是腦退化症」單張

甚麼是腦退化症？

- 腦退化症又稱「失智症」，是多種引致腦部功能不正常地衰退的病患之統稱。患者的記憶力及其他認知功能 (例如學習、理解、語言運用、方向感及判斷力等) 會逐漸失去
- 有些病人也會有抑鬱、幻覺或人格改變的病徵
- 此症的患者多屬老年人。世界各地的研究顯示，六十五歲或以上的人士中約有百分之五至十患上各種類型和不同程度的腦退化症發病率亦會隨年齡而增加，故此症常被稱為「老年腦退化症」。事實上，六十五歲或以下的人士也可能患上腦退化症醫學上稱這種情況為「早發性腦退化症」。一般來說，這些患者較多有家族病史，而疾病的進程也可能會較快

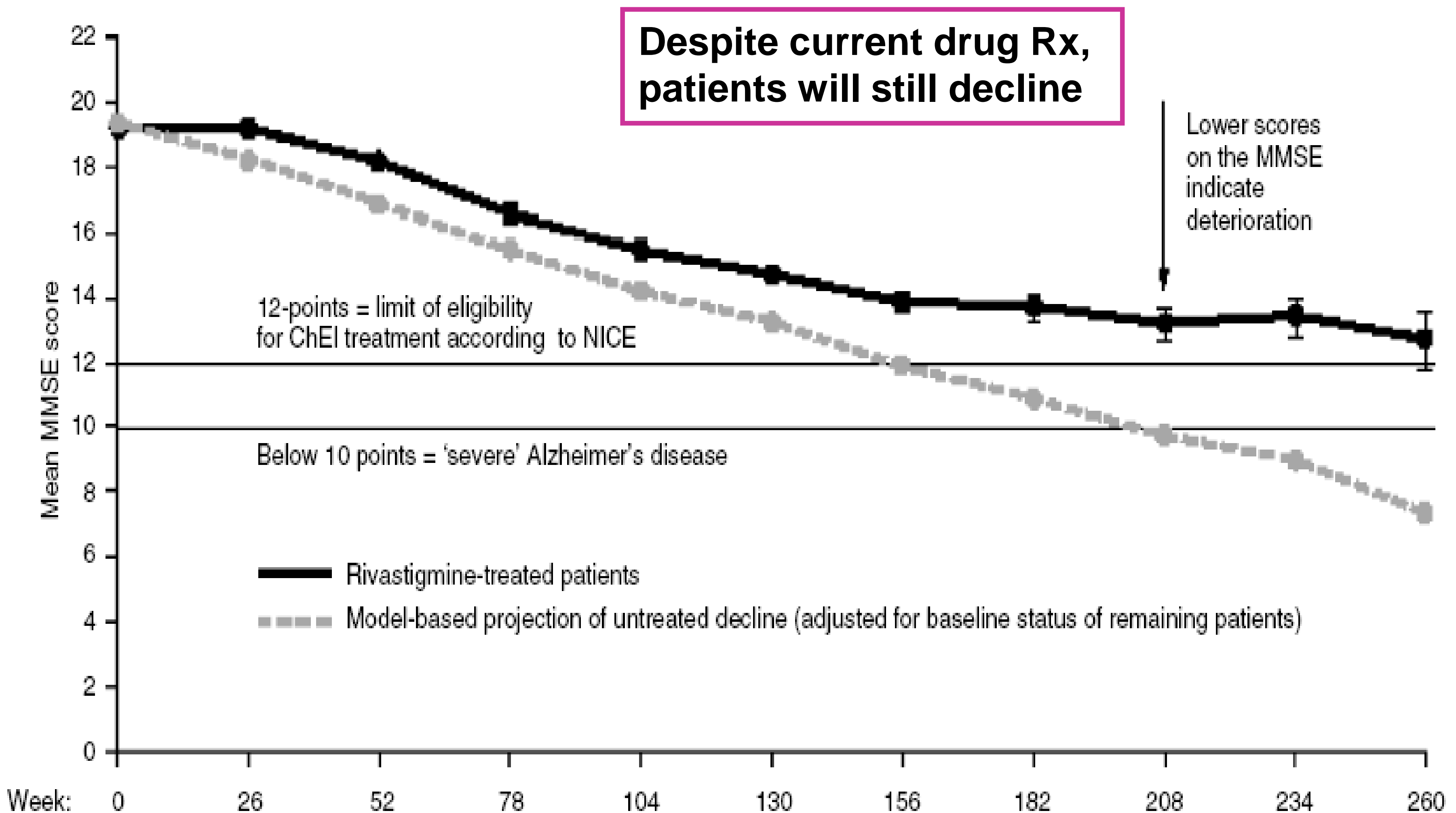
回到頁首

125%
17:46
16/1/2015

Stopping anti-dementia drug?

- No response:
  - Not all patients respond: ~ 30-50% (unlike DM drugs)
  - Consider static or slight improvement as good response
- Consider withdrawal if s/e, poor compliance, rapid decline, or when decline into advanced stage (e.g. bedridden, tube fed)
- Note: Some patients may remain static for years with/ without drug e.g. VaD

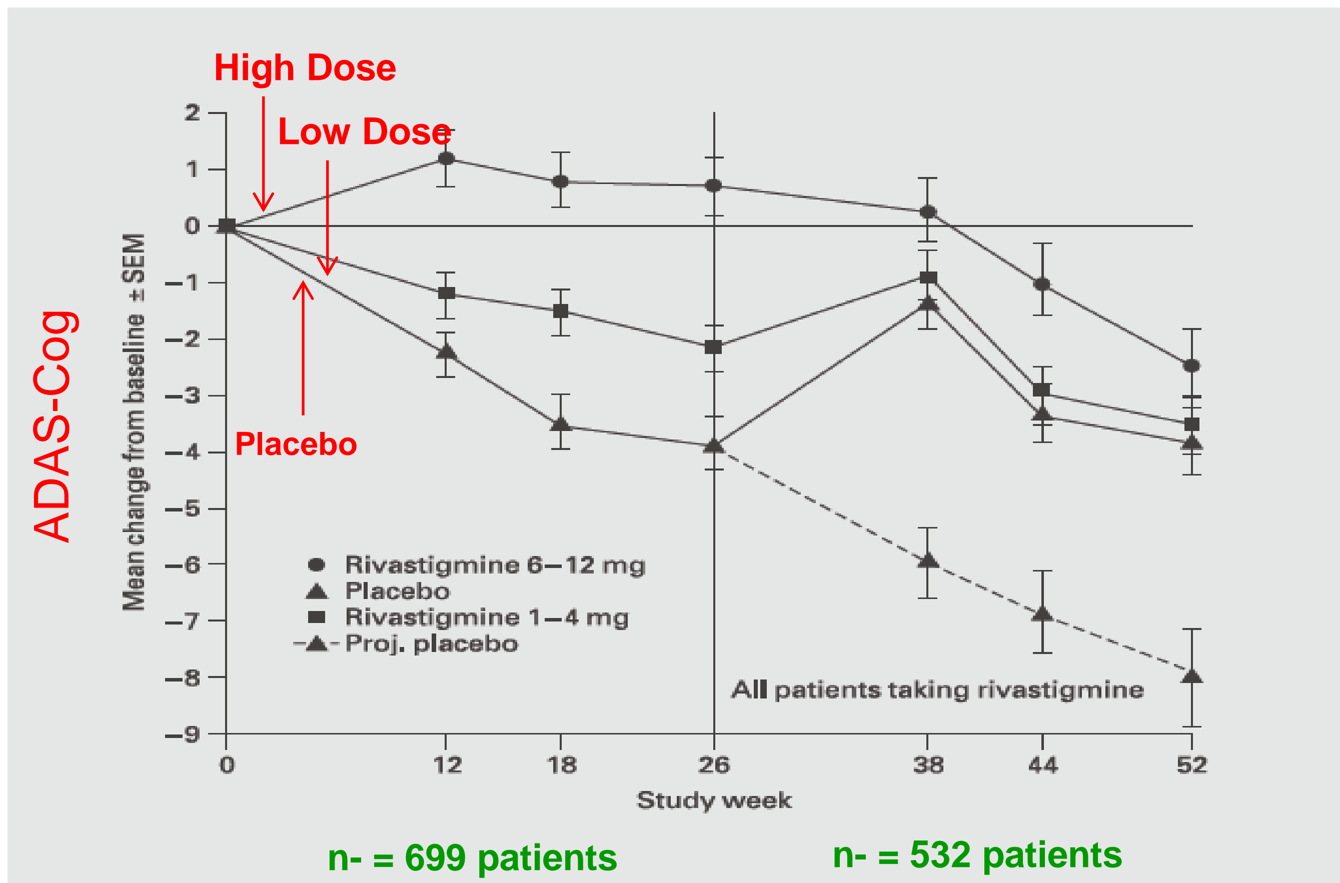
5-year decline in MMSE



Int J Clin Pract, July 2005, **59**, 7, 817–822

Why Early, High Dose Treatment?
To Optimize Long-term Outcomes for AD Patients

Initiate ChEI therapy later in the disease course do not ‘catch up’ with the functional or cognitive ability of those initiated earlier[1]



1. Grossberg G, *et al. Alzheimer Dis Assoc Disord* 2009;23:158–64; 2. Farlow M et al., *Eur Neurol* 2000; 44:236-41.

Other drugs – no evidence

- Ginkgo Biloba
- Vitamin E and other food supplements
- Piracetam (Nootropil)
- Aspirin

Anti-depressants

- ~ one-third to half have some mood problem during illness – mostly depression
- Depression may worsen cognition
- SSRI main-stay of treatment (e.g. sertraline, citalopram), SNRI (e.g. mirtazapine – very sedating)
- Choice of SSRI:
  - Anti-depressant effect mostly similar, differ in s/e profile
- S/E: monitor Na level; sedation and edema (mirtazapine)

BPSD (behavioural) drugs

- Delusion / hallucinations: nothing or anti-psychotics
- Aggression:
  - Anti-convulsants (e.g. valproate)
  - atypical anti-psychotics (e.g. risperidol, quetiapine)
- Irritability:
  - trazodone,
  - anxiolytic (e.g. xanax)
- Nightime behaviour / not sleeping:
  - sedatives (xanax, ativan), Z-sleeping drugs
  - trazodone
- BPSD and/or mod-advanced AD:
  - can also consider memantine
- *Notes: increased agitation possible with newly started AChEI – try decrease dose or take in morning for insomnia, or try rivastigmine*

Caution about anti-depressant & antipsychotics

- TCA:
  - retention of urine, arrhythmia, dry mouth
- Combinations of SSRI / SNRI / atypicial antipsychotics / herbs (e.g. ginseng)/ antihistamines:
  - serotonin syndrome (sweaty, tremoring/ twitching, ↑BP, HR, Temp, agitation/ hallucination)
- Anti-psychotics:
  - Extrapyrimidal Signs & Symptoms (EPS) –
    - tardive dyskinesia, dystonia, Parkinsonism

Vascular risk factor drugs

- BP, DM for Vascular Dementia patients
- Stroke prevention
- Over-controlled BP and blood sugar results in further cognitive impairment in elderly:
  - A1c of <6.5% too low for frail elderly (optimal 7 – 8% depends on frailty), 8% if very frail or brittle
  - SBP 160 best survival for 80+ patients

Drugs worsening Cognition

- Many…
- Psychoactive drugs:
  - Anti-cholinergic drugs (TCA)
  - Sedating drugs (benzodiazepines, Z-drugs: zopiclone, zolpiderm)
  - Antipsychotics (due to oversedation or EPS)
- Non-psychoactive drugs:
  - GI drugs:
    - H2 blockers (cimetidine, famotidine)
    - PPI (omeprazole)
    - Antispasmotics for cramps or diarrhoea
  - BP drugs e.g. beta-blockers, methydopa
  - Eye drops: topical timolol
  - Analgesics: narcotics, NSAID in renal impairment
  - Antibiotics: quinolones (excitatory), penicillins (including amoxicillin)
  - Urinary drugs: overactive bladder and urge incontinence drugs apart from estrogens
  - Parkinson Disease drugs: artane (strong anticholinergic), L-dopa (high doses)
  - Cough medications and decongestants for colds: new and old antihistamines or anti-cholinergics (e.g. chlopheniramine (piriton), cetirizine(Zyrtec), fexofenadine (Telfast))
  - DM drugs: due to hypoglycaemia

Drugs worsening Cognition

- Non-psychoactive drugs:
  - GI drugs:
    - H2 blockers (cimetidine, famotidine), PPI (omeprazole)
    - Antispasmotics for cramps or diarrhoea
  - BP drugs: beta-blockers, methydopa
  - Eye drops: topical timolol
  - Analgesics: narcotics, NSAID in renal impairment
  - Antibiotics: quinolones (excitatory), penicillins (e.g. amoxicillin)
  - Bladder & bowel drugs: overactive bladder and urge incontinence drugs, antispasmotics
  - Parkinson Disease drugs: artane, L-dopa (high doses)
  - Cough medications and decongestants for colds: new and old antihistamines (e.g. chlopheniramine (piriton), cetirizine(Zyrtec), fexofenadine (Telfast))
  - DM drugs: hypoglycaemic drugs, insulin

Drugs not expected to help (but may help)

- If worsened “confusion” or behaviour symptoms
- Look for causes other than dementia
  - Drugs
  - Acute illness
  - Physical distress
  - Psychological distress

Physical distress

- Many physical distress can induce delirium (or confusion) or result in agitation
- Basic: tiredness, hunger, restraints
- Pathological: pain, fever, itch, constipation, retention of urine, tachycardia, hypoxia, hypoglycaemia, hypotension, stroke, etc.

- Drugs (or management) that alleviate these will reduce so-called dementia symptoms

Psychological distress

- Psychological: fear, anxiety, sadness, excitement

- Reassurance
- May need medications

Advanced dementia

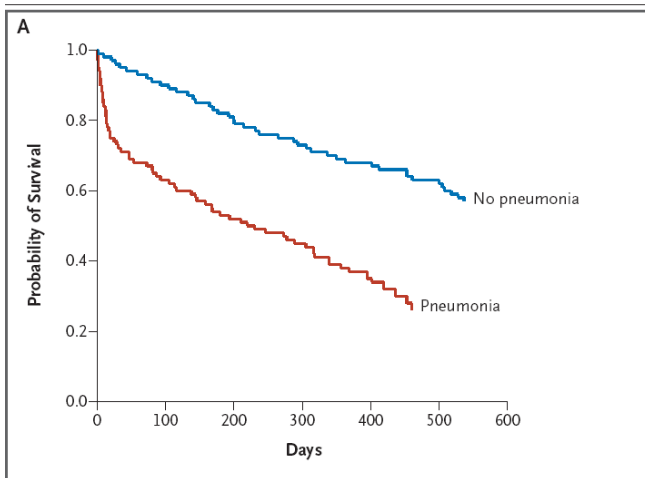
- When?
- FAST stage 7 or most ADLs dependent
- Example:
  - Double incontinent
  - Few words or no speech
  - Cannot self-feeding
  - Chair or bedbound

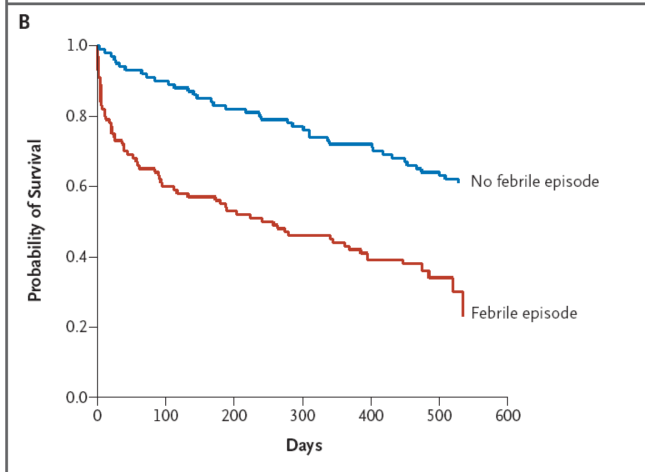
Advanced dementia

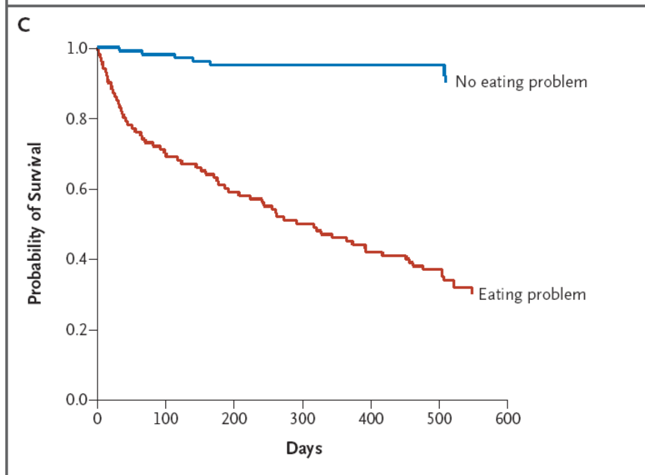
- Time for medication reduction
  - Over-control (glucose, BP, diet) difficult to detect (patient cannot complain)
  - Limited life expectancy – prognostic medications vs. symptomatic treatment
  - Diet and nutrition – maintenance of weight rather than restrictions
  - Comfort vs. Safety (pill load vs. feeding)
  - Cognition and BPSD drugs - ? Still needed

End of life in Dementia

- When?







Onset of pneumonia, febrile episodes and eating problems predicts end stage of life in dementia.

Mitchell et al. NEJM 2009

Palliation rather then “treatment”

- Complications:
  - Infections, pressure ulcers, pneumonia, other competing organ failure
- Dementia drugs ceased to be useful
- BPSD not prominent – off treatment
- Mainstay:
  - Analgesics (and pain detection), anti-pyretics, minimum risk factors control (HR, BP, glu), diuretics (edema), laxatives….

Conclusion

- Modify treatment as disease progress
- Minimize medications as prone to s/e esp CNS
- Dementia is incurable:
  - so palliation treatment becomes more important than cognitive treatment towards end of life

Thank you