An Approach to Delirium in LTC

FRASER HEALTH LONG TERM CARE ROUNDS

Feb 2023

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Delirium in LTC test question: Which of these is your favourite Marvel hero?

Loki

Black Widow

Captain America

Ant Man

Iron Man

Thor

You missed my fav.

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LEARNING OBJECTIVES

1) Recognition and prevention of delirium
2) Diagnosis and workup for delirium
3) Management of delirium

LEARNING OBJECTIVES

1) **Recognition and prevention of delirium**
2) Diagnosis and workup for delirium
3) Management of delirium

“This is not my mom”



Delirium is present in acute illness in up to 18-33% of LTC patients

- Early recognition is important - acute with sudden fluctuations
- Outside of the realm of normal for the patient

Hyperactive	*Hypoactive (65%)*	*Mixed*
Agitation Aggression Paranoia Hallucinations	Drowsy Not eating well Sleeping more Accelerated weakness / falls	Combination

Boockvar et al, JAMDA 2013.

Differential diagnosis for delirium

Lewy body dementia	Can be very dramatic fluctuations within hours; typically common to have previous fluctuations
BPSD or sundowning	Typically easier to identify a trigger with BPSD; delirium can present as increased agitation or aggression on a background of BPSD and more fluctuant
Progression of dementia	Typically more gradual progression or associated with focal neurologic deficits (in case of a stroke)
Disease specific fluctuations	Diabetes, CHF, hypertension, COPD

Delirium is often multifactorial



But we should rule out medical causes as well

Medication changes	Withdrawal or side effects
Infection	Viral, UTI, pneumonia, cellulitis, pressure sores, dental
Exacerbation of chronic medical conditions	CHF exacerbation, COPD exacerbation
Metabolic	Hypoglycemia or hyperglycemia, hyponatremia or hypernatremia
Acute medical conditions	Stroke, TIA, traumatic brain injury

The evidence is limited in treating and reducing delirium

- Outcomes from delirium are poor - higher mortality, more antidepressant and antipsychotic usage
- Cochrane review from 2019: moderate evidence that a medication review program was helpful but not enough evidence to look at other outcomes
- HELP (hospital elder life program) which has shown to help acute inpatients was studied in LTC patients who became acutely unwell to try to reduce delirium - no benefit

- Our best approach is likely *multifactorial* to address a number of triggers for delirium

Moon and Park, J Gerontol Nurs 2018.
Woodhouse et al, Cochrane 2019.
Boockvar et al, JAGS 2020.
Cheung et al, BMC Geriatrics 2018.

What sort of care can help to prevent delirium?

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Delirium prevention is also multifactorial



Delirium risk factors include patient factors and environmental factors

- Delirium is common, often prolonged, and often attributed to infection
- Risk factors for delirium in different studies showed: Regular benzodiazepine usage, vascular dementia, 2 or more new medications prescribed, pain, regular antipsychotic usage
- Environmental factors include:
  - *Lack of*: reading glasses, aids to orientation, family members, glass of water
  - *Presence of*: bedrails and other restraints

Skretteberg et al, JAMDA 2022.
McCusker et al, JAGS 2013.
Cheung et al, BMC Geriatrics 2018.

Medication reviews can follow a basic approach or use more structured tools

STOPPFRAIL tool can help as a guide to reducing polypharmacy in the severely frail with limited prognosis

- Review anticholinergic medications - antihistamines, H2 blockers (e.g. ranitidine), PRN medications like dimenhydrinate (anticholinergic burden scale for less risky alternatives)
- Review psychotropic medications - are these still needed at these same doses?
- Review time to benefit from medications - e.g. statins for primary prevention, diabetes medications (A1c targets of 8.5%), antihypertensives (SBP goals 140-160)
- Consider side effects of medications esp if weight loss - e.g. metformin or cholinesterase inhibitors causing diarrhea and weight loss

Environmental changes to promote safety

- Bright lighting
- Signs to reorient patients, memory box or pictures on the doors of their rooms
- Avoiding catheters/restraints as much as possible
- Mobility as much as able



Sleep hygiene

- Daytime activities to keep patients awake and mobility
- Quiet low-light environment at night
- Mixed evidence on timed bright light exposure - in the mornings it tends to lead to improved circadian rhythm, with patients more awake during the day and improved sleep in some studies
- Consideration of melatonin for circadian rhythm as well, but limited evidence for this in LTC patients
- Nature therapy (being outdoors)



Ancoli-Israel et al, JAGS 2002.
Martin et al, J Geront A Biol Sci Med Sci 2007.
Burns et al, Int Psychogeriatr 2009.
Gonzalez and Kirkevold, J Clinical Nursing 2013.

Structured drink rounds (hydration) reduced antibiotic usage and hospital admission

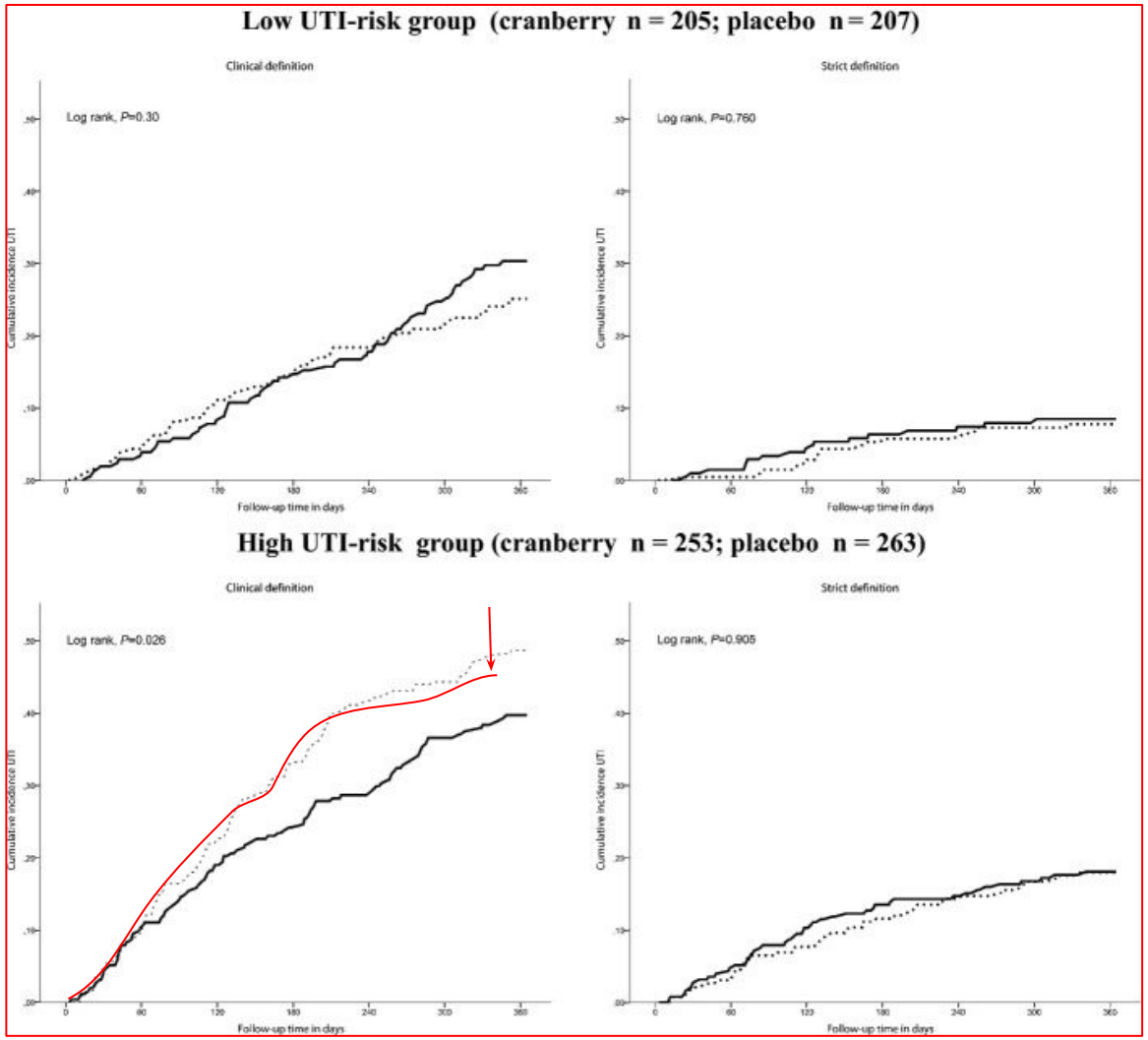
- Hydration status
- Reducing catheter usage as much as possible
- Adequate hygiene (peri-care)
- Vaginal atrophy can lead to more frequent UTIs - premarin cream 1g twice a week for a month, then 0.5g twice a week indefinitely



Meddings et al, J Hosp Med 2017.

Limited evidence for pharmacotherapy to prevent UTIs

- Cranberry capsules BID in high risk UTI patients in LTC reduced incidence of clinically defined UTIs, but in another study did not change pyuria and bacteriuria
- *D-mannose* has been shown to be more helpful than antibiotics in some studies in prevention of recurrent UTIs in general populations (no specific LTC evidence)
- Prophylactic antibiotic therapy is controversial - some studies have shown short-term benefit but they are generally not recommended in most patients



Caljouw et al, JAGS 2014. Juthani-Mehta et al. JAMA 2016.
Kyriakides et al, Eur Urol Focus 2020. Alterac and Papes, BJUI 2013. Porru et al, J Clin Urol 2014. Ahmed et al, BMJ Open 2017.

Edema prevention (to prevent cellulitis)

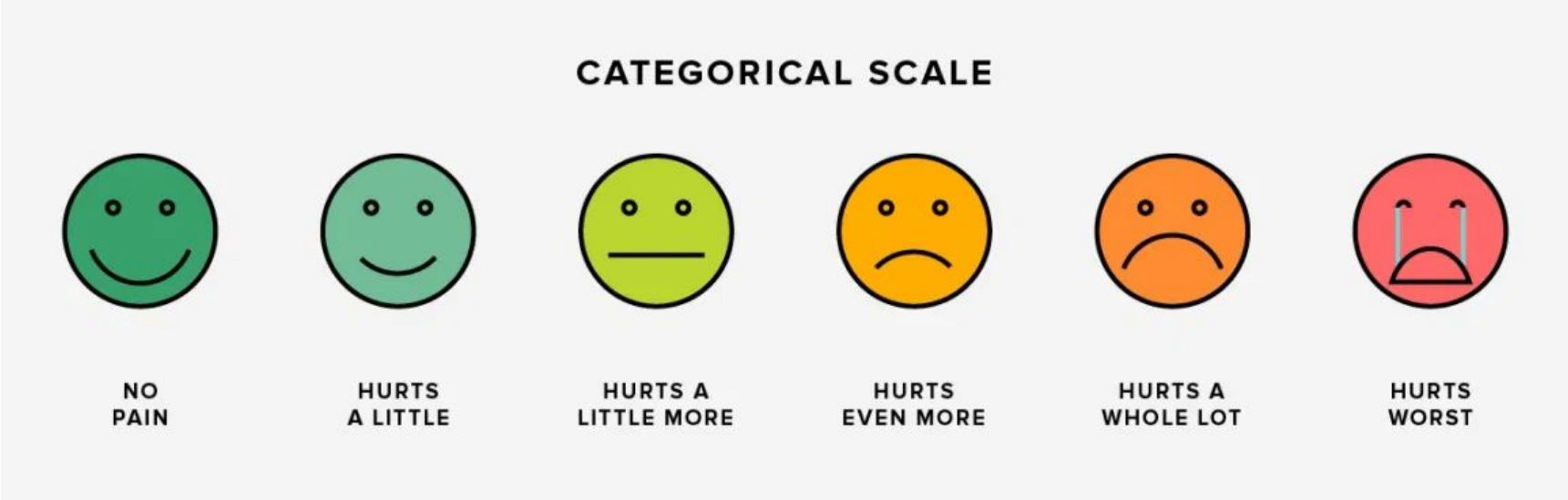
- Venous stasis edema - elevate the legs
- Compression stockings
- Diuretics if indicated



Pain is associated with delirium

Consider doing pain review - history of chronic pain conditions (e.g. chronic peripheral neuropathy but no medications for this, arthritis without any medications)

- Topical medications (diclofenac cream)
- Tylenol
- Gabapentin or pregabalin if indicated
- Venlafaxine for chronic neuropathic pain / anxiety / depression



Cheung et al, BMC Geriatrics 2018.

Adequate hydration and oral intake
Poll coming up at *pollev.com/brobinson676*

- Social meals
- Encouragement to eat during meals
- Look at dentition

- Look at their type of diet (e.g. dysphagia diets?)



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What is the evidence behind thickened liquid diets?

- Reduced incidence of aspiration pneumonia
- Reduced aspiration during video assessments
- Reduced mortality
- A and B
- A, B, and C
- None of the above

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Thickened fluids: they work in some patients with video fluoroscopy but don’t in others

- Video fluoroscopy showed less aspiration risk, but results were quite variable
- The more severe the dementia, the worse the patients did with any of the interventions
- Older patients seem to do better with a chin-down approach
- About half of patients didn’t seem to fit the pattern in generally that honey-thickened fluids, then nectar-thickened, then chin-down was best → need a personalized approach
- When honey-thick fluids were introduced last, it tended to be the least successful - likely represents fatigue from patients

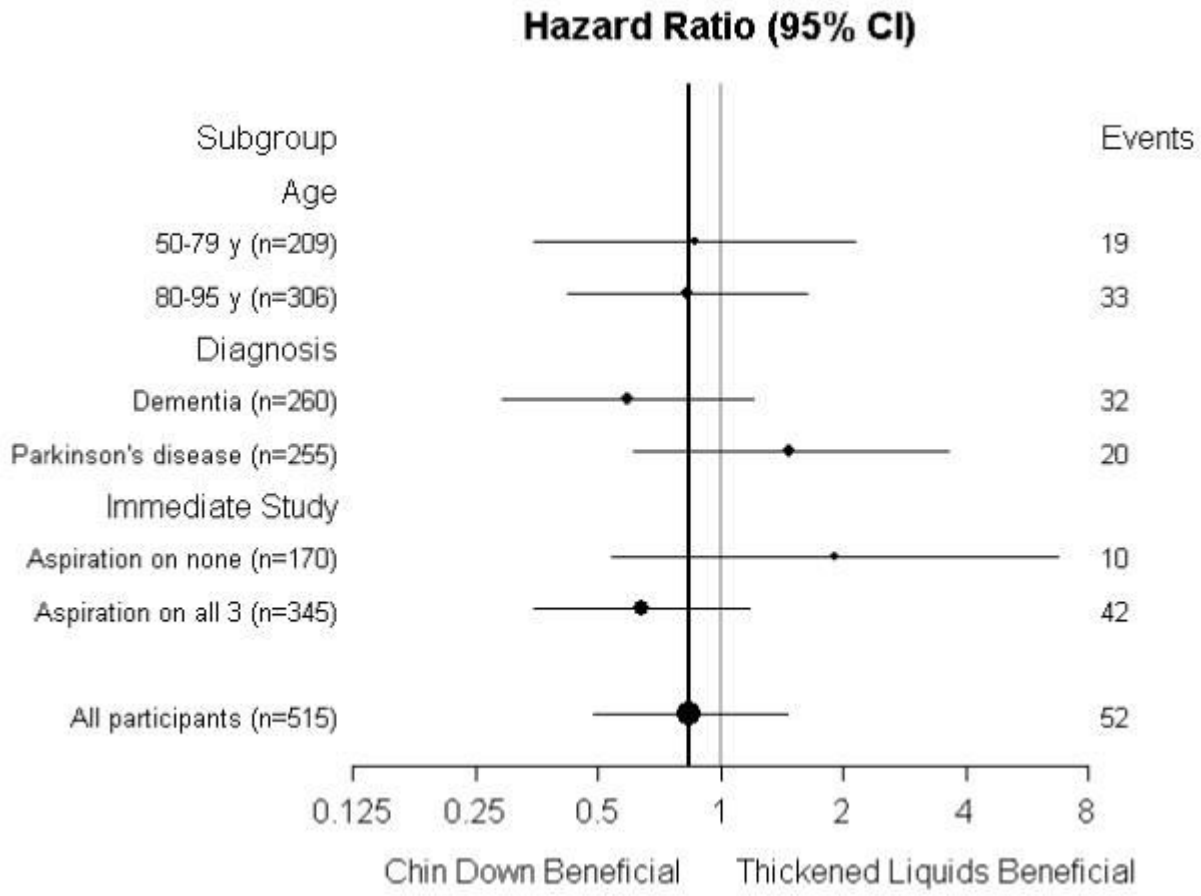
Logemann et al, J Speech Lang Hear Res 2008.

No difference in aspiration risk for thickened liquids vs. chin down

Systematic review shows no difference between chin down vs thickened liquids. Individual studies show:

- 3 month pneumonia incidence: comparing chin-down vs thickened liquids (dementia or Parkinson's) showed similar numbers of pneumonia, but higher UTI and dehydration risk in thickened liquids
- But this will likely involve more close monitoring during meals to ensure compliance

An alternate consideration for harm reduction - Frazier water protocol? Thickened liquids with meals, but regular fluids otherwise with good oral care



Robbins et al, Ann Intern Med 2008.
Sura et al, Clin Interv Aging 2002.
Beck et al, Clin Nutr 2018.

I tried to live through 24h of thickened liquids… it went poorly

- My first thought: “actually, this isn’t so bad. Maybe I was wrong. Maybe I should end my crusade…”
- At the end of the day: “I’m so thirsty but I just can’t drink any more of this.” (Luckily, I just had to wait until the next morning…)
- Dry food like bread was unappealing because I couldn’t quench my thirst afterwards
- I felt strangely bloated and had an aversion to drinking
- My mouth felt very dry, even after drinking
- I went on a 14 km hike and drank 75 mL of fluid along the way…



Perhaps reconsider thickened fluids in your patients

- Might increase risk of UTIs and dehydration
- Bioavailability of drugs is also affected by viscosity of fluid
- Could lead to less oral intake due to a sensation of fullness
- Limited evidence behind these diets long-term
- Each patient is quite individual with which approach works best for them

Clinical pearls: prevention of delirium is key

1) Deprescribing can reduce delirium (look at the Anticholinergic Burden Scale or consider the STOPPFRAIL criteria for polypharmacy)
2) Adequate hydration is important (perhaps reconsider thickened liquids!)
3) Ensure adequate pain control, especially in those with a history of pain



Case presentation: what could be contributing to her presentation? (Poll live at *pollev.com/brobinson676)*

89F in LTC with severe Alzheimer's, DM2 (no meds, A1c 7.0%), OAB, recurrent UTIs. Family visits daily.

Medications: On TID tylenol and multivitamin only.

Recent hospitalization 3 months ago for delirium and presumed UTI. Since last hospital stay:

- Not eating or drinking well, stand-by assist for mobility, continent at times.

Family: concerned that she's been more drowsy than usual, stating that she seems tired and weak.

Nursing: slightly decreased PO intake, a bit more drowsy than usual, perhaps more intermittent incontinence (unclear). Vitals WNL.

What could be contributing to her presentation?

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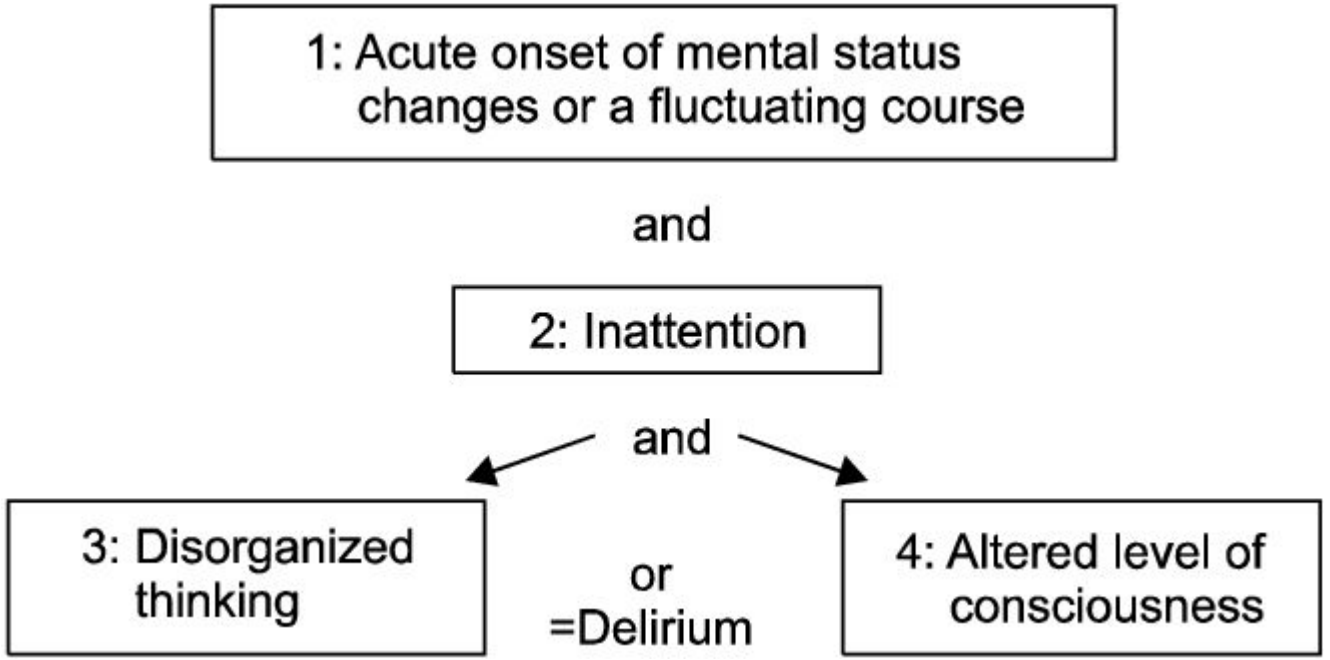
LEARNING OBJECTIVES

1) Recognize various presentations of delirium in the context of dementia
2) **Diagnosis and workup for delirium**
3) Management and when to refer to hospital

Core symptoms of CAM can be positive prior to the CAM being positive

- May represent a subsyndromal delirium
- Perhaps a sign that patients should be monitored more closely - marker of cognitive vulnerability
- CAM sensitivity reduced 70% and specificity 63% in severe dementia patients



Cole et al, JAGS 2012.
Wei et al, JAGS 2008.

Delirium workup - may be multifactorial!

- Behaviour charts, sleep logs, stool charts, oral intake charts
- Physical exam - look for constipation/retention (suprapubic fullness or tenderness), respiratory concerns, cellulitis, pressure sores, volume status
- Neurologic exam - focal neurological deficits, look for signs of encephalopathy (asterixis, jaundice)

- Check vitals and blood sugars
- Consider urinalysis and routine labs when available (CBC, renal profile)

O2 sats less than 94% can predict pneumonia

Small case control study of LTC patients (n=67)

O2 sats less than 94%

- 80% sensitivity and 94% specificity for pneumonia
- Negative likelihood ratio 0.22
- Positive likelihood ratio 8.8



Kaye et al, Am J Med Sci 2002.

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How do you manage possible delirium and positive urinalysis with no other symptoms?

Start antibiotics and await urine culture (if negative, stop)

Await urine culture and start antibiotics only if urine culture is positive

Search for other underlying causes - if none, then give antibiotics if culture positive

Do not give antibiotics - watch and wait

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UTI vs asymptomatic bacteriuria

Consider a UTI in a patient with delirium and worsening incontinence, frequency, dysuria, suprapubic pain, fever, chills, or hematuria (or if other reasonable causes are ruled out)

Choosing Wisely Canada:

- In catheterized patients, acute delirium without another cause
- In non-catheterized patients:
  - Acute dysuria or 2 or more of the following: (fever, urgency, frequency, suprapubic pain, gross hematuria, flank pain, incontinence)

The association between asymptomatic bacteriuria and delirium is limited

- There is an association between delirium and UTIs with urinary catheters, urinary retention, and dehydration separately. Beyond that, it becomes more unclear how to define UTIs.
- Retrospective cohort study looking at (general population) hospitalized patients with delirium and positive urinalysis (and no other symptoms) found that patients not treated with antibiotics had similar delirium resolution at 7 days and outcomes at 30 days
    - Only 25% of those were LTC patients, and the vast majority of LTC patients were treated with antibiotics
- There is limited clinician consensus on how to treat positive urine cultures in delirious LTC patients

Krinitski et al, JAGS 2021.
Joo et al, BMC Geriatrics 2022.
Teng et al, Drugs Real World Outcomes 2021.
Lague et al, CJEM 2022.

Case presentation: what is your next step to manage? (Poll live at *pollev.com/brobinson676)*

89F in LTC with severe Alzheimer's on thickened liquids, 2-3 days of drowsiness, and decreased PO intake

Physical exam shows:

- Slightly dry, nonspecific generalized abdo tenderness
- Drowsy when rousable, eats when fed
- Vitals stable. O2 sats 98%.
- Urine dip shows leukocytes.

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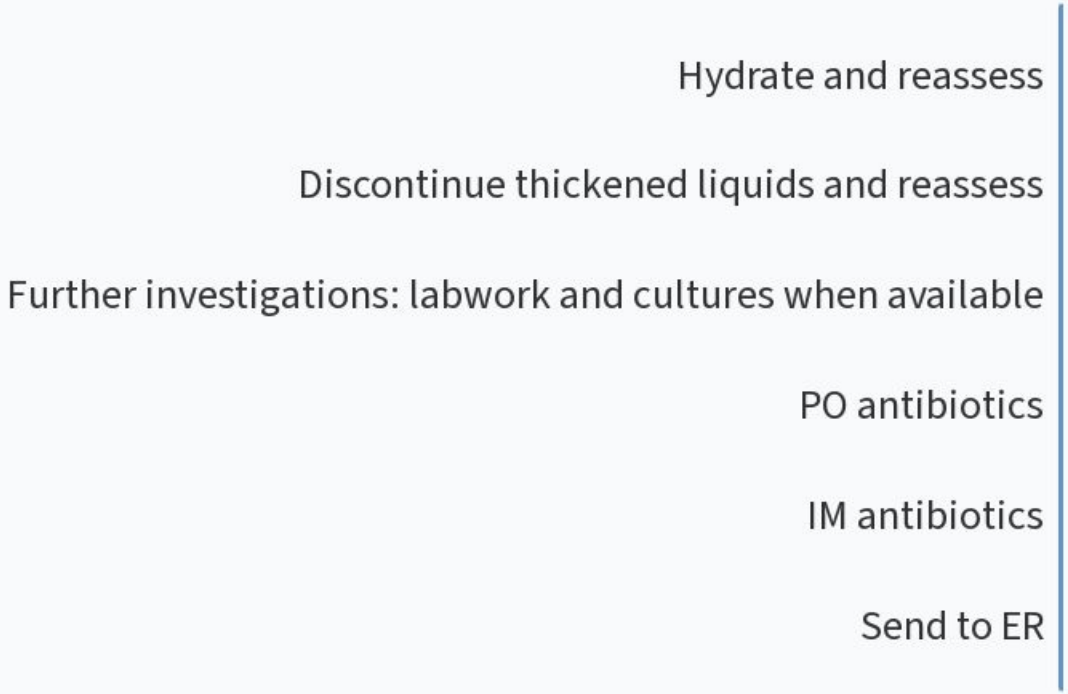
What is your next step in management? Choose as many as you like.



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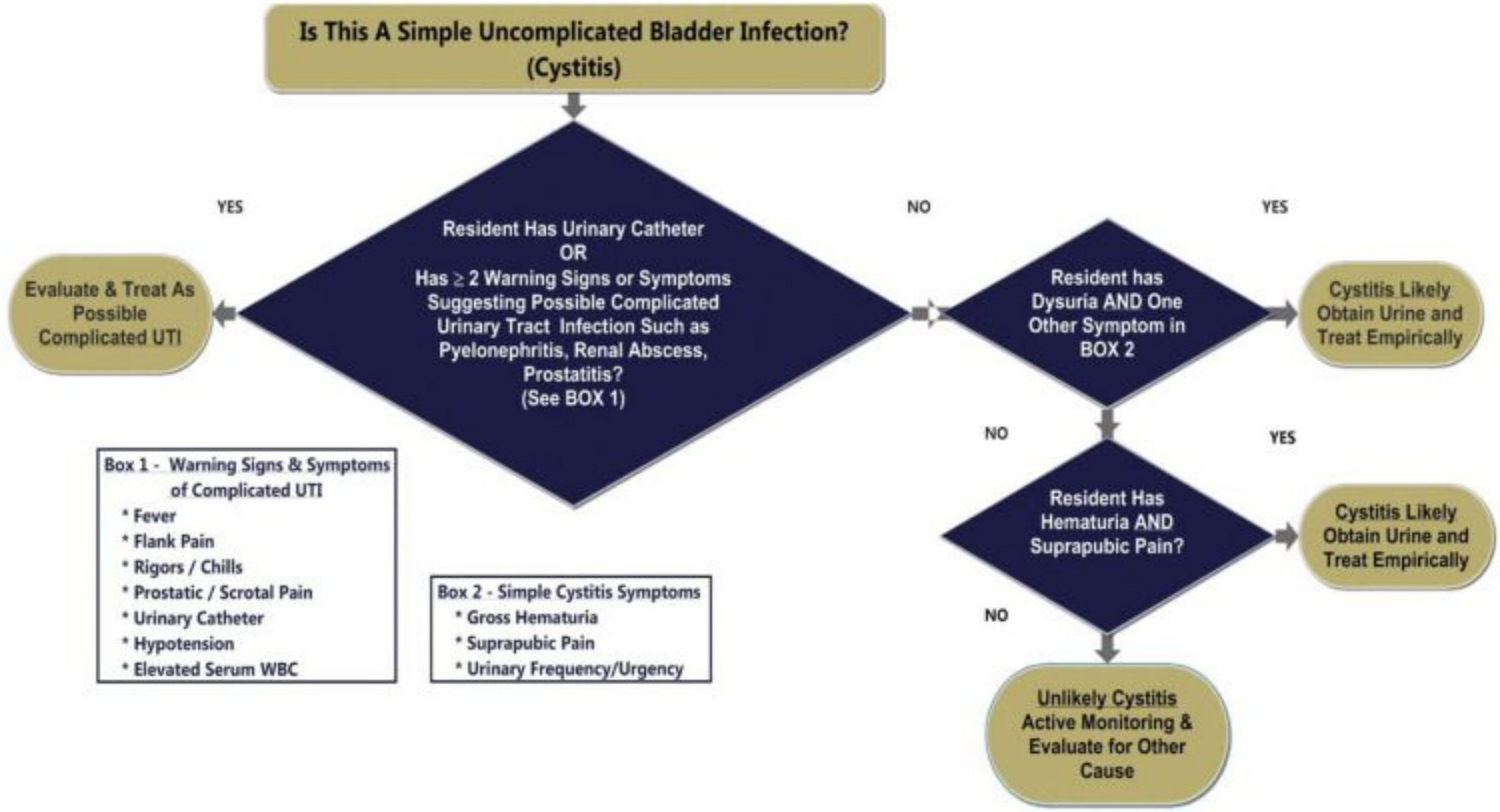
AMDA clinical practice guideline suggest to hydrate and wait if no symptoms or catheter



Clinical pearls

1. Low O2 sats have reasonable specificity for pneumonia
2. Rehydrate before considering antibiotics unless there are UTI symptoms associated with a positive urine dip
3. Consider UTI in patients with a catheter or urinary retention



LEARNING OBJECTIVES

1) Recognize various presentations of delirium in the context of dementia
2) Diagnosis and workup for delirium
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Management: treat the underlying cause

- Allow and encourage the family to visit, if at all possible
- Encourage hydration and mobility (prevent pressure sores, aspiration, and further deconditioning)
- Encourage nutrition as much as possible (prevent AKI)
- Consider pain control, bowel care, sleep hygiene
- Antibiotics for true infections
- Consider the underlying goals and care and prognosis

Goals of care should be revisited in advanced dementia with dysphagia or previous infections

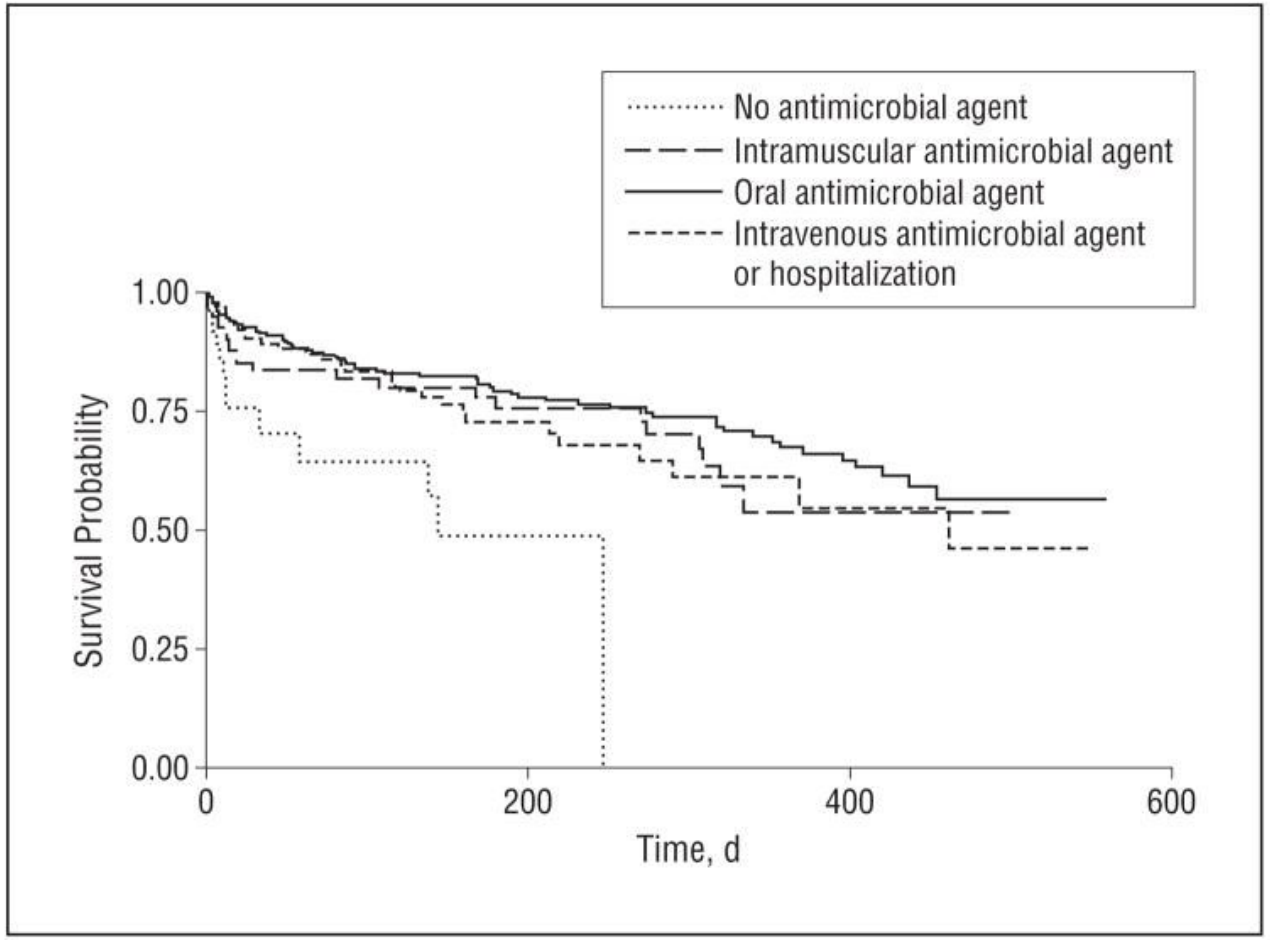
Signs to revisit goals of care discussions include end stage dementia:

- Median survival approximately 16 months for advanced dementia patients in nursing home
- 3 signs in severe dementia in LTC patients (mostly Alzheimer's) that are associated with end-stage dementia (without any other clear causes)
  - ~50% 6 month mortality if: *pneumonia* (47%), *swallowing problems* (39%), *febrile episodes* (45%)
- In final 3 months of their life, 90% had eating problems

Mitchell et al, NEJM 2009.

Any route of administration of antibiotics in pneumonia in severe dementia can prolong life

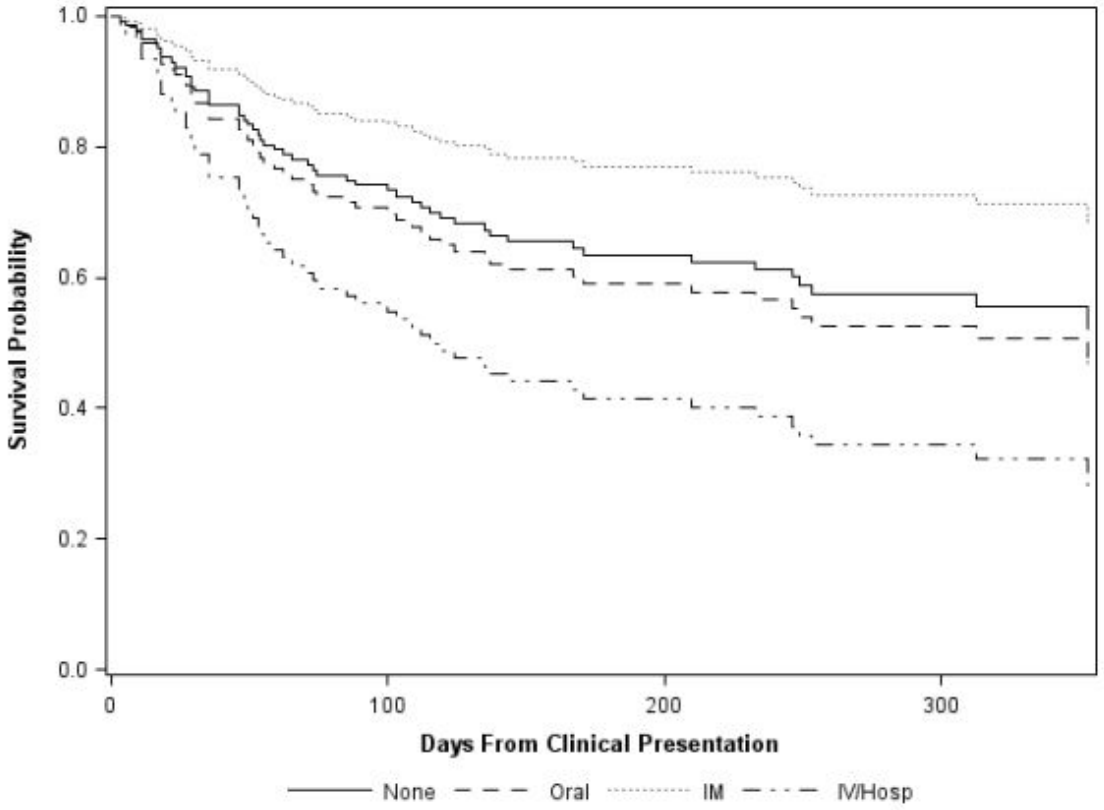
- Antibiotic therapy associated with lower mortality for any route of administration (increased survival time approximately 9 months)
- No survival difference between routes of administration
- For those who survived 90 days:
  - Greater comfort scores for those without antibiotics
  - Greater comfort scores for those with less aggressive care (IV significantly associated with lower comfort scores)



Givens et al, Arch Intern Med 2010.

PO or IM administration of antibiotics in UTI in severe dementia can prolong life

- 25% of patients died within 135 days of UTI
- No significant association between overall antibiotic use and mortality
- Hospitalization/IV antibiotic group associated with shorter survival (perhaps related to disease severity?)



Dufour et al, JAGS 2015.

Outcomes for LTC patients being transferred to hospital are generally poor

Systematic review from 2014 for LTC patients being transferred to hospital

- Most common reason was respiratory, infection, or fall
- Often associated with aspiration, adverse drug reactions, and multimorbidity

Mortality and functional decline was high for hospitalized LTC patients

- ~50% died within 3 months, 25% died within 30 days, 25% died in hospital, and 5% died within ER
- Higher association with functional decline
- More likely to acquire pressure ulcers
- More likely to develop delirium (38%); higher mortality in those who had delirium (46% vs 27%)
- 3x increased risk of hospital-acquired infection, higher risk of antibiotic resistant organisms

Dwyer et al, Age and Ageing 2014.

Hypernatremia may help risk stratify acute febrile illness

- Observational study of LTC patients who developed febrile illness found that sodium abnormalities were common.
- Rate of death higher in *hyper*natremic patients.
  - 35% who had hypernatremia died. Previous baseline sodium did not matter.
  - 23 of 28 (82%) of those who died had hypernatremia during their acute illness

Arizon et al, Arch Gerontol Geriatr 2005.

LRTI infections with higher respiratory rate is an indicator of higher mortality

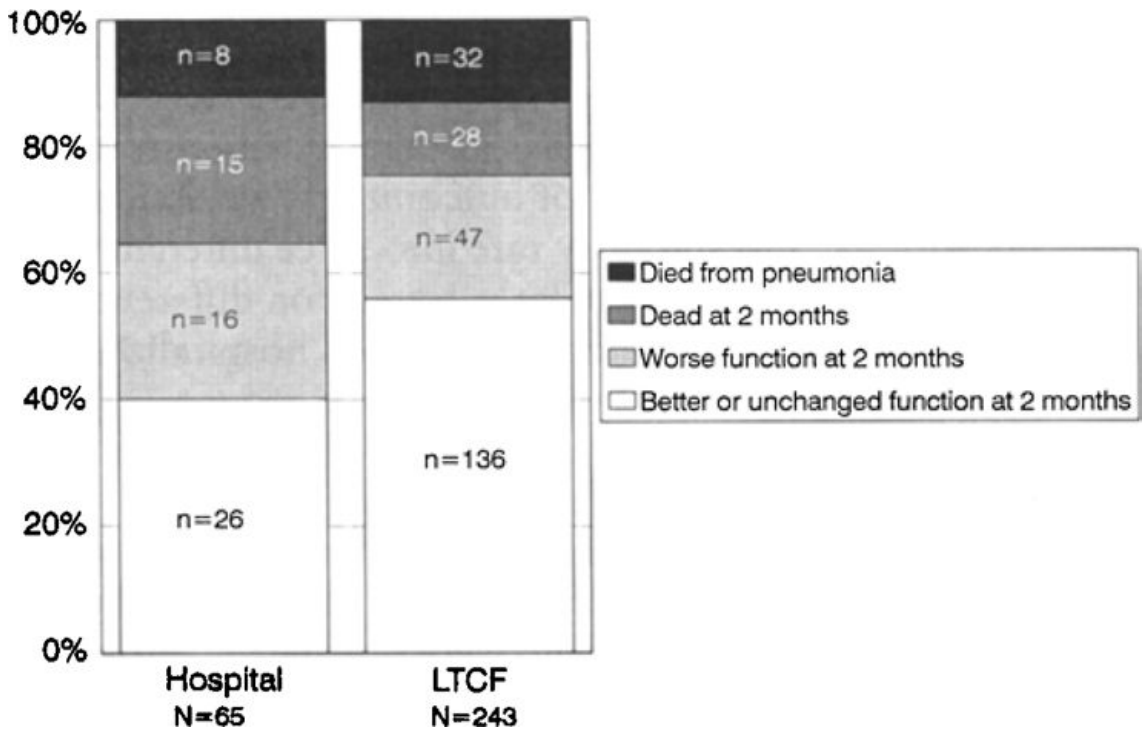
- Prospective cohort study of 1406 LRTI in LTC patients - hospitalization did not change mortality rates
- Observational study of 198 patients in LTC treated for LRTI - predictors of failure were: needing feeding by staff, altered diets, and sepsis
  - Failure rate (requiring hospital admission) was 11% for no factors, 23% for 1-2 factors, and 60% for 3 factors
- Observational study of 316 patients who were in LTC - elevated respiratory rate patients tended to die more when they were treated in LTC vs hospital
  - More frail patients also tended to die more often

Degelau et al, JAGS 1995.
Kruse et al, Med Care 2004.
Fried et al, J Gen Intern Med 1995.

Patients who go to hospital with LRTI may have worse short-term functional outcomes

312 patients who were in LTC and developed LRTI

- 79% treated in LTC and 21% treated in hospital
- Equal proportions died
- Higher proportion of those who went to hospital died at 2 months or had functional decline at 2 months
- This remained true even when adjusting for disease severity
- For patients who were less sick (lower respiratory rate), they tended to do better in LTC than in hospital



Fried et al, JAGS 1997.

A set clinical pathway for treatment of LRTI can be helpful in the LTC facility

Nursing homes in Hamilton, Ontario looked at a standard set of clinical protocols for hospital transfer

Treated in LTC if:

- Able to eat and drink
- HR <100
- RR <30
- SBP >90 (or a decrease of less than 20 mmHg from baseline)
- O2 sats of 92% or above (90% or above in COPD)

But LTC treatment included hypodermoclysis in patients who appeared hypovolemic (up to 60 mL/hr of normal saline)

Similar outcomes for mortality and reduced hospitalizations and costs

Loeb et al, JAMA 2006.

Summary of antibiotic therapy

- Any route of treatment appears to be beneficial, though this is likely also a marker of illness
- Patients treated in LTC may do better, especially if they are able to receive some amount of subcutaneous hydration
- Higher respiratory rate in LRTI and hypernatremia in acute febrile illness may predict mortality

Case presentation: she is declining. What next? (Poll live at *pollev.com/brobinson676)*

89F in LTC with severe Alzheimer's on thickened liquids, 2-3 days of drowsiness and decreased PO intake

- Was started on PO antibiotics for 2 days
- Becoming drowsier and eating less.
- Too drowsy or refusing to take her PO meds now and becoming combative with care.
- On exam, looks unwell and appears dry. Slightly tachypneic, O2 sats 90%, and crackles at bases on auscultation.

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She's not getting better. What do we do now? Pick as many as you like.

- Send to ER
- Antipsychotics for delirium
- Change to IM antibiotics
- Transition to comfort care (with family consent)

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Antipsychotic therapy in delirium may be needed in the short-term

- Sleep hygiene - melatonin, timed bright light exposure, daytime activities as much as possible
- Antipsychotics can be indicated for severe agitation/restlessness but come with increased risk of stroke and death in dementia patients
- Choice of antipsychotics depends upon availability, route of administration, and side effect profile

Antipsychotics can treat hyperactive delirium

Antipsychotic choice should be made based on routes of administration and sedation effects

- Oral only: quetiapine
- Oral, SC, and IM: haloperidol, loxapine, methotrimeprazine

Try to avoid antipsychotics if at all possible in Parkinson's disease and Lewy Body Dementia

- Can use trazodone (oral only) or benzodiazepines instead (if SC needed)
- Loxapine has less EPS and can also be used

Ideally, we want our patients awake during the day but not combative

- Quetiapine is most sedating and has least risk of EPS, but is only oral (use in evening)
- Haloperidol and loxapine tend to be less sedating and have PO and SC options (use in daytime)

My typical approach to antipsychotics is to start with PRNs and increase to scheduled

1) Start with oral PRN options if possible:
   - Quetiapine 6.25-12.5 mg PO q4h PRN for severe agitation and restlessness
   - Haloperidol 0.25-0.5 mg SC q4h PRN for severe agitation and restlessness (if not taking PO) OR loxapine 2.5-5mg SC q4h PRN or for severe agitation and restlessness (if not taking PO)
2) If consistently needing PRNs: look at the timing and schedule based on behaviour timings

	AM (08:00)	*Afternoon (1600-1700)*	*HS (2000-2100)*
Nocturnal agitation	PRN only	PRN only	quetiapine 12.5-25 mg PO *or* loxapine 5 mg SC
Sundowning	PRN only	quetiapine 6.25-12.5 mg PO *or* loxapine 2.5 mg SC	quetiapine 12.5-25 mg PO *or* loxapine 5 mg SC
Throughout the day	quetiapine 6.25-12.5 mg PO *or* loxapine 2.5 mg SC	quetiapine 6.25-12.5 mg PO *or* loxapine 2.5 mg SC	quetiapine 12.5-25 mg PO *or* loxapine 5 mg SC

If you have significant concerns about Parkinsonism, alternatives include

- Oral: Trazodone 12.5-25 mg PO q4h PRN or Quetiapine 6.25-12.5 mg PO q4h PRN
- SC: Loxapine 2.5-5 mg SC q4h PRN
- SEVERE neuroleptic sensitivity (e.g. Lewy Body Dementia with neuroleptic sensitivity) can consider lorazepam 0.5-1 mg SC/SL q4h PRN (but can have paradoxic agitation)

	AM (08:00)	*Afternoon (1600-1700)*	*HS (2000-2100)*
Nocturnal agitation	PRN only	PRN only	trazodone 25-50 mg PO *or* loxapine 5 mg SC
Sundowning	PRN only	trazodone 12.5-25 mg PO *or* loxapine 2.5 mg SC	trazodone 25-50 mg PO *or* loxapine 5 mg SC
Throughout the day	quetiapine 6.25-12.5 mg PO *or* loxapine 2.5 mg SC	trazodone 12.5-25 mg PO *or* loxapine 2.5 mg SC	trazodone 25-50 mg PO *or* loxapine 5 mg SC

Side effects based on antipsychotic

	EPS (D2 receptor)	Sedation (H1 receptor)	Anticholinergic / deliriogenic (M1 receptor)	Orthostatic hypotension (α1 and α2 receptor)
Quetiapine **- least EPS, fairly sedating**	++	++++	+	+++
Haloperidol **- most EPS**	+++++	+	+	+
Loxapine **- middle ground**	++++	+++	++	+
Methotrimeprazine **- very sedating**	+++	+++++	?	?
Olanzapine	+++	++++	++++	++
Risperidone	+++++	+++	+/-	++++

Other considerations with longer-term use of antipsychotics

- QTc interval prolongation (in descending order):
  - Quetiapine, risperidone, olanzapine, haloperidol
- MI risk higher in first 30 days and decreases over time
  - HR 2.19; higher in typicals RR 1.2 compared to atypicals
  - At 3 months, back to baseline risk
- CHF reported in olanzapine and quetiapine
- Ventricular arrhythmias
  - Higher in typicals than atypicals RR 1.1

Vieweg, Prim Care Companion J Clin Psychiatry 2003.

Case presentation: the finale

Ended up admitted to hospital with UTI +/- aspiration pneumonia and placed on ceftriaxone

Seen by SLP → NPO

Developed mixed delirium, treated with quetiapine 6.25 mg PO q4h PRN haldol 0.5 mg SC q4h PRN

Required quetiapine 6.25 mg at 0800, 1400, and 12.5 mg at 2000

Developed a small pressure sore after ~3 weeks in hospital, fluctuating delirium and poor PO intake

Gradually improving - SLP changed to dysphagia thickened liquids but still poor oral intake

Geriatrics consulted: family meeting held → opted to feed at risk and slowly started eating better

Revisited goals of care in end-stage dementia: DNR M2 and discharged home at wheelchair level

What could have been done differently in her case?

- Was this even a “UTI” as initially thought? Hydration is key!
- Discussed signs of end-stage dementia after her hospitalization a few months prior to admission and readdressed goals of care
- Reassessed thickened liquid diets
- Discussion about feeding at risk prior to initiation of thickened liquid diet (family didn’t recall being told of this option at first admission)

Clinical pearls

1. Any route of administration of antibiotics in severe dementia seem to work, but subcutaneous hydration tends to help produce better outcomes
2. Antipsychotics can be given regularly based on their side effect profile - quetiapine has the least EPS and is the most sedating
3. Trazodone or lorazepam are alternate options in severe Parkinson's or Lewy Body Dementia with neuroleptic sensitivity



LEARNING OBJECTIVES (completed!)

1) Recognize various presentations of delirium in the context of dementia
2) Diagnosis and workup for delirium
3) Management and when to refer to hospital



Key points



1. Delirium prevention is key and the best approach is likely multifactorial, including medication review, hydration, and pain control
2. Ideally, treatment in LTC facility seems to be most beneficial (especially if subcutaneous hydration can be given)
3. Signs of end-stage dementia that may warrant a goals of care discussion include: pneumonia, swallowing problems, and febrile episodes
4. Quetiapine is a fairly safe PO option for delirium, with loxapine or haloperidol options for subcutaneous

Thank you!

Questions or comments?