Delirium

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What will be covered

- What is delirium and how best to detect it
- Delirium and poor outcomes
- Prevention and treatment of delirium
- Drugs to avoid in delirium and in those at risk

What is delirium ?

Based on DSM-V criteria (updated 2013)

- Sudden onset
- New or worsened cognitive impairment
- Fluctuates over hours or days
- Inattention is a key feature
- May be hallucinations, perceptual disturbances, misinterpreting environment
- Altered conscious level
  - Hypervigilant (wandersome, agitated = hyperactive)
  - Sleepy / withdrawn = hypoactive delirium (dangerous)
  - May be mixed picture

- Delirium and dementia are not the same thing (more later)
- They can (and frequently do) co-exist

- Asking a friend or relative the SQiD has high sensitivity for detecting delirium
  - "Do you think [*patient*] has been more confused lately"?
  - 80% sensitivity for delirium

Sans et al. Palliat Med 2010; 24: 561-565

Detecting inattention

- Months of the year backwards (MOTYB)
  - If able to reach July without error, attention likely intact
- Dementia reduces specificity of this test
- MOTYB in >69yo *without* dementia
  - 84% sensitivity
  - 90% specificity for delirium
- MOTYB in those *with* dementia
  - 88% sensitive (for delirium)
  - Low specificity

(O'Reaghan JNNP 2014;85:1122-1131)

Size of the problem – why is delirium important

- Estimates of delirium occurrence in hospitals vary according to specialty and patient age
- Rates of any delirium during admission (any age) are **consistently above 20%**
- In some specialties rates are **>50%**, and incidence increases with age
- **One third of patients over 80** will experience delirium during their hospital stay

Ryan et al BMJOpen 2014, Pendlebury BMJOpen 2015

- Rates also high in orthopaedic surgery and ICU
- 50% of delirious patients had a prior diagnosis of dementia (point prevalence survey)

Ryan et al BMJOpen 2014

Delirium is associated with poor outcomes

- The development of delirium is associated with:
  - mortality rates of 25 to 33%
  - increased morbidity
  - functional and cognitive decline
  - considerably extended lengths of hospital stay
  - increased requirement for institutional care at discharge

(Siddiqi et al Age Ageing 2006;35:350-364)

- **Delirium can be prevented in about one third of patients**

Delirium prevention strategies

- Multicomponent delirium prevention interventions can reduce incident delirium by about **a third**

  (Meta analyses: Hshieh 2015, Martinez 2015)

- NICE Clinical Guideline for Prevention and Treatment of Delirium (2010) recommends widespread adoption of multicomponent delirium prevention interventions

- High quality, individualised patient centred care

- Combining data from recent systematic reviews of delirium prevention (RCTs and observational studies)
  - No statistically significant reduction in
    - In hospital mortality (RR 0.98 [95%CI 0.62-1.55])
    - 6-month mortality (RR 1.10 [95%CI 0.8-1.46])
    - Admission to long term care (RR 0.84 [95%CI 0.67-1.04])

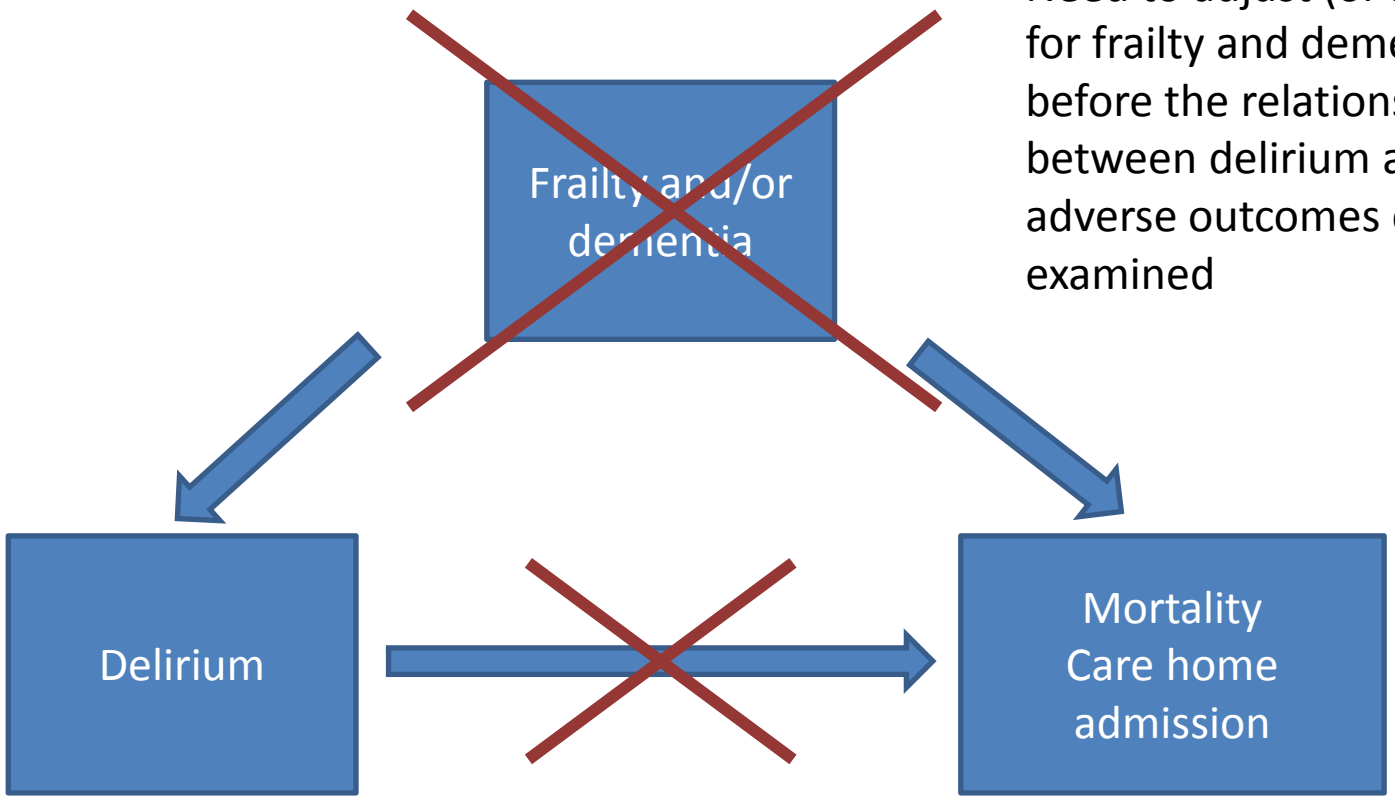
(Teale et al A&A 2015)

- *This is despite effective delirium prevention*

- Disconnect between prevention of delirium and longer term outcomes

Why might this be?

- Methodological
  - Rare (usually secondary) outcomes – underpowered studies
- Difficulty measuring / identifying delirium
  - Ascertainment bias
  - Often unblinded assessments in trials
  - Lack of objective measures (no biomarkers)
- Confounding factors of
  - Frailty
  - Dementia
  - Underlying pathological processes (as yet poorly understood)



Need to adjust (or stratify) for frailty and dementia before the relationship between delirium and adverse outcomes can be examined

This might explain the lack of improvement in medium and long term outcomes despite effective delirium prevention

Frailty and delirium

- Frailty cut-offs determined using the cumulative deficit model of frailty (the frailty index – FI)
- Frailty defined as FI>0.25

- 273 patients followed up after an acute medical admission
- Daily assessments for delirium
- 162 fit (29 had delirium), 111 frail (72 had delirium)
- Median survival significantly longer for patients who were fit compared with those who were frail
  - Fit: 1,368 days (95% CI: 1014-1722)
  - Frail: 207 days (95% CI: 88-326)

- Survival attenuated for those with delirium regardless of frailty status
  - Fit with delirium: 359 days (95% CI: 118-600)
  - Frail with delirium: 88 days (95% CI:5-171)

Eeles et al A&A 2012

Dementia and delirium

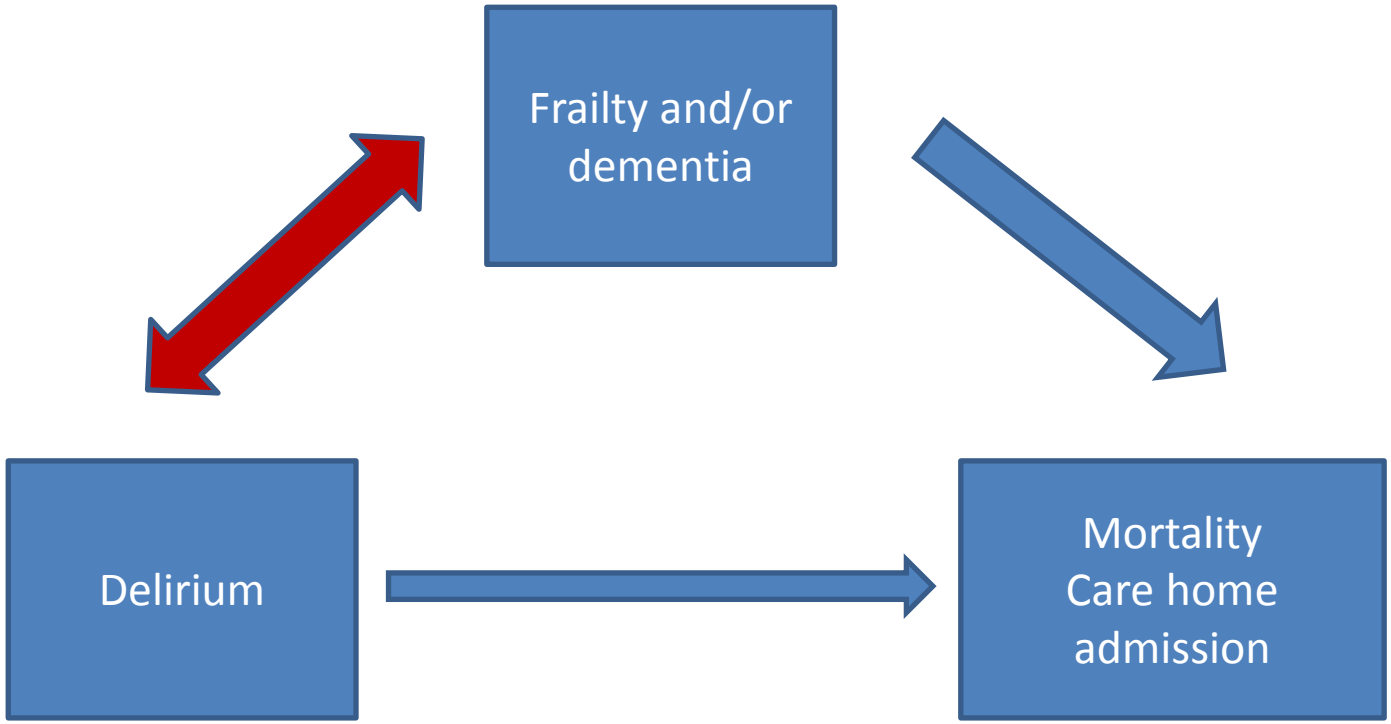
- Delirium may persist for months
  (associated with particularly poor outcomes)
- An episode of delirium carries increased risk of subsequent dementia
- May alter the trajectory of cognitive decline (rate of deterioration)
- Increased risk of incident dementia following delirium after controlling for confounders
  - Adj RR 5.7 (95% CI: 1.3-24.0) (241 patients)
  - Worse cognitive outcomes following delirium for patients on ICU / post surgery
- Increased risk of death or institutionalisation for patients with dementia and delirium over those with dementia alone (771 patients)
  - Mortality RR 5.4 (95% CI: 2.3-12.5)
  - Institutionalisation RR 9.3 (95% CI: 5.5-15.7)

Fong, Davis, Growdon, Albuquerque, Inouye Lancet 2015

Is delirium simply a symptom of dementia / frailty ?

Perhaps…

- Is transient delirium on admission to hospital for patients with dementia a consequence of a change in environment, with assciated disruption to routine?
- Are frailty and dementia acting as true confounders in the relationship between delirium and poor outcomes?
- Can delirium uncover ‘latent’ frailty / dementia and cause worsening of these conditions?
- Does delirium cause permanent neuronal damage and progression to dementia?



Relationship is complex:
Delirium may worsen existing cognitive impairment or result in lasting cognitive decline

Can we predict who is going to get delirium?

- Several risk stratification models
- Observational study to externally validate four delirium risk stratification models (308 patients)
- Acutely ill older medical inpatients
- Can predict who is most at risk from delirium
  - AUC between 0.69 and 0.76
  - No clearly superior model
  - Based on combinations / weighted scoring of accepted risk factors

Pendlebury et al A&A 2016

Delirium risk factors

- Risk factors are remarkably consistent across observational studies of delirium

- Some are modifiable:
  - Illness severity
  - Catheterisation
  - Polypharmacy
  - Electrolyte disturbance / abnormality of urea / creatinine ratio

- Some are partly modifiable
  - Visual impairment

Ahmed, Leurent, Sampson A&A 2014

- Some are likely related to co-morbidity
  - Low albumin
  - Length of hospital stay

- Some are not-modifiable and reflect the key associations with risk of onset of delirium
  - Older age
  - Co-morbidities
  - Cognitive impairment

Frailty

Person-centred care
Non-confrontational environment
Avoid noise overstimulation
Keep everything as calm as possible

i.e. good dementia friendly care!

- Multicomponent delirium prevention interventions should aim to improve modifiable risk factors for delirium and enhance the experience / quality of care for the person at risk or with delirium
- High quality basic care
- Don’t assume this just happens – make sure it does.
- Individuals with frailty and delirium are particularly at risk – target interventions

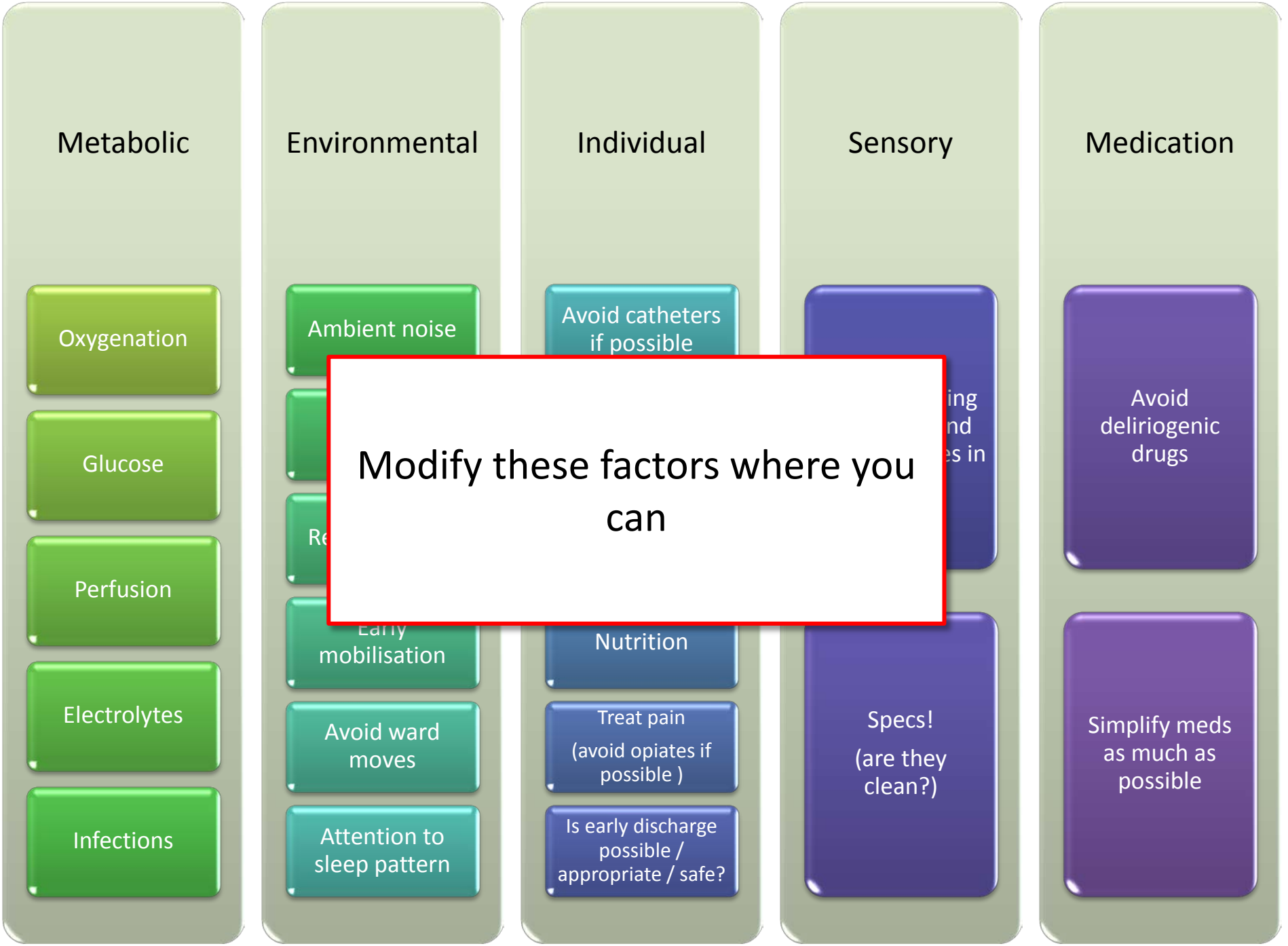
Drugs to avoid in delirium

Drug class (studies)	No risk			
Neuroleptics (4)	✓			
Opioids (7)				
Benzodiazepines (7)		✓		
Dihydropyridines (1)		✓		
Antihistamines (2)			✓	
Digoxin (1)	✓			
Steroids (1)				✓
NSAIDS (1)				✓
TCAs (1)				✓
Parkinsons meds				✓

A recent ICU (observational) study suggested an association between haloperidol and delirium – prone to bias – interpret with caution

Pisani *Crit Care Med* 2015; 43:996–1002

Try and avoid drugs with anticholinergic properties


Metabolic
Oxygenation
Glucose
Perfusion
Electrolytes
Infections
Environmental
Ambient noise
mobilisation
Avoid ward moves
Attention to sleep pattern
Individual
Avoid catheters if possible
Nutrition
Treat pain
(avoid opiates if possible)
Is early discharge possible / appropriate / safe?
Sensory
Specs!
(are they clean?)
Medication
Avoid deliriogenic drugs
Simplify meds as much as possible
Modify these factors where you can

Drugs and delirium prevention / treatment

- Evidence remains limited – no clear benefit from any pharmacological therapies for treatment or prevention of delirium in non-ICU settings

- There is a need for further trials to identify agents that are safe for older people, and that have efficacy in the treatment / prevention of delirium in non-ICU settings

- Meta-analysis of melatonin no overall benefit for delirium prevention (4 trials)
- Some benefit in medical patients (subgroup analysis)
  - Not conclusive, and not currently recommended

- **Antipsychotics**
  - Evidence is largely low quality and trials subject to bias
  - Routine use of antipsychotics not recommended for the treatment or prevention of delirium in the NICE delirium prevention and treatment guideline (2010)
  - No convincing new evidence generalisable to general medical patients to support routine use of haloperidol or other antipsychotics since NICE guidelines were published (2010)

- **Acetylcholinesterase Inhibitors (AChE-i)**
  - Trial of rivastigmine vs placebo (2010)
  - Usual care included treatment with haloperidol (not usual care in the UK)
  - Multicentre placebo controlled double blind trial
  - Critical care setting (Netherlands)
  - Halted early
    - After recruitment of 104 /target 440
    - Excess mortality in the intervention group (12 vs 4 p=0.07).
    - Median duration of delirium longer in intervention group than in the placebo group (5.0 days vs 3.0 days p=0.06)

Van Eijk et al The Lancet 2010

Conclusions

- Delirium is an unpleasant experience and is preventable
- Patients with frailty or dementia are particularly at risk and should be targeted for multicomponent delirium prevention strategies
- Still no robust evidence to support pharmacological options for treatment or prevention of delirium
- An episode of delirium may uncover and worsen underlying dementia or frailty
- Patients may not return to functional or cognitive baseline (delirium not as reversible as we initially thought?)
- The pathological processes involved in delirium are poorly understood
- There is a lot of work to be done