Management of delirium in older persons

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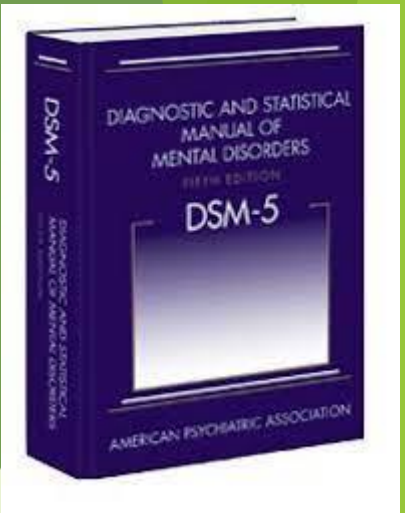
Delirium

- A 80-year-old women is admitted for a hip fracture surgery. She is functionally independent, and known with mild forgetfulness. There are no events during the first day of hospitalization, however, on the 2th postoperative day, she develops severe confusion and agitation.

Delirium: DSM V classification (1/2)



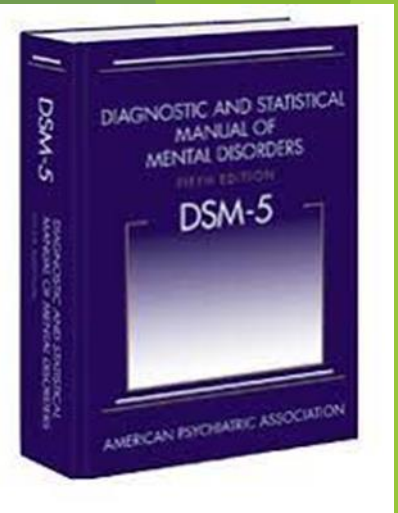
- Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).

- An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability or perception)

- The disturbance develops over a short period of time (usually hours to a few days), represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day

(American Psychiatric Association, 2013)

Delirium: DSM V classification (2/2)



- Disturbances are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.

- There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

(American Psychiatric Association, 2013)

Epidemiology (1/5)

In nursing homes:

- Prevalence rates: 1,4% to 70,3%
  - Depending on the used diagnostic criteria + the population being studied (ie. aged 65+ years vs. 85+ years, prevalence of dementia)

De Lange E et al. 2013, Boorsma et al. 2012, Siddiqi et al. 2009

In home setting:

- Prevalence rates: 1-2% (in population 65+ years old) to 10% (in population 85+ years old)

De Lange E et al. 2013

Epidemiology (2/5)

Hospital:

- Medical older inpatients
  - prevalence of delirium at admission
    - from 10 to 31%
  - incidence of new delirium per admission
    - from 3 to 29%

(Siddiqi et al. Age and Ageing 2006; 35: 350–364; Marcantonio 2011)

- Up to 70% occurrence of delirium in an older medical intensive care unit (ICU) patients (inclusive post-ICU period)

Epidemiology (3/5)

- Surgical older inpatients
  - Occurrence postoperative delirium from 5% to 52%
  - cardiothoracic surgery and repair of hip fracture consistently associated with high rates

(Lindesay et al. Delirium in Old Age. Oxford, UK: Oxford University Press; 2002:27-50; Marcantonio 2012)

Epidemiology (4/5)

- In patients with advanced cancer (e.g. acute palliative care unit)
  - Prevalence
    - on admission to hospital = 28% to 48%
    - In the hours to days before death = approximately 90%
  - 49% of delirium episodes is reversible
    - 56% in a first episode
    - 26% in a repeated episode

(Lawlor et al., 2000; Lawlor & Bruera, 2002)

Epidemiology (5/5)

- Incidence/prevalence increases with
  - High age
  - Pre-existing cognitive decline
    - e.g. dementia, depression, parkinson, …
  - Severity of co-morbidity

Outcomes – patients (1/4)

- Incontinence; Pressure ulcers, …
- Falls
- Decline in ADL performance
- Nursing home admissions
- Increased mortality
  - hospital mortality ranging from 10% to 65%
  - twice as likely to be dead 6 months post-discharge

(Brannstrom et al., 1988; Breitbart et al., 2002; Bush et al., 2018; Cole et al., 2009; Eeles et al., 2010; Inouye et al., 1998; Levkoff et al., 1992; O'Keefe & Levan, 1997; Pompei et al., 1994; Rockwood et al., 1999; Sullivan-Marx, 1994, Witlox et al., 2010)

Outcomes – patients (2/4)

- Highly distressing experience
  - 53,5% recall delirium with 80% reporting severe distress
- Hinders
  - Assessment & control of symptoms
    - Pain
    - Psychologic symptoms
  - Participation in therapeutic decision making process
  - Meaningfull communication among patient and family

(Breitbart et al., 2002; Bush et al., 2018; Lawlor & Bruera, 2002)

Outcomes – family (3/4)

- Highly distressing experience
  - 76% report severe distress
  - Often required to assume additional responsibility
    - e.g.: Participation in decisions with regard to intensity & nature of therapeutic intervention

Outcomes – other impact (4/4)

- High intensity of nursing care
  - increases nurses' workload and frustration
  - more use of physical restraints
- Increased health care expenditure
  - increased length of hospital stay
  - 30% increase in hospital cost
  - higher rates of new nursing home placement

Delirium management
= multicomponent approach

Delirium management

- Determine the risk of each patient
- Implement preventive measures
- Identify prodromal signs of delirium
  - Systematic screening
- Treat etiological factors
- Symptom management

Prevention

Treatment

(Bush et al, 2018; Hshieh et al. 2015; Marcantonio 2017; Martinez et al. 2015; Milisen et al., 2005; Young et al., NICE guidelines, 2010)

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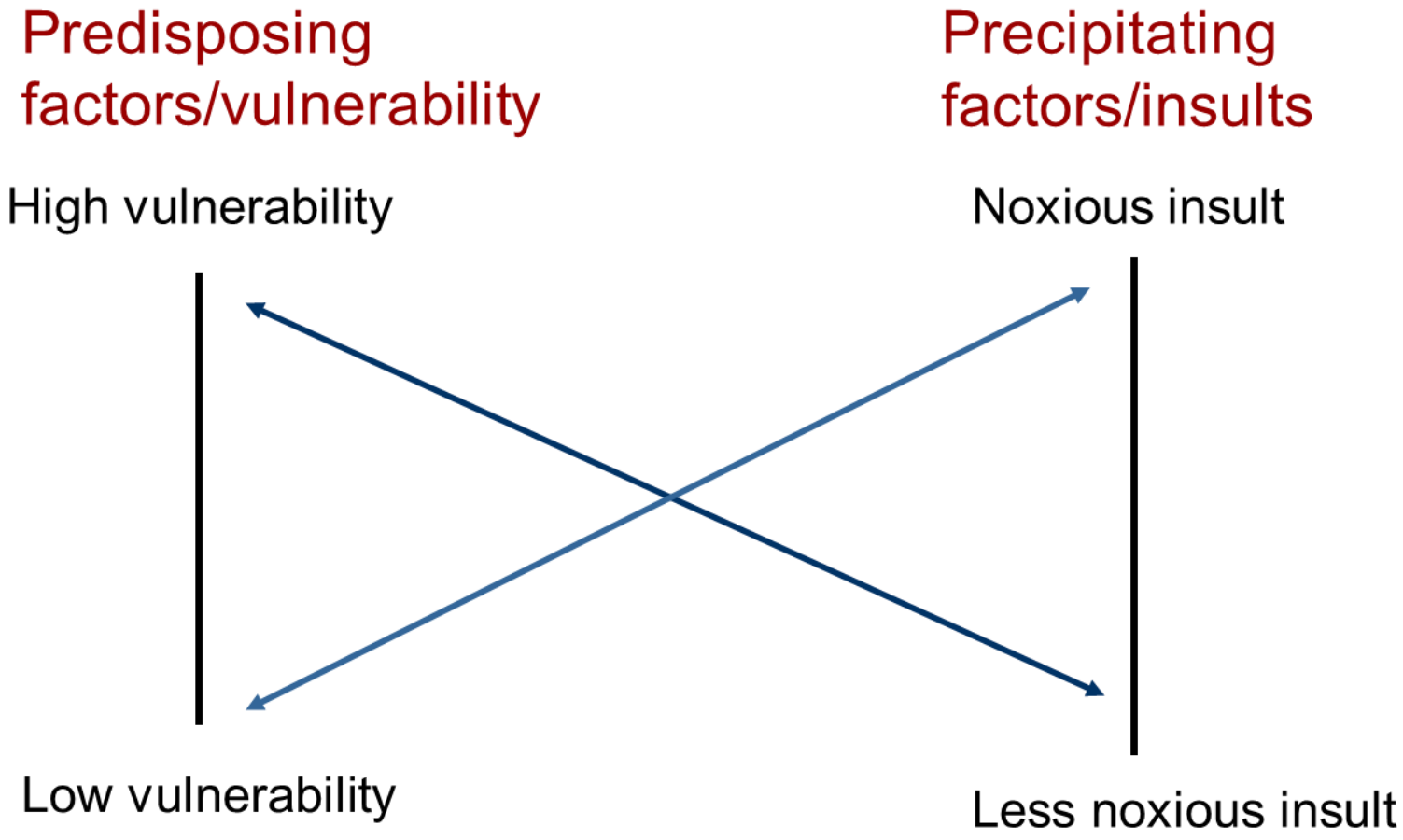
Multifactorial etiology



(Inouye et al., 1996)

Patients at risk – predisposing factors

- pre-existing cognitive impairment
  - e.g. dementia, stroke, depression, …
- 2 or more of the following risk factors
  - advanced age (+ 80 years)
  - severe illness
  - high comorbidity
  - dehydration / malnutrition
  - sensory impairments
  - decline in ADL functioning
  - previous delirium episode

Box 5 | Common risk factors and precipitants for delirium

Risk factors

Old age (over 65 years), physical frailty, severe illness, multiple diseases, dementia, admission to hospital with infection or dehydration, visual impairment, deafness, polypharmacy, alcohol excess, renal impairment, malnutrition

Precipitants (more than one may be present)

Lower respiratory tract infection, urinary infection/ catheters, constipation, electrolyte disturbance (dehydration, renal failure, hyponatraemia or hypernatraemia), drugs (especially those with anticholinergic activity or psychoactive drugs), alcohol withdrawal, pain, neurological disorder (stroke, epilepsy, subdural haematoma), hypoxia, sleep deprivation, surgery (such as fractured neck of femur), environmental (see text)

John Young and Sharon K Inouye

BMJ 2007;334;842-846
doi:10.1136/bmj.39169.706574.AD

Specific risk populations in the hospital

- Intensive care unit patients
- Oncology patients in terminal stage
- Older hip fracture patients
- Cardiac surgery in older patients

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Non- pharmacological interventions (1/2)

- **Minimize risk factors for delirium**
  - Optimize pain management
    - Systematic monitoring of pain
    - Use preferably nonopioid medications
  - Treat urinary retention (i.e. globus vesicalus) and fecal impaction / constipation
  - Adequate fluid and nutrition intake
    - Supplement as necessary, cave aspiration
  - Eliminate / avoid precipitating medication such as
    - anti-cholinergic & psycho-active drugs, benzodiazepines, high-dose opioids, anti-histamines

Non- pharmacological interventions (2/2)

- Stimulate early mobilization
- Create a therapeutic environment
  - Continuity of care
  - Cues for orientation, familiarity, and meaning
    - Provide newspaper, clock, calendar, pictures of relatives
  - Balancing environmental stimulation
    - Cave sensory overload
    - Promote sleep hygiene

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(Bush et al, 2018; Hshieh et al. 2015; Marcantonio 2017; Martinez et al. 2015; Milisen et al., 2005; Young et al., NICE guidelines, 2010)

Under detection of delirium

- In 33% to 72% cases
  - Transient changes in cognition often misattributed to:
    - Dementia
    - Depression
  - No systematic and standardized evaluation of a patient's cognitive function

(Fick & Foreman, 2001; Inouye et al., 2014; Milisen et al., 2002)

Systematic screening – early recognition

- Delirium Observation Screening Scale (DOS)
  - 13 items based on DSM-IV criteria
  - Evaluation of patient's behavior during regular care
  - Completion requires on avarage 2 minutes
  - No specific knowledge/training required

(Schuurmans et al., 2001 & 2003)

DELIRIUM OBSERVATION SCREENING (DOS) SCALE
(version 0 - 1)

Date:
Patient Name:

	OBSERVATION The patient	Day shift			Evening shift			Night shift			TOTAL SCORE TODAY (0 - 39)
		never	sometimes - always	unable	never	sometimes - always	unable	never	sometimes - always	unable	
1	Dozes off during conversation or activities	0	1	-	0	1	-	0	1	-	
2	Is easily distracted by stimuli from the environment	0	1	-	0	1	-	0	1	-	
3	Maintains attention to conversation or action	1	0	-	1	0	-	1	0	-	
4	Does not finish question or answer	0	1	-	0	1	-	0	1	-	
5	Gives answers that do not fit the question	0	1	-	0	1	-	0	1	-	
6	Reacts slowly to instructions	0	1	-	0	1	-	0	1	-	
7	Thinks they are somewhere else	0	1	-	0	1	-	0	1	-	
8	Knows which part of the day it is	1	0	-	1	0	-	1	0	-	
9	Remembers recent events	1	0	-	1	0	-	1	0	-	
10	Is picking, disorderly, restless	0	1	-	0	1	-	0	1	-	
11	Pulls IV tubing, feeding tubes, catheters etc.	0	1	-	0	1	-	0	1	-	
12	Is easily or suddenly emotional	0	1	-	0	1	-	0	1	-	
13	Sees/hears things which are not there	0	1	-	0	1	-	0	1	-	
	TOTAL SCORE PER SHIFT (0 - 13)										
	DOS SCALE FINAL SCORE = TOTAL SCORE TODAY / 3										

⇓

DOS SCALE Final Score	< 3	Not delirious
	≥ 3	Probably delirious

https://www.health.belgium.be/nl/delirium-observation-screening-scale

Diagnosis

- 3D-Confusion Assessment Method (3D **CAM *or CAM -ICU***)
  - 3 minute diagnostic assessement developed for detection by non-psychiatric clinicians
  - 4 core diagnostic criteria for delirium
    1. Acute onset and fluctuation
    2. Inattention
    3. Disorganised thinking
    4. Altered level of consciousness
  - Diagnostic criteria by CAM require presence of features (1), (2), and either (3 or 4)

(Inouye et al., 1990; Marcantonio et al. 2014 https://www.hospitalelderlifeprogram.org/delirium-instruments)

New kid on the block; 4AT

4AT

Patient name:

Date of birth:

Patient number:

Assessment test for delirium & cognitive impairment

Date: Time:

Tester:

		CIRCLE
[1] ALERTNESS		
This includes patients who may be markedly drowsy (eg. difficult to rouse and/or obviously sleepy during assessment) or agitated/hyperactive. Observe the patient. If asleep, attempt to wake with speech or gentle touch on shoulder. Ask the patient to state their name and address to assist rating.		
	Normal (fully alert, but not agitated, throughout assessment)	**0**
	Mild sleepiness for <10 seconds after waking, then normal	**0**
	Clearly abnormal	**4**
[2] AMT4		
Age, date of birth, place (name of the hospital or building), current year.		
	No mistakes	**0**
	1 mistake	**1**
	2 or more mistakes/untestable	**2**
[3] ATTENTION		
Ask the patient: "Please tell me the months of the year in backwards order, starting at December." To assist initial understanding one prompt of "what is the month before December?" is permitted.		
Months of the year backwards	Achieves 7 months or more correctly	**0**
	Starts but scores <7 months / refuses to start	**1**
	Untestable (cannot start because unwell, drowsy, inattentive)	**2**
[4] ACUTE CHANGE OR FLUCTUATING COURSE		
Evidence of significant change or fluctuation in: alertness, cognition, other mental function (eg. paranoia, hallucinations) arising over the last 2 weeks and still evident in last 24hrs		
	No	**0**
	Yes	**4**

4 or above: possible delirium +/- cognitive impairment
1-3: possible cognitive impairment
0: delirium or severe cognitive impairment unlikely (but delirium still possible if [4] information incomplete)

4AT SCORE ☐

Bellelli et al. 2014
https://www.the4at.com/4at-download

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Precipitants (more than one may be present)

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PINCHME mnemonic
to help identify potential causes of delirium


Pain


Infection


Nutrition


Constipation


Hydration


Medication


Environment

Delirium management

- Determine the risk of each patient
- Implement preventive measures
- Identify prodromal signs of delirium
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Prevention

Treatment

(Bush et al, 2018; Hshieh et al. 2015; Marcantonio 2017; Martinez et al. 2015; Milisen et al., 2005; Young et al., NICE guidelines, 2010)

Non-pharmacological interventions (1/2)

- Be calm and reassuring to patient
- Same interventions as in the prevention:
  - Stimulate early mobilization
  - Create a therapeutic environment
    - Continuity of care
    - Cues for orientation, familiarity, and meaning
      - Provide newspaper, clock, calendar, pictures of relatives
    - Balancing environmental stimulation
      - Cave sensory overload
      - Promote sleep hygiene

Non-pharmacological interventions (2/2)

- Avoid physical restraints

  = independent risk factor for delirium persistence at discharge (Inouye et al 2007)

- Educate patient and family about delirium
  - Description and explanation of delirium and its experience

Pharmacological interventions (1/7)

Antipsychotic Medication for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis

Karin J. Neufeld, MD, MPH,[*a] *Jirong Yue, MD,*[§a] *Thomas N. Robinson, MD, MPH,*[‖] *Sharon K. Inouye, MD, MPH,*[**††b] *and Dale M. Needham, MD, PhD*[†‡b]

RESULTS: Screening of 10,877 eligible records identified 19 studies. In seven studies comparing antipsychotics with placebo or no treatment for delirium prevention after surgery, there was no significant effect on delirium incidence (OR = 0.56, 95% confidence interval (CI) = 0.23–1.34, I^2 = 93%). Using data reported from all 19 studies, antipsychotic use was not associated with change in delirium duration, severity, or hospital or ICU LOS, with high heterogeneity among studies. No association with mortality was detected (OR = 0.90, 95% CI = 0.62–1.29, I^2 = 0%).

Pharmacological interventions (2/7)

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CONCLUSION: Current evidence does not support the use of antipsychotics for prevention or treatment of delirium. Additional methodologically rigorous studies using standardized outcome measures are needed. J Am Geriatr Soc 2016.

ratios (ORs) were calculated for dichotomous outcomes (delirium incidence and mortality), and mean or standardized mean difference for continuous outcomes (delirium duration, severity, hospital and intensive care unit (ICU) length of stay (LOS)). Sensitivity analyses included postoperative prevention studies only, exclusion of studies

standardized outcome measures are needed. J Am Geriatr Soc 2016.

Key words: delirium; pharmacological prevention; pharmacological treatment; adult

Pharmacological interventions (3/7)

The decision whether to use such agents must consider the trade-off between an immediate reduction of agitation, hallucinations, and delusions versus the risks of sedation and antipsychotic-induced complications

(Marcantonio, N Engl J Med 2017;377:1456-66)

Pharmacological interventions (4/7)

Table 5. Pharmacologic Therapy of Agitated Delirium.*

Agent	Drug Class	Dosing†	Routes	Degree of Sedation	Risk of EPS	Adverse Effects	Comments
Haloperidol	Typical antipsychotic	Initial: 0.25–0.5 mg Maximum: 3 mg	Oral, IM, or IV	Low	High	Risk of EPS increases if daily dose exceeds 3 mg	Longest track record in delirium; several large trials are ongoing
Risperidone	Atypical antipsychotic	Initial: 0.25–0.5 mg Maximum: 3 mg	Oral or IM	Low	High	Slightly less risk of EPS than with haloperidol at low doses	Small trials; considered to be very similar to haloperidol
Olanzapine	Atypical antipsychotic	Initial: 2.5–5 mg Maximum: 20 mg	Oral, sublingual, or IM	Moderate	Moderate	More sedating than haloperidol	Small trials; oral route is less effective than other routes for management of acute symptoms
Quetiapine	Atypical antipsychotic	Initial: 12.5–25 mg Maximum: 50 mg	Oral	High	Low	Much more sedating than haloperidol; risk of hypotension	Small trials; can be used, with caution, in patients who have parkinsonism
Ziprasidone	Atypical antipsychotic	Initial: 5–10 mg Maximum: 40 mg	Oral or IM	Moderate	Moderate	More sedating than haloperidol; risk of cardiac arrhythmia, heart failure, and agranulocytosis	Owing to risks, used primarily in ICU; large trial is ongoing
Lorazepam	Benzodiazepine	Initial: 0.25–0.5 mg Maximum: 2 mg	Oral, IM, or IV	Very high	None	More paradoxical excitation and respiratory depression than with haloperidol	Second-line agent; use in sedative and alcohol withdrawal or if patient has a history of the neuroleptic malignant syndrome

* Use of all these drugs for delirium is off-label in the United States. Atypical antipsychotic agents have been tested primarily in small noninferiority trials with haloperidol and recently in small placebo-controlled trials in the intensive care unit (ICU). The Food and Drug Administration (FDA) requires a "black box" warning for all atypical antipsychotics because of increased risks of cerebrovascular events (e.g., stroke) and death among patients with dementia. Typical antipsychotic agents have an FDA "black box" warning because of an increased risk of death among patients with dementia. EPS denotes extrapyramidal symptoms, IM intramuscular, and IV intravenous.

† The doses recommended in this table are for older adults. "Initial" represents the initial dose for an acutely agitated older patient; the dose may need to be repeated. "Maximum" represents the maximum recommended cumulative daily dose — that is, the sum of all as-needed and scheduled doses over a period of 24 hours. Somewhat higher doses may be used in younger patients if the side-effect profile is acceptable.

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Marcantonio, N Engl J Med 2017;377:1456-66

Pharmacological interventions (7/7)

- Regardless of drug selected, initial dose should be LOW!
  - wide variability in response
- Additional doses administered every 30 to 60 minutes
  - until desired behavioral end point is achieved (e.g. patient no longer hallucinating)
  - thereafter, doses can be administered on an as-needed basis
- Drugs should be stopped as soon as possible

Marcantonio, N Engl J Med 2017;377:1456-66

What about the evidence for a multicomponent approach? (1/3)

Effectiveness of Multicomponent Nonpharmacological Delirium Interventions

A Meta-analysis

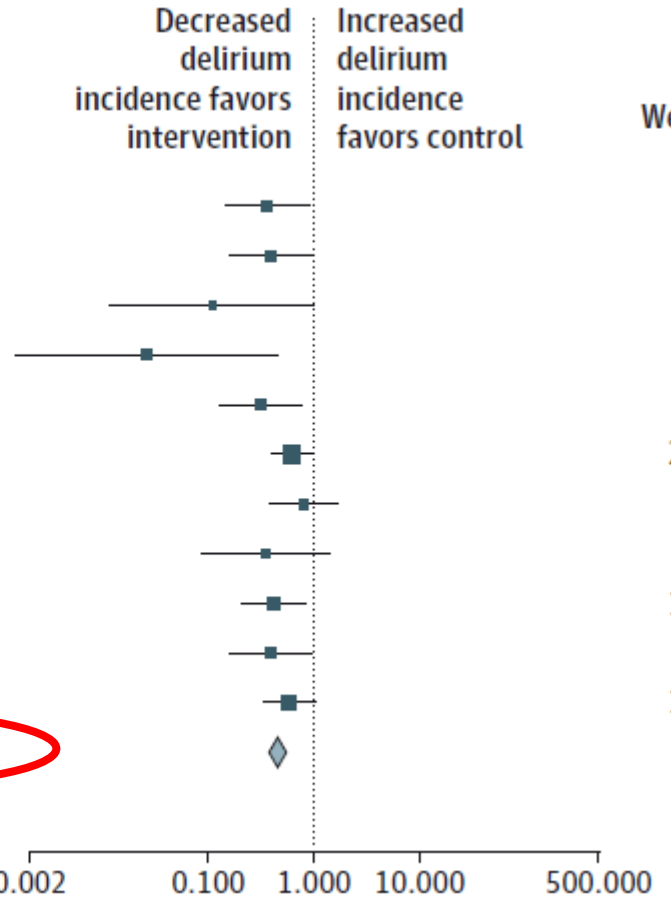
Tammy T. Hshieh, MD; Jirong Yue, MD; Esther Oh, MD; Margaret Puelle; Sarah Dowal, MSW, MPH; Thomas Travison, PhD; Sharon K. Inouye, MD, MPH

JAMA Intern Med. doi:10.1001/jamainternmed.2014.7779
Published online February 2, 2015.

What about the evidence for a multicomponent approach? (2/3)

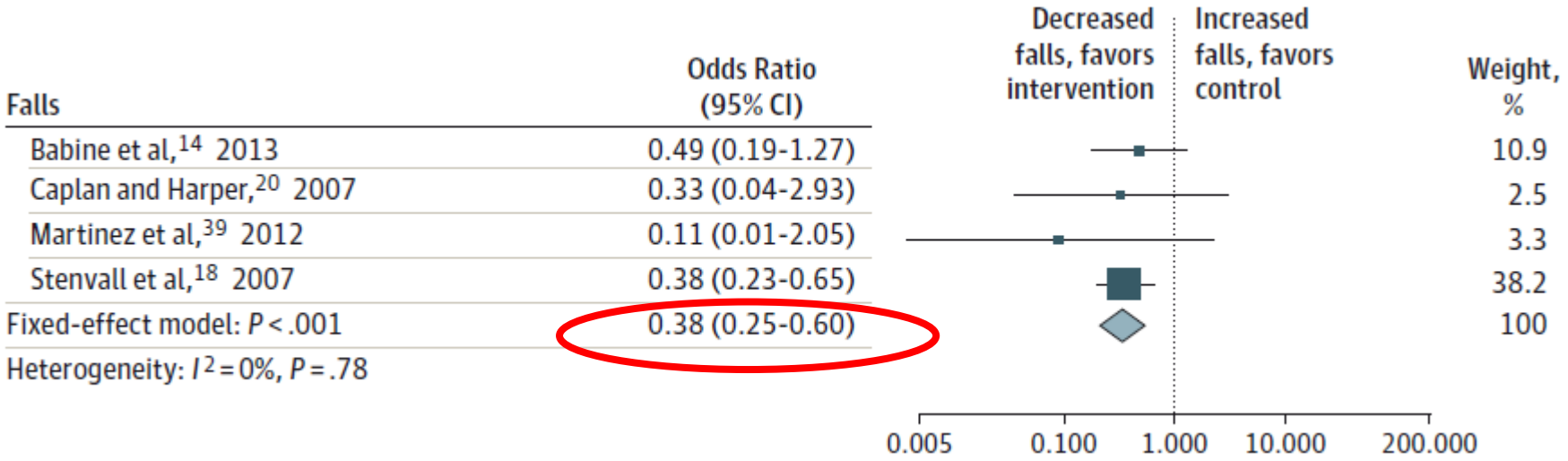
- Delirium incidence - about 50% odds reduction !

Delirium Incidence	Odds Ratio (95% CI)	Weight, %
Andro et al,[34] 2011	0.36 (0.15-0.89)	7.0
Bo et al,[35] 2009	0.39 (0.17-0.93)	7.3
Caplan and Harper,[20] 2007	0.11 (0.01-0.99)	2.6
Chen et al,[16] 2011	0.03 (0.00-0.44)	5.7
Holt et al,[36] 2013	0.31 (0.13-0.74)	9.1
Inouye et al,[5] 1999	0.62 (0.41-0.94)	23.4
Jeffs et al,[37] 2013	0.79 (0.40-1.57)	7.6
Kratz,[38] 2008	0.35 (0.09-1.39)	3.1
Lundström et al,[17] 2007	0.42 (0.21-0.80)	11.3
Martinez et al,[39] 2012	0.38 (0.16-0.91)	7.3
Vidán et al,[26] 2009	0.59 (0.34-1.00)	15.5
Fixed-effect model: $P < .001$	0.47 (0.38-0.58)	100
Heterogeneity: $I^2 = 18\%$, $P = .27$	NNT = 14.3 (95% CI, 11.1-20.0)	



What about the evidence for a multicomponent approach? (3/3)

- Falls - greater than 60% odds reduction !



Falls	Odds Ratio (95% CI)	Weight, %
Babine et al,[14] 2013	0.49 (0.19-1.27)	10.9
Caplan and Harper,[20] 2007	0.33 (0.04-2.93)	2.5
Martinez et al,[39] 2012	0.11 (0.01-2.05)	3.3
Stenvall et al,[18] 2007	0.38 (0.23-0.65)	38.2
Fixed-effect model: $P < .001$	0.38 (0.25-0.60)	100
Heterogeneity: $I^2 = 0\%$, $P = .78$		

Additional information

- British Geriatrics Society: https://www.bgs.org.uk/topics/delirium
- Nice guidelines: https://www.rcplondon.ac.uk/guidelines-policy/delirium-prevention-diagnosis-and-management-nice-guideline
- Belgische Vereniging voor Gerontologie en Geriatrie – richtlijn delier: https://geriatrie.be/nl/de-bvgg/activiteiten/werken-en-bijdragen/publicaties/delier-richtlijn/

Thanks for your attention!

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