Come sedare un paziente agitato e disorientato in reparto e in terapia intensiva.

DELIRIUM

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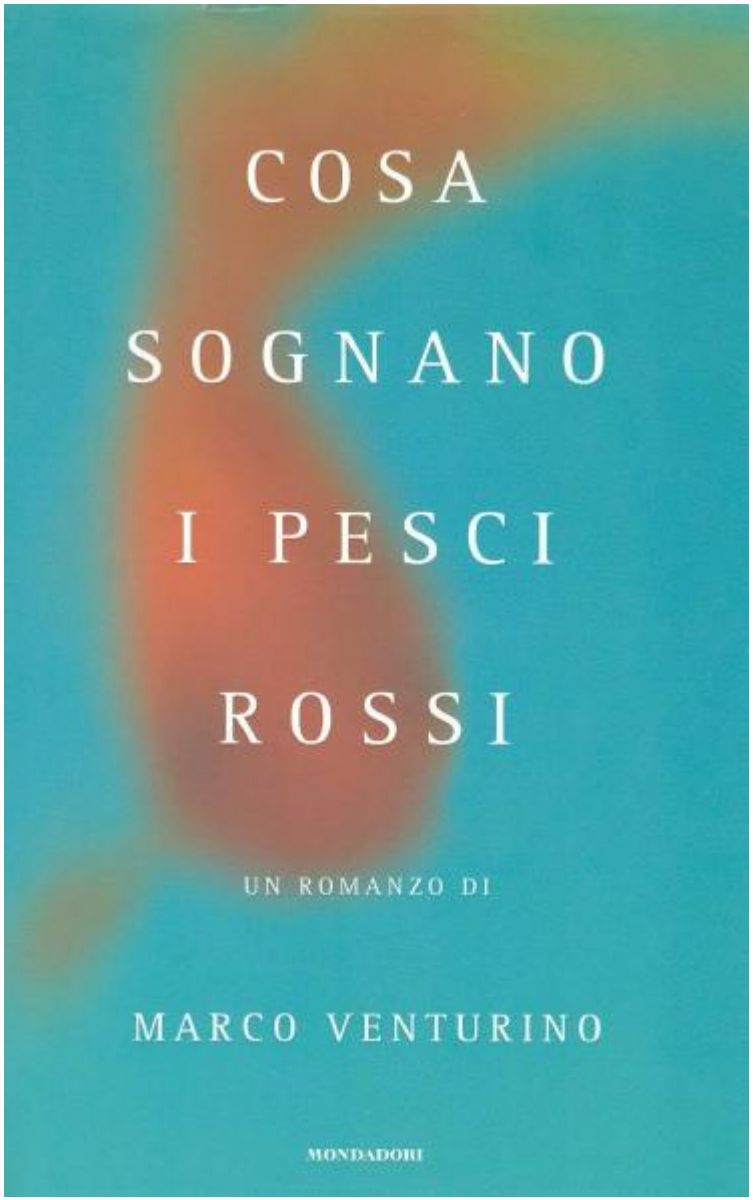
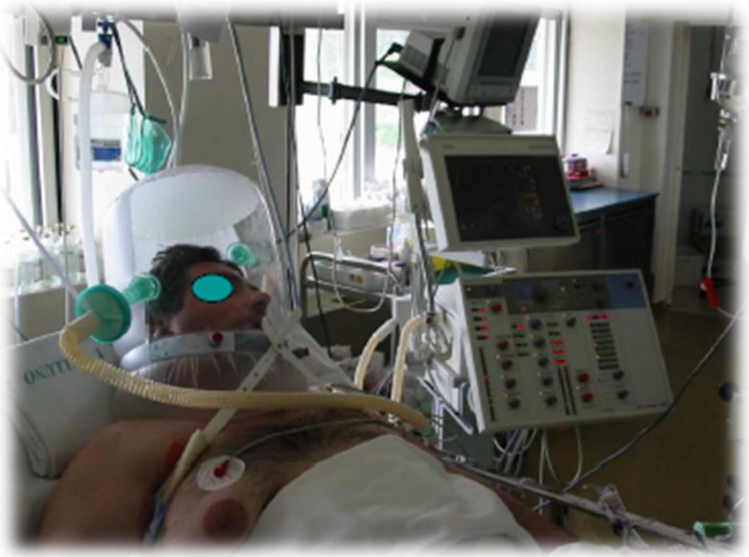
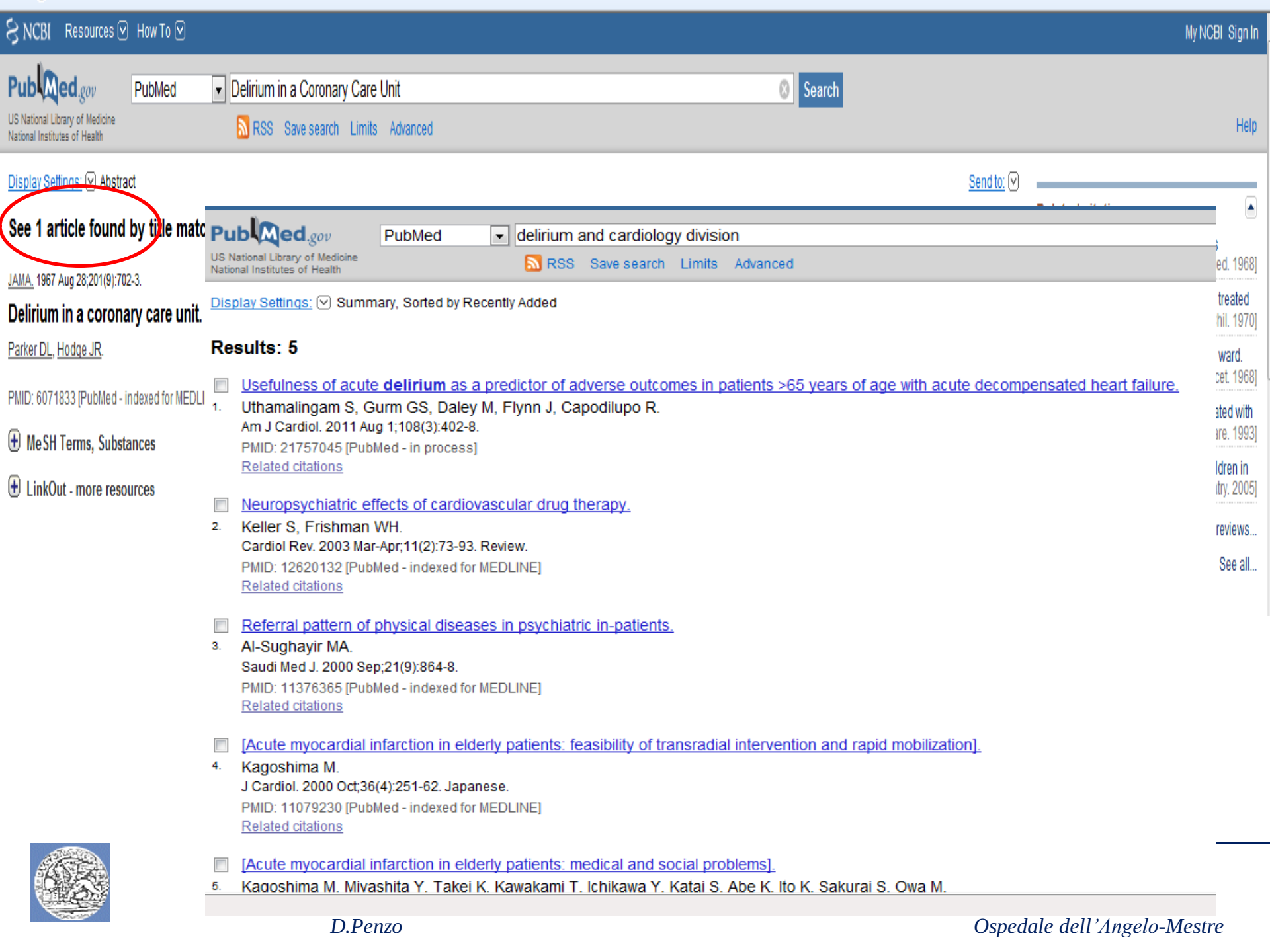
“if you don’t look, you won’t find”



"Adesso ne ho la certezza: sono proprio nei guai. E' un complotto! Mi tengono prigioniero…
….mi hanno fatto qualcosa qui al collo, per impedirmi di parlare. Ma non riescono ad impedirmi di pensare."

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Usefulness of acute delirium as a predictor of adverse outcomes in patients >65 years of age with acute decompensated heart failure.
1. Uthamalingam S, Gurm GS, Daley M, Flynn J, Capodilupo R.
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Risk factors associated with early reintubation in trauma patients: a prospective observational study.

1. Brown CV, Daigle JB, Foulkrod KH, Brouillette B, Clark A, Czysz C, Martinez M, Cooper H.
J Trauma. 2011 Jul;71(1):37-42.
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2. Pol RA, van Leeuwen BL, Visser L, Izaks GJ, van den Dungen JJ, Tielliu IF, Zeebregts CJ.
Eur J Vasc Endovasc Surg. 2011 Jul 31. [Epub ahead of print]
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3. Pun BT, Boehm L.
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Diagnostic Accuracy of HMGB-1, sTREM-1, and CD64 as Markers of Sepsis in Patients Recently Admitted to the Emergency Department.

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Acad Emerg Med. 2011 Aug;18(8):807-815. doi: 10.1111/j.1553-2712.2011.01113.x. Epub 2011 Jul 18.
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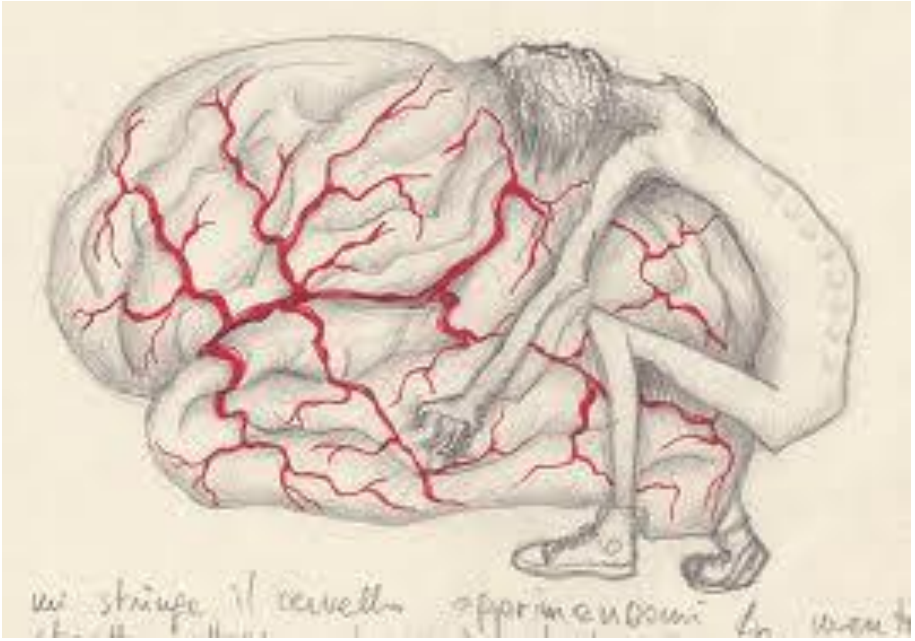
Perché dobbiamo preoccuparci del Delirium ?



- **20 -50%** dei pz. non ventilati (lower severity ICU pz)
- **60 -80%** dei pz. ventilati

Sequelae of Delirium

During the ICU/Hospital Stay

- Increased mortality
- Longer intubation time
- Average 10 additional days in hospital
- Higher costs of care

After Hospital Discharge

- Increased mortality
- Development of dementia
- Long-term cognitive impairment
- Requirement for care in chronic care facility
- Decreased functional status at 6 months

Delirium and Outcomes

- Increased ICU Length of Stay (8 vs 5 days)
- Increased Hosp Length of Stay (21 vs. 11days)
- Increased time on the Ventilator (9 vs 4 days)
- Higher costs ($22,000 vs $13, 000 in ICU costs)
- Estimated $4 to $16 **billion** associated U.S. costs
- 3-fold increased risk of death
- Possibly increased Long-Term Cognitive Impairment (aka, ICU accelerated dementia)

What Is Delirium?

DSM-IV°

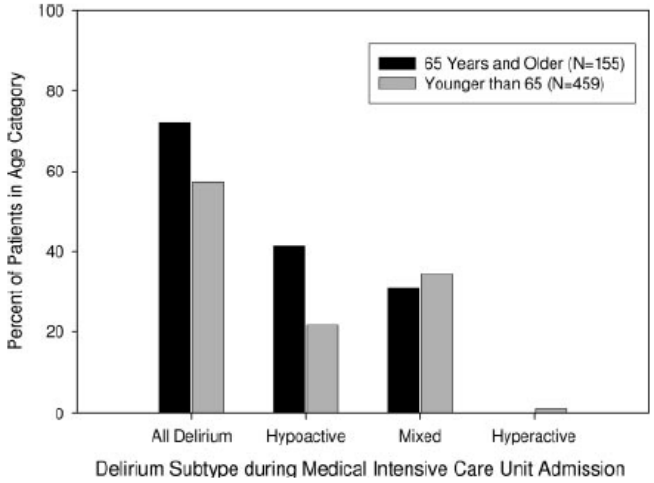
… as an acute brain dysfunction with a fluctuating change in consciousness, attention, perception, and cognition ..

Delirium is often "invisible"

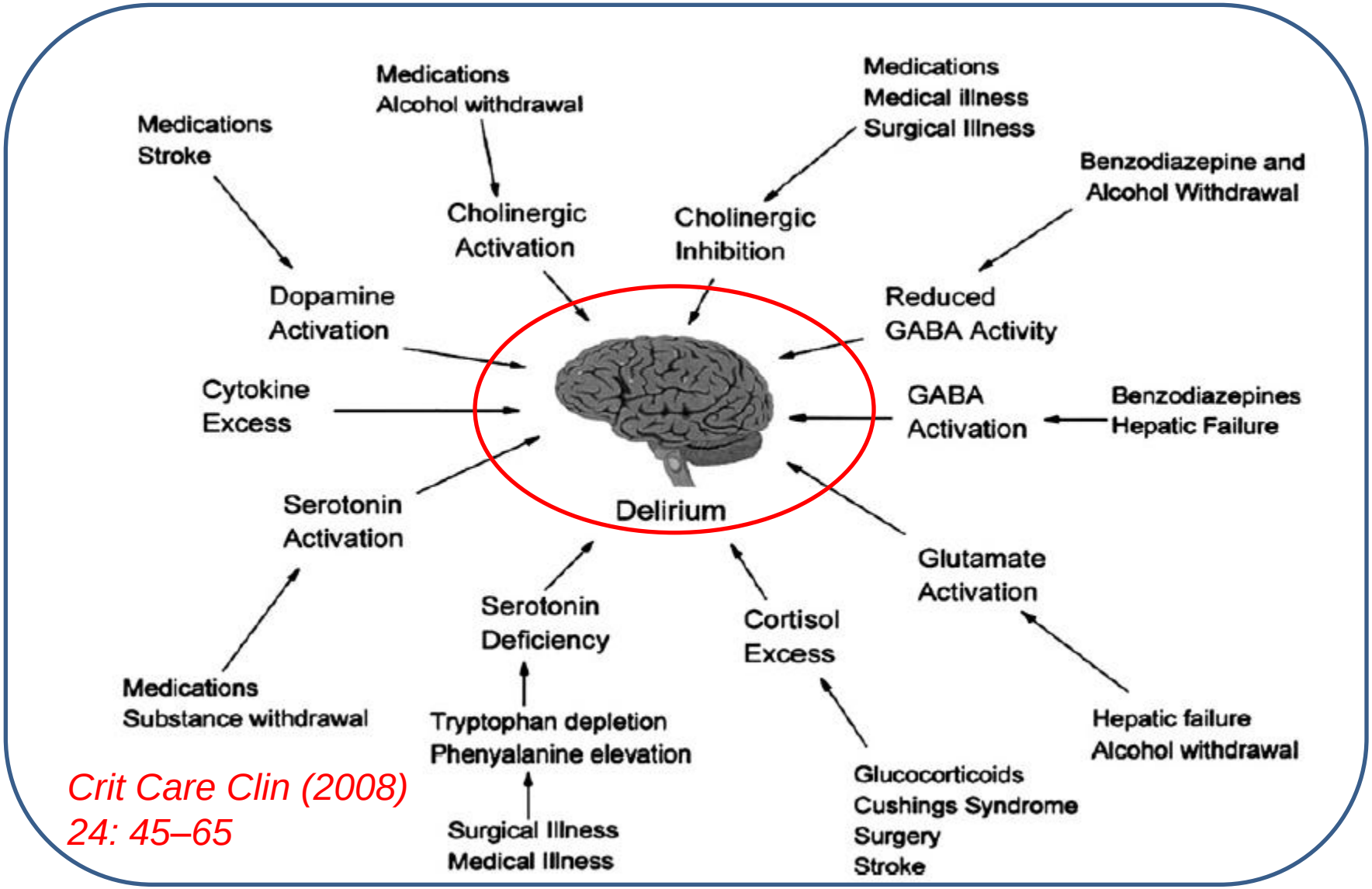
(unless you look for it)

- "quiet" ***hypoactive*** subtype (35%)
- ***Hyperactive*** subtype (1%)
- ***Mixed*** (64%)

Older age is the strong predictor



PATHOPHYSIOLOGY

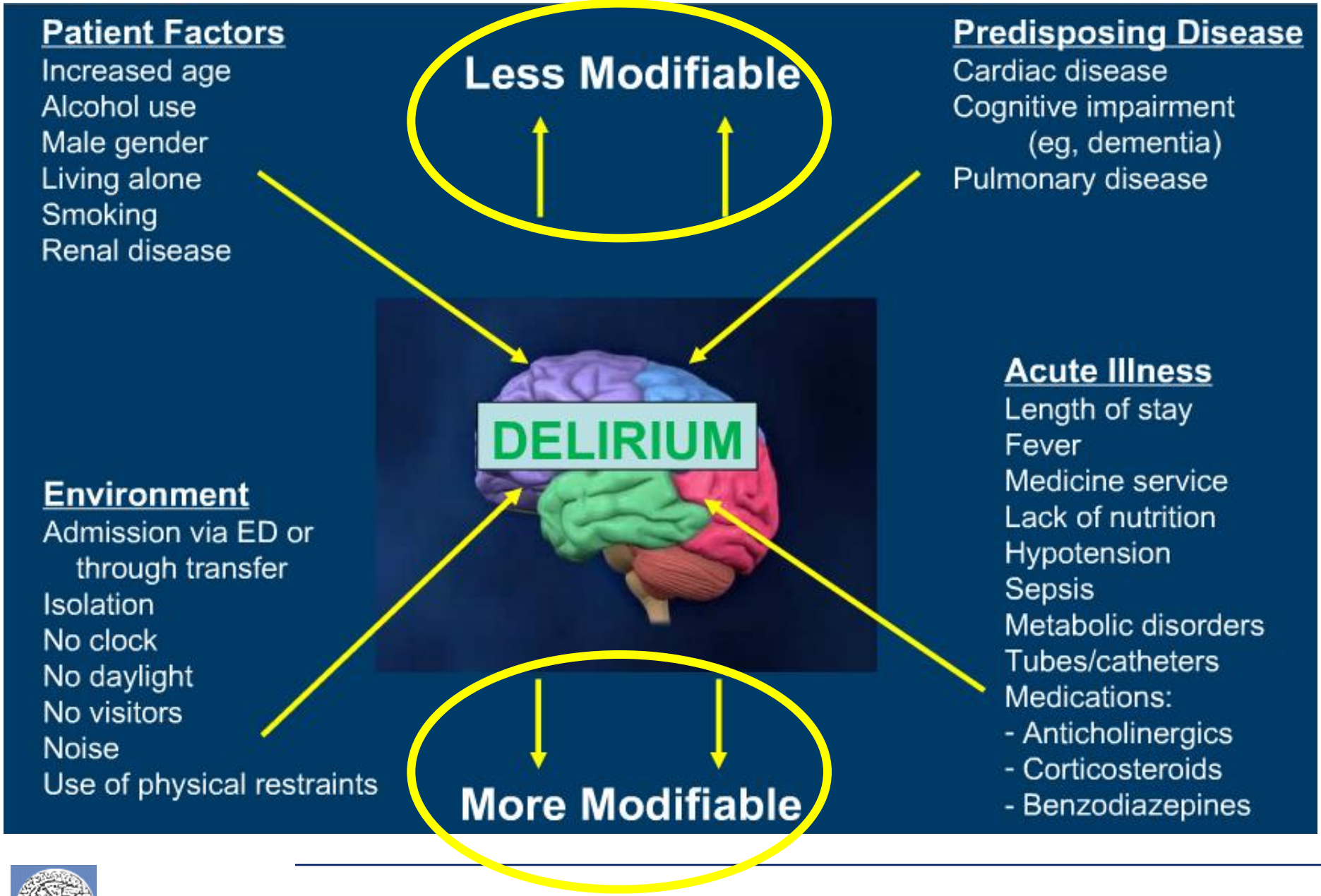


Crit Care Clin (2008)
24: 45–65

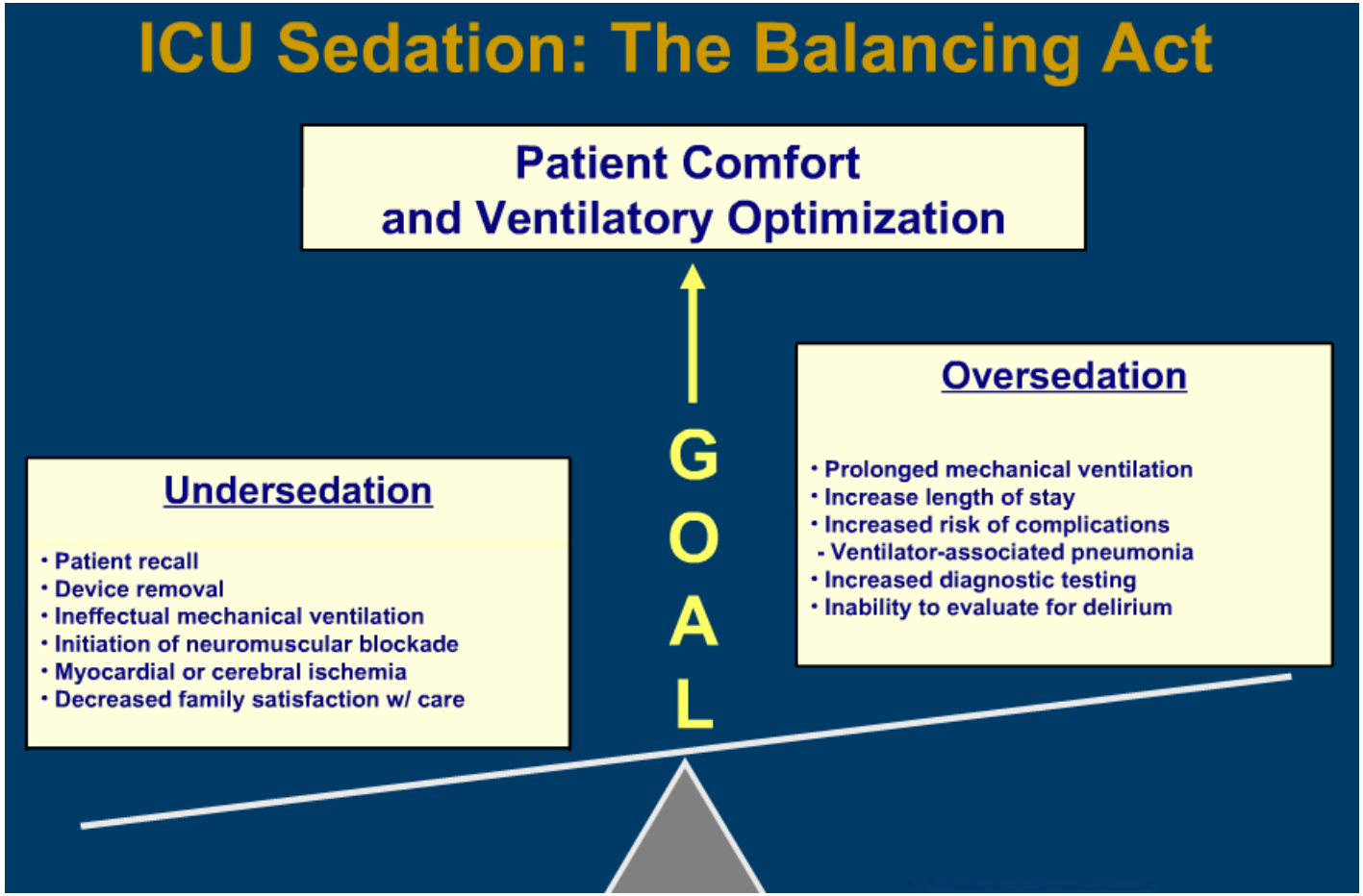
Table 4—*Risk Factors Associated With ICU Delirium*

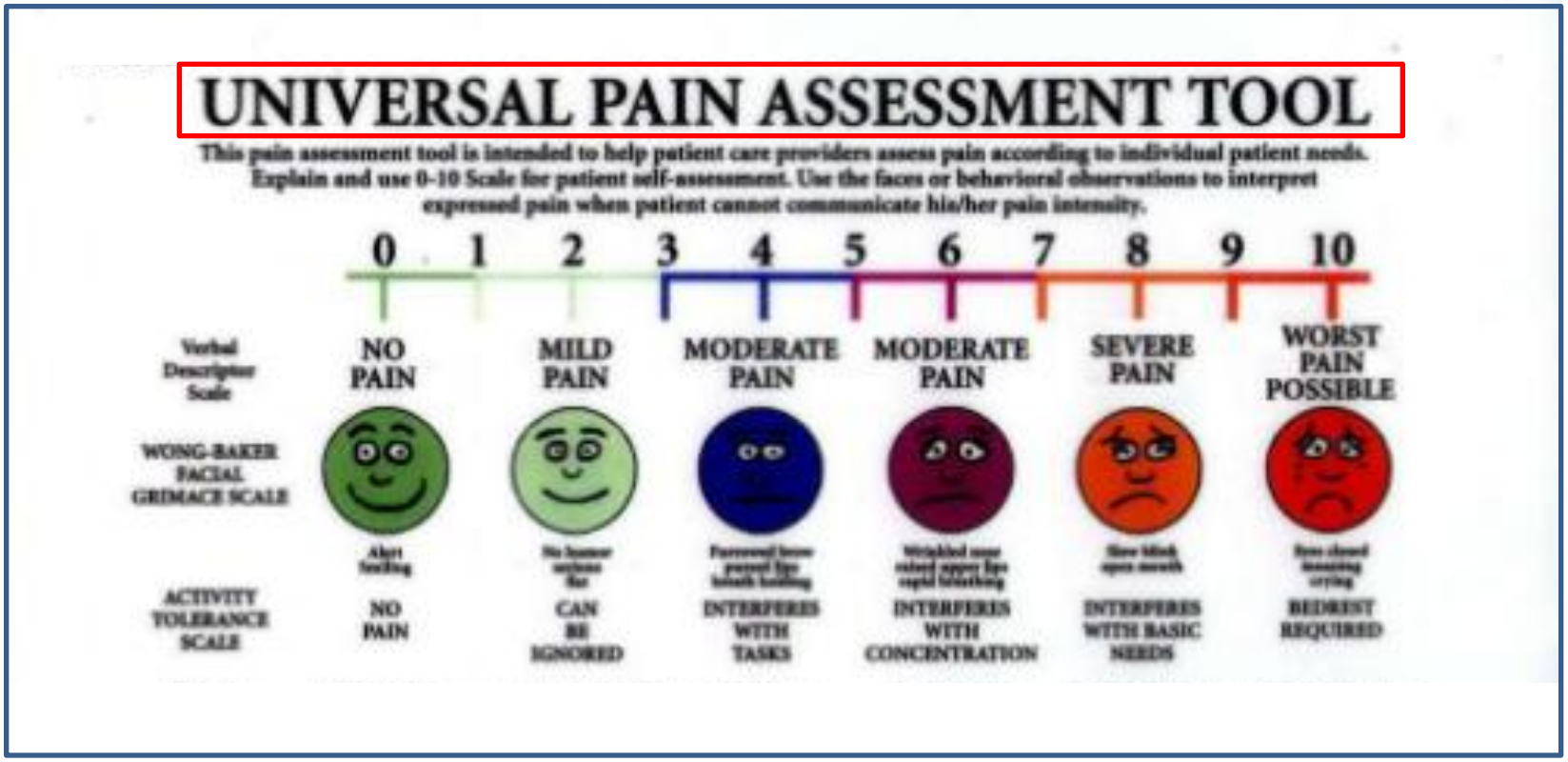
Preexisting risk factors (baseline vulnerability)
- Dementia
- Apolipoprotein E4 phenotype
- Chronic illness (including hypertension)
- Advanced age
- Depression
- Smoking
- Alcoholism
- Severity of illness on hospital admission

Precipitating risk factors (hospital related or iatrogenic)
- Hypoxia
- Metabolic disturbances
- Electrolyte imbalances
- Sleep deficits*
- Congestive heart failure
- Sepsis
- Prolonged restraint use and immobility
- Withdrawal syndromes
- Acute infections (systemic and intracranial)
- Seizures
- Dehydration
- Hyperthermia
- Head trauma
- Vascular disorders
- Intracranial space-occupying lesions
- Medications
  - Benzodiazepines
  - Morphine/fentanyl
  - Meperdine†
  - Propofol


Patient Factors
Increased age
Alcohol use
Male gender
Living alone
Smoking
Renal disease
Less Modifiable
Predisposing Disease
Cardiac disease
Cognitive impairment
(eg, dementia)
Pulmonary disease
DELIRIUM
Environment
Admission via ED or
through transfer
Isolation
No clock
No daylight
No visitors
Noise
Use of physical restraints
Acute Illness
Length of stay
Fever
Medicine service
Lack of nutrition
Hypotension
Sepsis
Metabolic disorders
Tubes/catheters
Medications:
- Anticholinergics
- Corticosteroids
- Benzodiazepines
More Modifiable

Monitoring Sedation, Pain and Diagnosing-monitoring the Delirium





- **Numeric Rating Scale (NRS)**
- **Visual Analogue Scale (VAS)**
- **Verbal Rating Scale (VRS)**
- **Behavioral Pain Scale(BPS)**

Strumenti per la Diagnosi del Delirium

- **CAM-ICU** (Confusion Assesment Method for Intensive Care Unit)
- **CTD** (Cognitive Test for Delirium)
- **ICDSC** (Intensive Care Delirium Screening Checklist)
- **DDS** (Delirium Detection Score)
- **NEECHAM** confusion scale in intensive care delirium assessment

Intensive Care Delirium Screening Checklist

1. Altered level of consciousness
2. Inattention
3. Disorientation
4. Hallucinations
5. Psychomotor agitation or retardation
6. Inappropriate speech
7. Sleep/wake cycle disturbances
8. Symptom fluctuation

Score 1 point for each component present during shift

- Score of 1-3 = Subsyndromal Delirium
- Score of ≥ 4 = Delirium

Metodologia di valutazione “delirium” con uso di CAM-ICU

- **1° Fase**

- *Valutazione della sedazione* (RASS)

- **2° Fase**

- *Valutazione del Delirium*

a. Modificazioni acute della coscienza/decorso fluttuante
b. Disattenzione
c. Pensiero disorganizzato
d. Alterato livello di coscienza

Riker Sedation-Agitation Scale (SAS)

Score	Term	Descriptor
7	Dangerous Agitation	Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side-to-side
6	Very Agitated	Requiring restraint and frequent verbal reminding of limits, biting ETT
5	Agitated	Anxious or physically agitated, calms to verbal instructions
4	Calm and Cooperative	Calm, easily arousable, follows commands
3	Sedated	Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
2	Very Sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

Guidelines for SAS Assessment

1. Agitated patients are scored by their most severe degree of agitation as described
2. If patient is awake or awakens easily to voice ("awaken" means responds with voice or head shaking to a question or follows commands), that's a SAS 4 (same as calm and appropriate – might even be napping).
3. If more stimuli such as shaking is required but patient eventually does awaken, that's SAS 3.
4. If patient arouses to stronger physical stimuli (may be noxious) but never awakens to the point of responding yes/no or following commands, that's a SAS 2.
5. Little or no response to noxious physical stimuli represents a SAS 1.

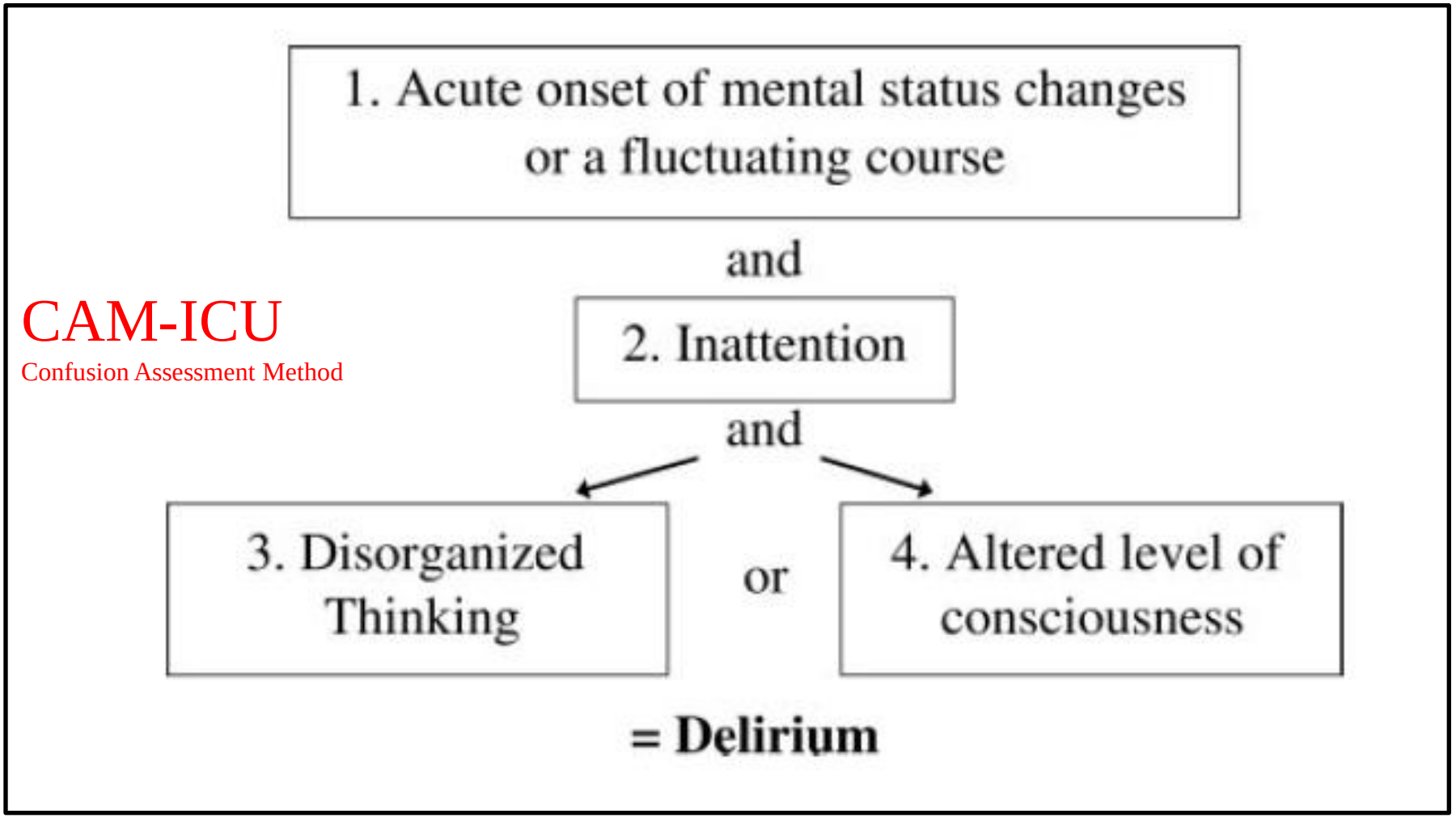
This helps separate sedated patients into those you can eventually wake up (SAS 3), those you can't awaken but can arouse (SAS 2), and those you can't arouse (SAS 1).

Richmond Agitation Sedation Scale (RASS)

Score	State	
+ 4	Combative	
+ 3	Very agitated	
+ 2	Agitated	
+ 1	Restless	
0	Alert and calm	
-1	Drowsy	eye contact > 10 sec
-2	Light sedation	eye contact < 10 sec
-3	Moderate sedation	no eye contact
-4	Deep sedation	physical stimulation
-5	Unarousable	no response even with physical

Verbal Stimulus

Physical Stimulus



CAM-ICU

Confusion Assessment Method

The Society of Critical Care Medicine (SCCM) Guidelines recommend monitoring delirium routinely in patients receiving mechanical ventilation

❖*Delirio **se il pz è positivo***
a entrambi i punti A e B, e
ad almeno uno dei punti C o D

Confusion Assessment Method (CAM)
Shortened version

The diagnosis of delirium by CAM requires the presence of **BOTH** features **A** and **B**		
CAM Confusion Assessment Method	**A.** **Acute onset** **and** **Fluctuating course**	Is there evidence of an acute change in mental status from patient baseline? Does the abnormal behavior: ➢ come and go? ➢ fluctuate during the day? ➢ increase/decrease in severity?
	B. **Inattention**	Does the patient: ➢ have difficulty focusing attention? ➢ become easily distracted? ➢ have difficulty keeping track of what is said?
	AND the presence of EITHER feature C or D	
	C. **Disorganized thinking**	Is the patient's thinking ➢ disorganized ➢ incoherent For example does the patient have ➢ rambling speech/irrelevant conversation? ➢ unpredictable switching of subjects? ➢ unclear or illogical flow of ideas?
	D. **Altered level of consciousness**	Overall, what is the patient's level of consciousness: ➢ alert (normal) ➢ vigilant (hyper-alert) ➢ lethargic (drowsy but easily roused) ➢ stuporous (difficult to rouse) ➢ comatose (unrousable)

(Adapted with permission: Inouye, SK, et.al. (1990). Clarifying Confusion: The Confusion Assessment Method. A new method for detection of delirium. Ann Intern Med, 113: 941-8.)

1) MODIFICAZIONI IMPROVVISE DELLO STATO MENTALE

C'è stato un cambiamento acuto nello stato mentale del paziente rispetto alla situazione di base?	Sì	No

2) RIDOTTA CAPACITÀ DI ATTENZIONE

a) Il paziente presenta difficoltà a concentrarsi (per esempio è facilmente distraibile), non riesce a mantenere il filo del discorso o ha difficoltà nel ricordare ciò che è stato detto:

- ❑ Mai durante l'intervista
- ❑ Presente a tratti durante l'intervista, ma in forma lieve
- ❑ Presente a tratti durante l'intervista, in forma marcata
- ❑ Non definibile

b) Se c'è ridotta capacità di attenzione durante l'intervista, il comportamento è oscillante o tendead aumentare o diminuire nella sua severità?

- ❑ Si
- ❑ No
- ❑ Incerto
- ❑ Non applicabile

c) Se c'è ridotta capacità di attenzione, descrivere il comportamento.

3) PENSIERO DISORGANIZZATO

Il pensiero del paziente è disorganizzato e incoerente, passa da un argomento all'altro senza filo logico e in modo imprevedibile ?	Sì	No

4) ALTERATO LIVELLO DI COSCIENZA

In generale come valuteresti il livello di coscienza del paziente?

- ❑ Attento (normale)
- ❑ Vigile (iperallerta, eccessivamente sensibile agli stimoli ambientali, si spaventa facilmente)
- ❑ Letargico (assopito, ma facilmente risvegliabile)
- ❑ Stato stuporoso (difficilemente risvegliabile)
- ❑ Coma (non risvegliabile)
- ❑ Non applicabile

5) DISORIENTAMENTO

Il paziente durante tutta la durata dell'intervista è disorientato nel tempo e nello spazio; pensa di essere in un altro luogo; in un letto non suo.	Sì	No

6) DIMINUZIONE DELLA MEMORIA

Il paziente durante l'intervista ha presentato disturbi della memoria, come difficoltà a ricordare gli eventi accaduti durante il ricovero, o difficoltà nel ricordare le istruzioni ricevute?	Sì	No

7) PERCEZIONE ALTERATA

Il paziente ha presentato un disturbo percettivo, come allucinazioni/illusioni, o interpretazioni errate tali da associare qualcosa di reale a qualcosa di irreale?	Sì	No

8) AGITAZIONE PSICOMOTORIA (PARTE 1)

Il paziente durante l'intervista presenta un'agitazione motoria crescente, quasi irrefrenabile, come il disfare il letto, tamburellare le dita o cambiare in modo frenetico posizione?	Sì	No

8) RALLENTAMENTO PSICOMOTORIO (PARTE 2)

Il paziente durante l'intervista presenta una riduzione dell'attività motoria con rallentamento e letargia, come il mantenere a lungo la stessa posizione o muoversi molto lentamente?	Sì	No

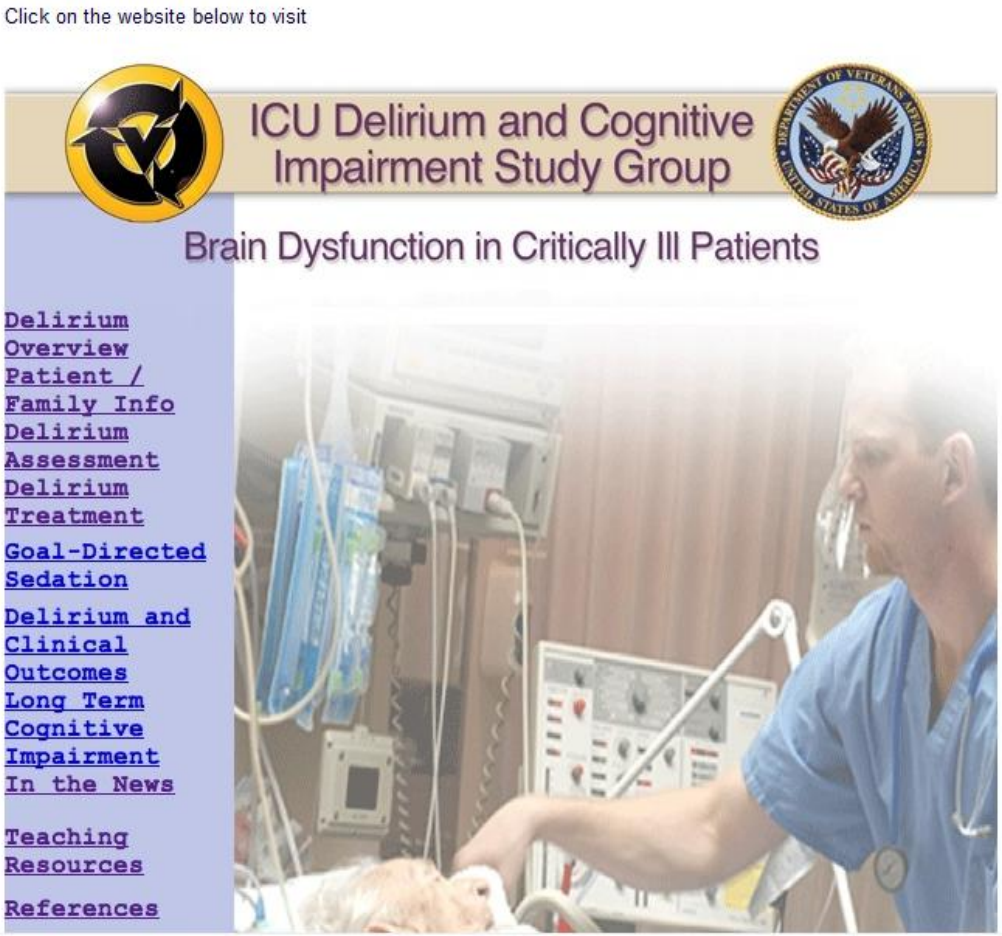
9) ALTERAZIONE DEL RITMO SONNO-VEGLIA

Il paziente presenta un evidente alterazione del ritmo sonno/veglia come un'eccessiva sonnolenza diurna o insonnia notturna?	Sì	No

CAM-ICU

- Validata per l'uso infermieristico in TI con eccellente compliance anche dopo breve training
- Sensibilità e specificità > 90%
- La valutazione richiede pochi minuti

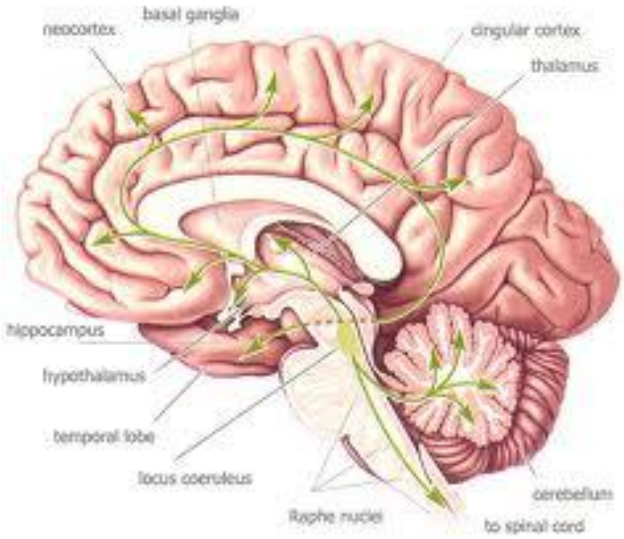
www.ICUdelirium.org



How Should We Approach This Multifaceted Problem?

- **<u>Non pharmacologic</u> Prevention and Treatment**

- **<u>Pharmacologic</u> Prevention and Treatment**



- Reorientamento con calendario e orologio
- Presenza dei famigliari
- Mantenimento ciclo sonno/veglia - notte/giorno
- Uso televisione/radio
- Controllare il rumore
- Mantenere giusto microclima
- Utilizzare precocemente occhiali, apparecchi acustici
- Eventuale interprete

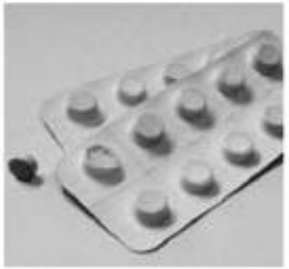
Prevention and intervention

Avoid dehydration

Avoid high levels of noise

Normal sleep-wake cycle

Facilitate orientation

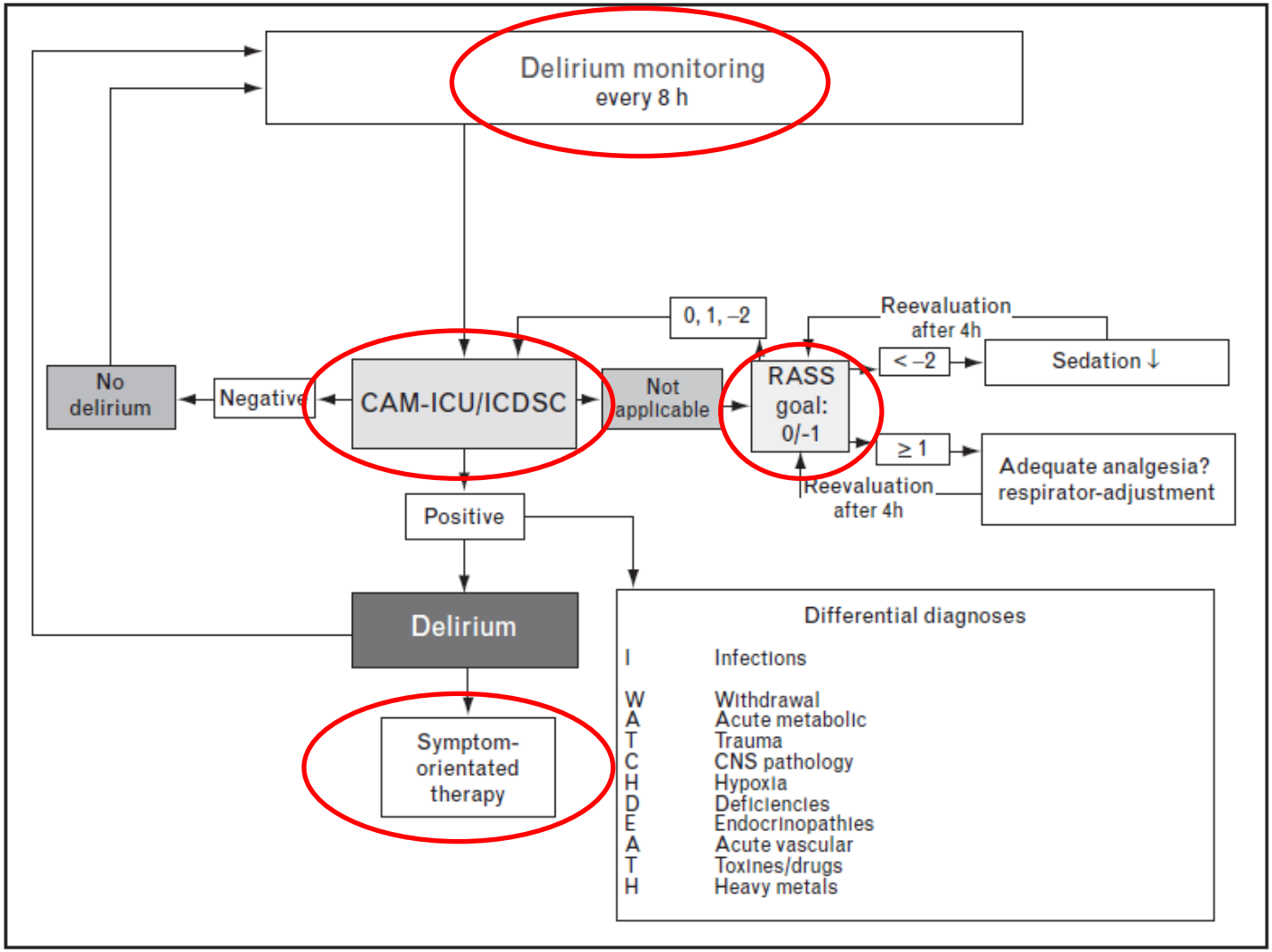


Conservative therapy vs. pharmacological therapy

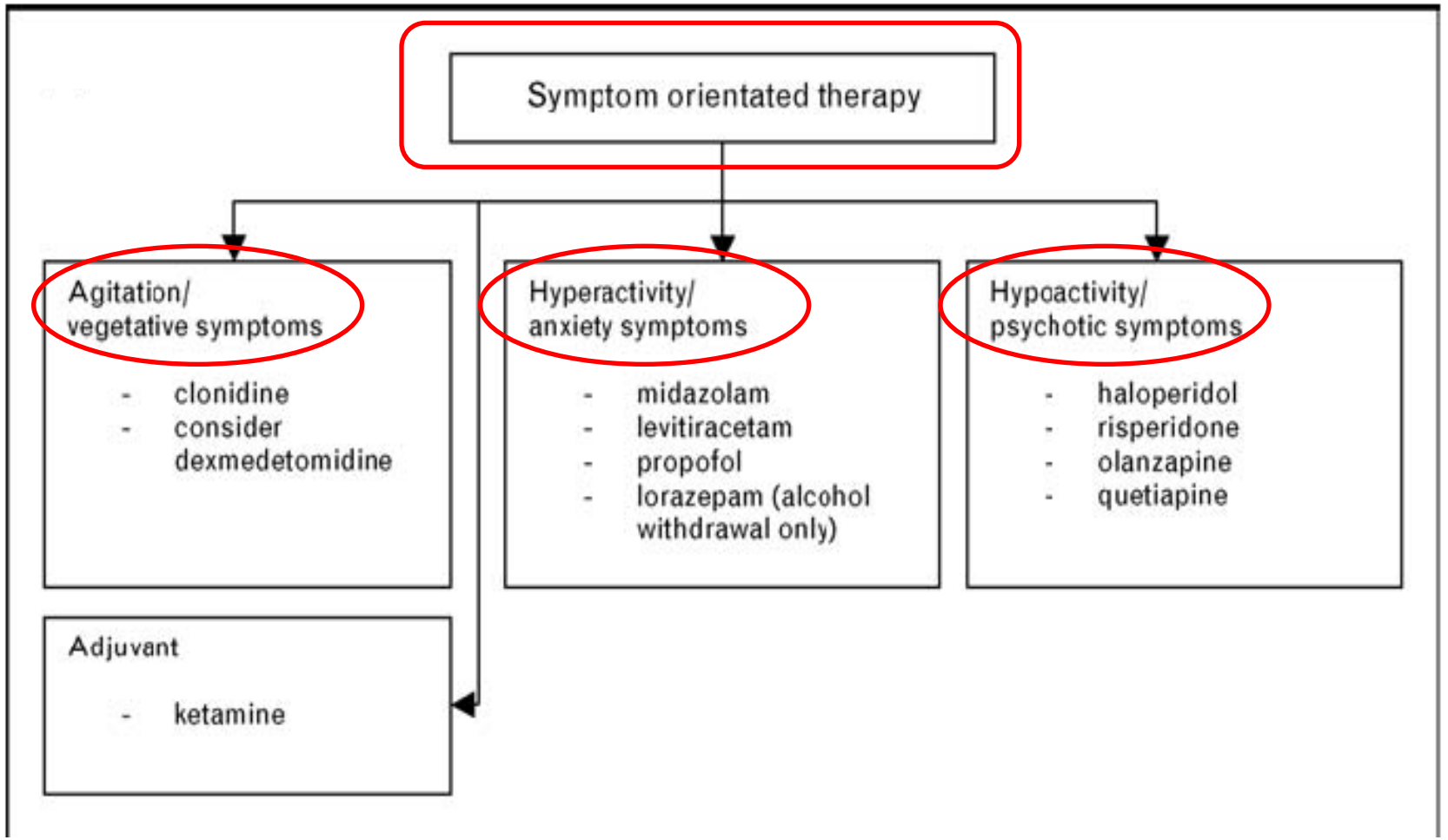
Define targets for sedation and analgesia

Figure 1 Algorithm to manage ICU delirium

Current Opinion in Critical Care 2011,17:131–140



Treatment of delirium



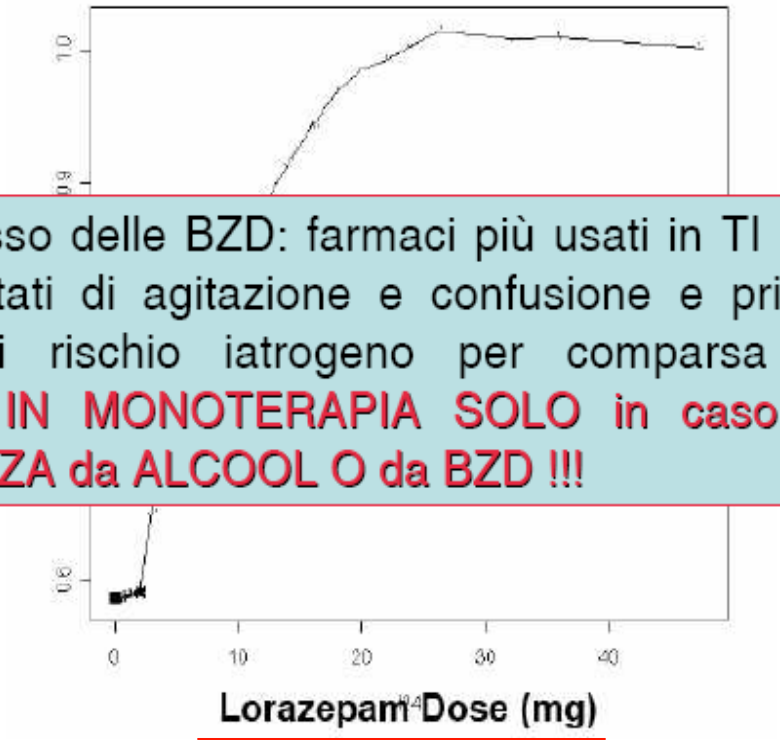
❑ Pharmacologic Prevention and Treatment

- **Benzodiazepin**e: *midazolam,lorazepam, diazepam*
- *Propofol*
- **Oppiace**i: *morfina, fentanyl, remifentanil*
- ***FANS***: *ketoprofene, ketoralac, paracetamolo, tramadolo*
- **Neurolettic**i: *aloperidolo, deidroperidolo, clorpromazina*
- **Antipsicotici atipici**: *quetiapine,olanzapine, risperidone*
- **Adiuvanti**: *clonidina, dexmedetomidine, ketamina*
- *Alogenati*: *Sevofluorane* (sistema AnaConDa®)

✓Limitare l'impiego delle BZD

✓Prediligere BZD a breve-brevissima durata d'azione

Risk factors you can control...medications

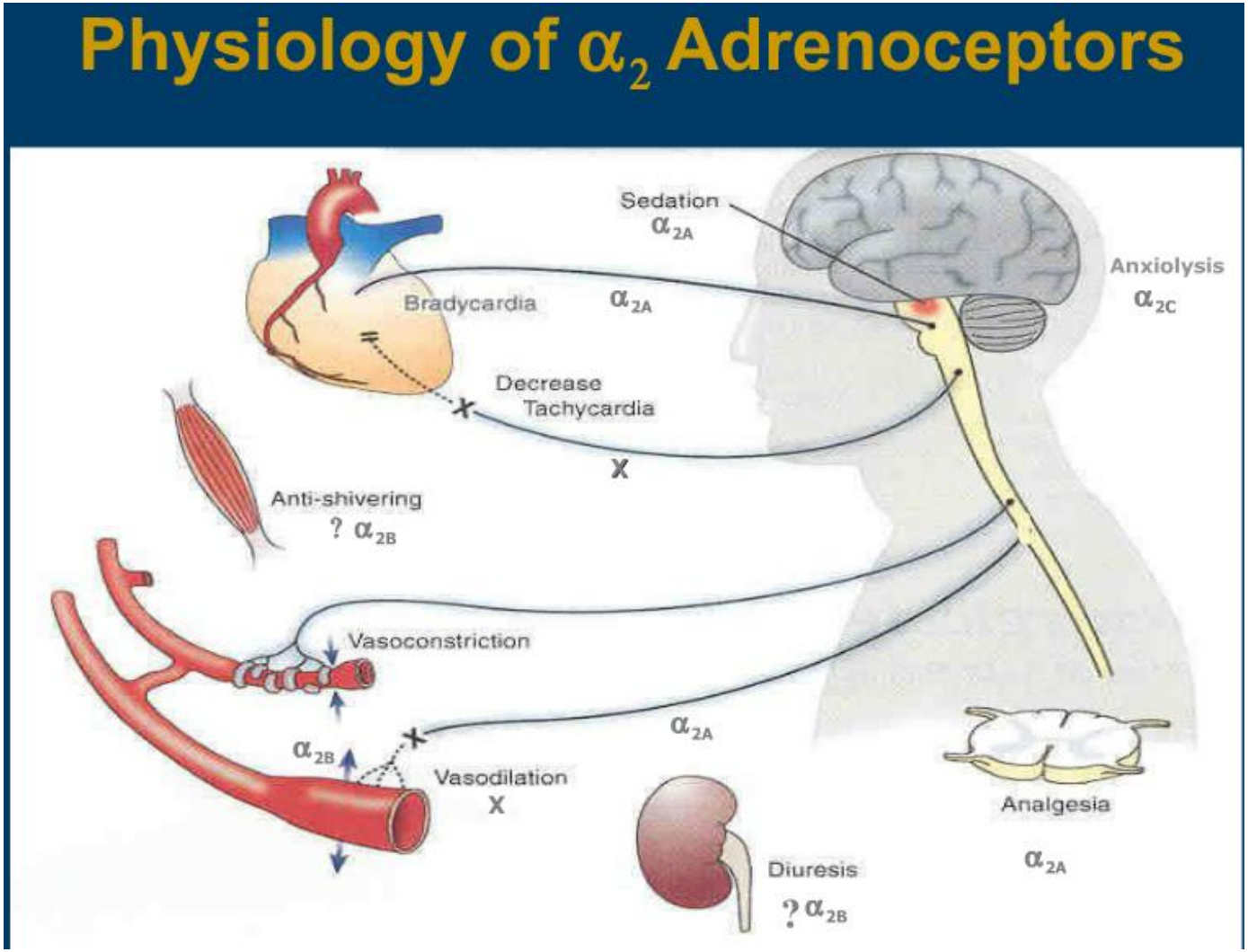


De

Il paradosso delle BZD: farmaci più usati in TI per trattare stati di agitazione e confusione e primo fattore di rischio iatrogeno per comparsa di delirium. IN MONOTERAPIA SOLO in caso di ASTINENZA da ALCOOL O da BZD !!!

Pandharipande, Anesthesiology 2006;104:21-26

- ***Clonidina***
- ***Dexmedetomidina***



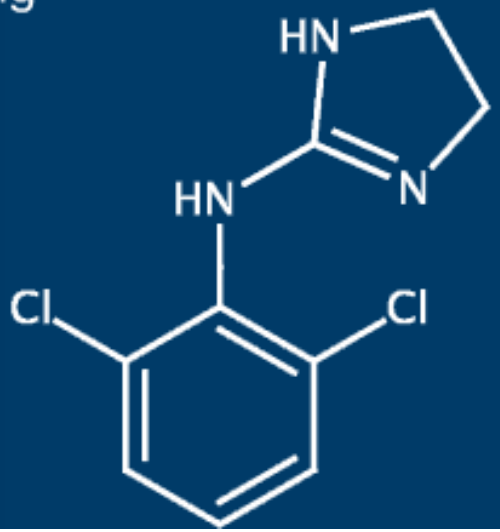
α_2 Agonist Clonidine

Clinical Effects

- Antihypertensive
- Analgesia
- Sedation
- Decrease sympathetic activity
- Decreased shivering

Adverse Effects

- Bradycardia
- Dry mouth
- Hypotension
- Sedation



CLONIDINA

- Già noto come adiuvante analgesico nel postoperatorio e nelle sdr . astinenziali
- Buon controllo della pressione arteriosa e della frequenza cardiaca associato alla sedazione
- Myles et al. hanno evidenziato miocardioprotezione, stabilità emodinamica e metabolica
- Effetti positivi sulle sindromi da sospensione della sedazione
- **Dosaggio** : 0.5 mcg/Kg ev all'ingresso in ICU seguito da infusione di 1 – 2 mcg/Kg/h *

** A.S.Rubino et al. Impact of on delirium and relate respiratory weaning after surgical correction of acute type –A aortic dissection. Interact CardioVasc Thorac Surg;2010 ;10:58-62*

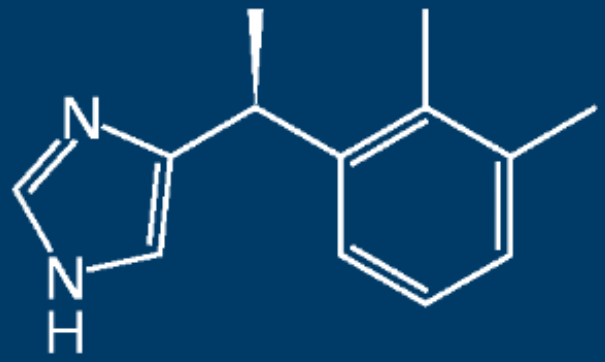
α_2 Agonist Dexmedetomidine

Clinical Effects

- Antihypertensive
- Sedation
- Analgesia
- Decreased shivering
- Anxiolysis
- Patient arousability
- Potentiate effects of opioids, sedatives, and anesthetics
- Decrease sympathetic activity

Adverse Effects

- Hypotension
- Hypertension
- Nausea
- Bradycardia
- Dry mouth
- Peripheral vasoconstriction at high doses



Dexmedetomidina

- **Dose di carico**: non raccomandata
- **Mantenimento**: 0.2 - 1.4 mcg/kg/h iniziando da 0.2 e titrando ogni 30 min.
- **Onset**: > 5 – 10 min.
- **Durata dose intermittente**: 60 – 120 min.
- **Vantaggi**: Sedativo con buona ansiolisi e moderata analgesia. Il paziente è risvegliabile e in grado di intereagire.Riduzione del brivido nel rewarming.
- **Svantaggi**: ipotensione e bradicardia non rapidamente risolvibile dopo interruzione. Riduzione dei dosaggi nell'insufficienza epatica. Approvato dalla US-FDA solo per *sedazione a breve termine*

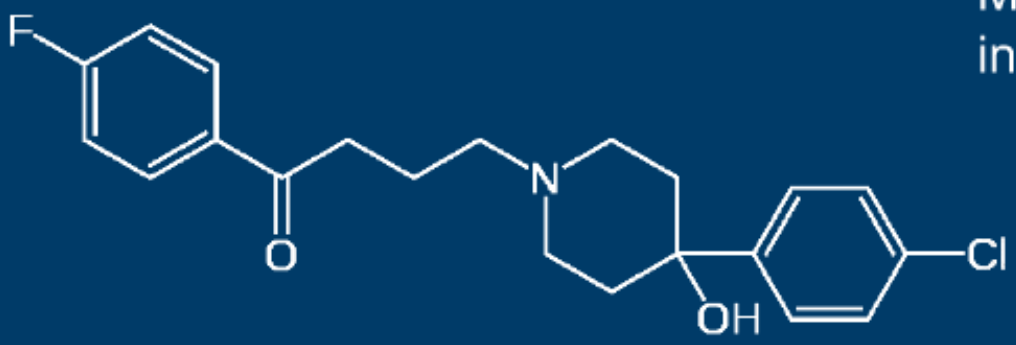
Dopamine Antagonist Haloperidol

Clinical Effects

- Hypnotic agent with antipsychotic properties[1]
  - For treatment of delirium in critically ill adults[1]
- Does not cause respiratory depression[1]

Adverse Effects

- Dysphoria[2]
- Adverse CV effects include QT interval prolongation
- Extrapyramidal symptoms, neuroleptic malignant syndrome (rare)[1]
- Metabolism altered by drug-drug interactions[2]

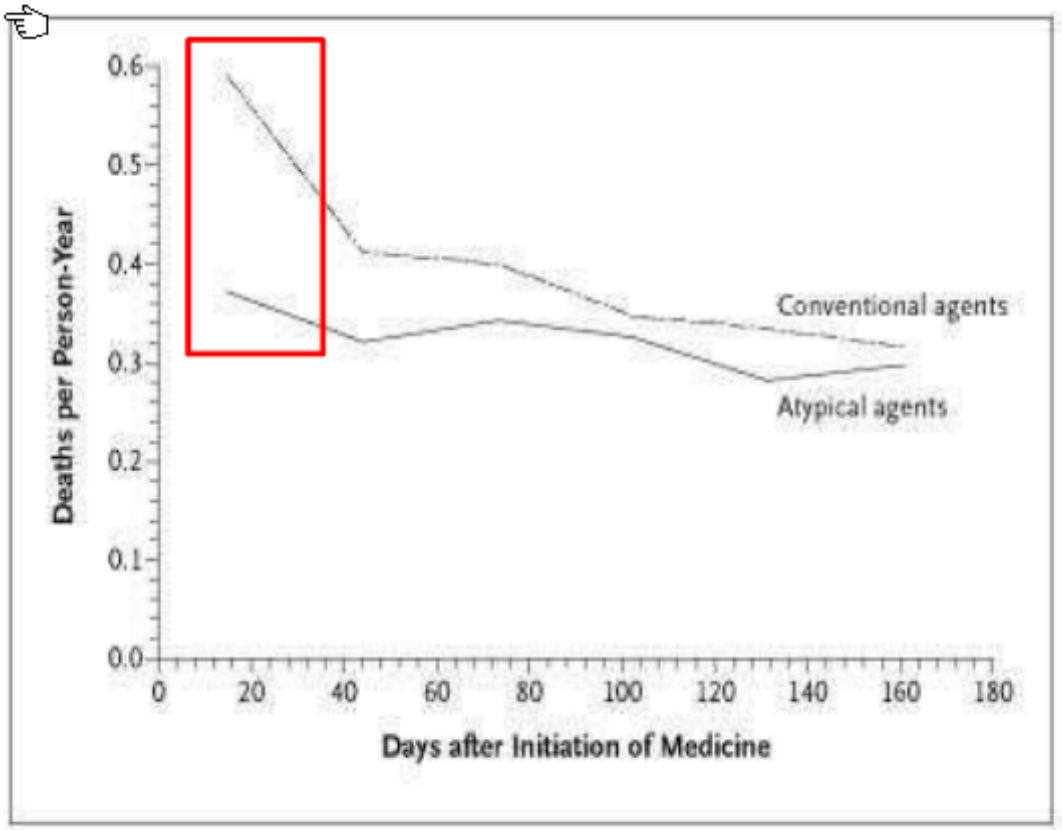


Aloperidolo

- **Dose di carico** ***: 0.03 – 0.15 mg/kg (2 – 10 mg)***
- **Mantenimento** : ***0.03 – 0.15 mg/ Kg ogni 30' – 6 h; nell'anziano 0.25 - 0.50 mg ogni 2 – 4 h; possibile l'infusione continua a 5 – 10 mg/h***
- **Onset** : 30 – 60 min
- **Durata dose intermittente** : da 30 a più di 360 min.
- **Vantaggi** : Antagonismo recettori D2 della dopamina spt. a livello mesolimbico per il controllo dei sintomi da delirium e psicotici. Minimo l'effetto cardiovascolare nei pazienti emodinamicamente stabili.

  Svantaggi : incremento dell'emivita a dosi ripetute; prolungamento QT ed ipotensione risultano essere dose-dipendenti; interferenza metabolica con i comuni farmaci da ICU con effetto sul prolungamento QT. Rari la sindrome neurolettica maligna e la distonia.
- *Comunemente usato per il delirium o la prevenzione dello stesso in ICU, spt. in vista del weaning da ventilazione meccanica*

Potential Advantages of Atypical Antipsychotics
vs Conventional Antipsychotics



- Decreased extrapyramidal effects
- Little effect on the QTc interval (with the exception of ziprasidone)
- Less hypotension/fewer orthostatic effects
- Less likely to cause neuroleptic malignant syndrome
- Unlikely to cause laryngeal dystonia
- Lower mortality when used in the elderly to treat agitation related to dementia

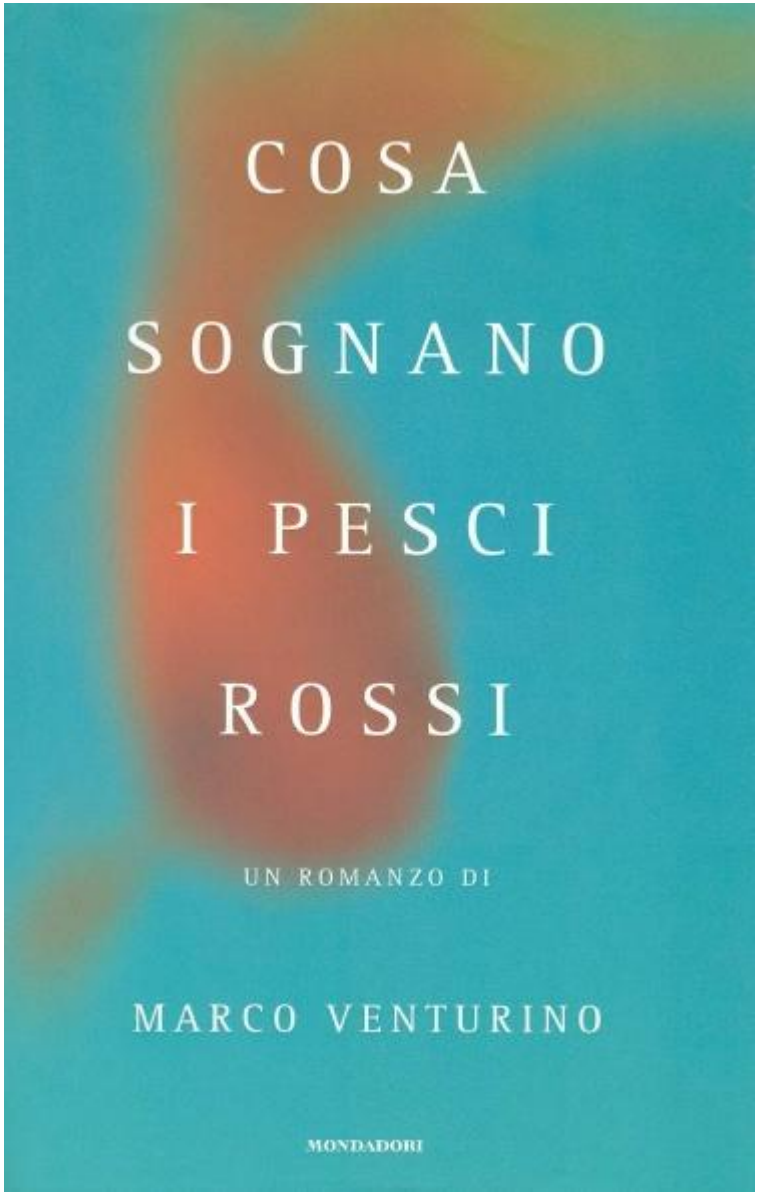
❖ ***Olanzapine, Quetiapine, Risperidone, Ziprasidone***

Quetiapina

- **Dose di carico**: nessuna
- **Mantenimento**: ***iniziare con 50 mg per os ogni 12 ore, aumentare ogni 24 ore fino a 400 mg/die***
- **Onset**: 24 h
- **Vantaggi** : rischio minore di sintomi extrapiramidali e meno prolungamento QT dell'aloperidolo
- **Svantaggi**: richiede via enterale, lento onset; Metabolizzata epaticamente dal CYT P450-3A4 a metaboliti sia attivi che inattivi. Riduzione del dosaggio se insufficienza epatica.
- ***Possibile l'associazione ad aloperidolo nel trattamento e prevenzione del delirio. In attesa di ulteriore validazione.***

❖ ***Summary Points on Management of Delirium in the ICU***

- Monitor delirium regularly in ICU patients using a valid, reliable tool (*eg*, The Delirium Screening Checklist or the CAM-ICU). Remember that the most is hypoactive and will be missed if not actively "looked for"
- Discuss results of delirium assessments on all patients daily on interdisciplinary rounds.
- Identify patients with high number of risk factors for the development or persistence of delirium (*eg*, electrolyte imbalance, fever, addition of new medications; especially those with anticholinergic properties, uncontrolled pain, new onset of congestive heart failure or nosocomial infection, prolonged immobility and restrain use, sleep/wake cycle disturbance).
- Review sedation and analgesia therapy, and ensure that the patient is receiving the minimum doses needed to achieve comfort, realizing that narcotics are often used for the double effect of analgesia and sedation. Implement strategies for tight titration (*eg*, nurse-driven, patient-targeted sedation delivery with daily sedation vacations).
- Consider the benefit and risk profile of adding medications that might spare the use of sedatives and avoid respiratory suppression (*eg*, haloperidol or atypical antipsychotics).



"Già, perché, se pure mi trovo spesso a fluttuare in uno stato di semincoscienza o di sopore, capisco benissimo e ho imparato a capire dai rumori cosa accade intorno a me, ma soprattutto…

… ***ho imparato a vedere bene negli occhi di chi mi si avvicina cosa c'è dentro al cuore a cui quegli occhi appartengono."***

Grazie per l'attenzione

PROTOCOLLI

❖ ***Paziente ventilato meccanicamente, agitato che tende al "disadattamento", instabile emodinamicamente***

- (Propofol) - Remifentanil (0.05–0.08 mcg/Kg /min) – (Midazolam 3-5 mg durante nursing)
- Aloperidolo 0.25 – 0.50 mg /ogni 2-4h – [valutare + Droperidolo (2,5 mg)]
- quando via enterale disponibile: Quetiapina, (*iniziare con 50 mg per os ogni 12 ore, aumentare ogni 24 ore fino a 400 mg/die)*
- ("Weaning" oppiacei: Clonidina (0.5 – 1 mcg/kg/h)
  Dexmedetomidina

❖ ***Paziente in Ventilazione Meccanica, stabile emodinamicamente***

- Remifentanil (0.05– mcg/Kg /min) - Propofol
- Droperidolo (bolo iniziale 2.5 – 5 mg) + Aloperidolo 0.25 – 0.50 mg/6 h
- Quando via enterale disponibile: Quetiapina, (*iniziare con 50 mg per os ogni 12 ore, aumentare ogni 24 ore fino a 400 mg/die)*

❖ Paziente in respiro spontaneo

- (weaning oppiacei-analgesia transizionale)
- Droperidolo 2.5 – 10 mg ev
- Aloperidolo 0.25 – 0.50 mg im ogni 6 h
- Quetiapina, (*iniziare con 50 mg per os ogni 12 ore, aumentare ogni 24 ore fino a 400 mg/die)*