



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

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di Confindustria

**Auditorium
della Tecnica**

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1 Ottobre
2022**



“Questioni” di Utic

“DELIRIUM CORDIS”.

La gestione in terapia intensiva cardiologica

Daniela Pedicino



Disturbo dell'attenzione e della coscienza, accompagnato da alterazioni cognitive o disturbi percettivi, che si sviluppa in un breve lasso di tempo (ore o giorni) ad andamento altalenante

definition
defə'niSH(ə)n

noun

a statement of the exact meaning of a word, especially in a dictionary.



FISIOPATOLOGIA

MICROGLIA

(primed by prior degenerative pathology)

Secret: *IL-1 β , TNF- α , NO, ROS*

Neuronal dysfunction & injury

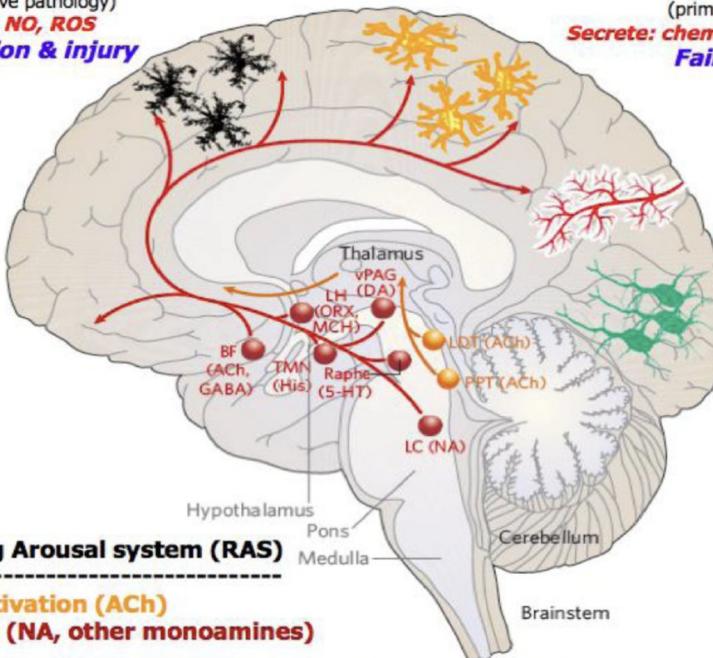
DRUGS

GABAergic sedatives
Anti-cholinergic drugs
Anti-histamine drugs

↓
Neurotransmitter Disturbance

↑
Reticular Ascending Arousal system (RAS)

Thalamocortical activation (ACh)
Cortical integration (NA, other monoamines)



ASTROCYTES

(primed by prior degenerative pathology)

Secret: *chemokines (immune cell infiltration)*

Failure of metabolic support

VASCULAR

Endothelial/BBB injury
Impaired neurovascular coupling
Microvascular dysfunction

Metabolic Insufficiency

NEURONAL DYSFUNCTION

Brain Network Disintegration

↓
DELIRIUM

SYSTEMIC TRIGGERS

Acute systemic inflammation

Hypoxemia (∇O_2), blood flow (shock, impaired perfusion)

Metabolic derangement (Na^+ , hypoglycemia)



Delirium cordis

Stato confusionale acuto

Psicosi cardiaca

Psicosi da terapia intensiva

Insufficienza cerebrale acuta

Delirio post-pericardiotomico

Encefalopatia



Intensive Care Med (2020) 46:1020–1022
<https://doi.org/10.1007/s00134-019-05907-4>



WHAT'S NEW IN INTENSIVE CARE

Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies

Arjen J. C. Slooter^{1*} , Wim M. Otte², John W. Devlin^{3,4}, Rakesh C. Arora^{5,6}, Thomas P. Bleck⁷, Jan Claassen⁸, Matthew S. Duprey^{3,4}, E. Wesley Ely^{9,10}, Peter W. Kaplan¹¹, Nicola Latronico¹², Alessandro Morandi^{13,14}, Karin J. Neufeld¹⁵, Tarek Sharshar¹⁶, Alasdair M. J. MacLullich¹⁷ and Robert D. Stevens¹⁸

- 
1. The term *acute encephalopathy* refers to a rapidly developing (over less than 4 weeks, but usually within hours to a few days) pathobiological process in the brain. **This is a preferred term**
 2. *Acute encephalopathy* can lead to a clinical presentation of subsyndromal delirium, delirium, or in case of a severely decreased level of consciousness, coma; all representing a change from baseline cognitive status
 3. The term *delirium* refers to a clinical state characterized by a combination of features defined by diagnostic systems such as the DSM-5. Delirium according to the DSM-5 is defined if criterium A-E are fulfilled: A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment). B. The disturbance develops over a short period of time (usually hours to a few days) represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of the day. C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception). D. The disturbances in criteria A and C are not explained by another pre-existing, established, or evolving neurocognitive disorder, and do not occur in the context of a severely reduced level of arousal, such as coma. E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal (i.e., because of a drug of abuse medication), or exposure to a toxin, or is because of multiple etiologies. **This is a preferred term**
 4. The term *coma* refers to a clinical state of severely depressed responsiveness defined by diagnostic systems such as the GCS or FOUR score. **This is a preferred term**
 5. The term *acute confusional state* **should not be used** in addition to the terms delirium and acute encephalopathy
 6. The term *acute brain dysfunction* **should not be used** in addition to the terms delirium and acute encephalopathy
 7. The term *acute brain failure* **should not be used** in addition to the terms delirium and acute encephalopathy
 8. The term *altered mental status* is not synonymous with *delirium* and **should not be used**



TI generaliste ☽ 32-87%

TI cardiochirurgiche ☽ 50%

Greaves D, et al. Int J Cardiol. 2019.
doi: 10.1016/j.ijcard.2019.04.065.

TI cardiologiche ☽ 15-50%

Falsini, G. et al (DELIRIUM CORDIS). European heart journal.
Acute cardiovascular care 7, 661-670 (2018)

Epidemiologia





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Acute cardiovascular care 7, 661-670 (2018)

Delirio subsindromico ☽ fino a 2/3
degli over 65 ricoverati

Cole M, et al. The prognostic significance of subsyndromal delirium in elderly medical inpatients. Journal of the American Geriatrics Society 51, 754-760 (2003).

Epidemiologia





TI cardiologiche ☽ 15-50%

Delirium post TAVI

à 7.2% (95% CI=5.4-9.1%) TF-TAVR

à 21.4% (95% CI=10.3-32.5%) non TF-TAVR

Abawi M, et al. Postoperative Delirium in Individuals Undergoing Transcatheter Aortic Valve Replacement: A Systematic Review and Meta-Analysis. J Am Geriatr Soc. 2018. doi: 10.1111/jgs.15600.

Epidemiologia





Sottotipi

IPERATTIVO ⚡ agitazione incontrollata, aggressività, allucinazioni e disorientamento. Comune nell'astinenza da alcol, rara nel delirium acquisito in ospedale (<2% dei casi);

IPOATTIVO ⚡ letargia, sonnolenza, lentezza nei movimenti, asocialità, apatia. Forma più comune di delirio acquisito in ospedale (45-64% dei casi); prognosi infastidita (mortalità a 6 mesi fino al 32% vs 8% circa per le altre forme)

MISTO





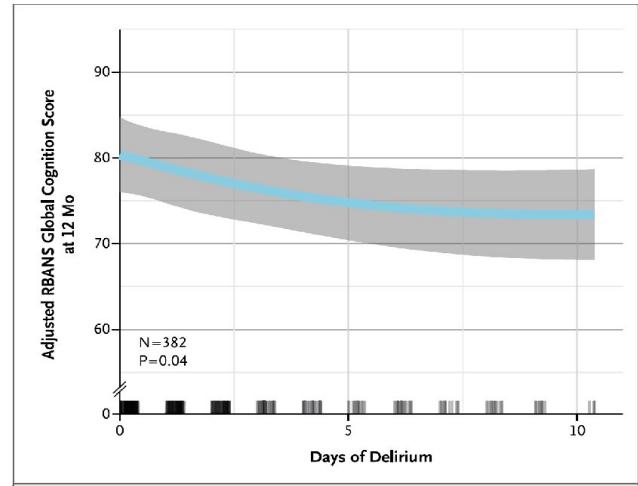
DELIRIO PERSISTENTE vs DELIRIO RAPIDAMENTE REVERSIBILE

La durata del delirio è indipendentemente associata a mortalità, nuove ospedalizzazioni, demenza

Prognosi



Durata degenza
Durata ventilazione
Costi



Goldberg TE, et al. Association of Delirium With Long-term Cognitive Decline: A Meta-analysis. JAMA Neurol. 2020. doi: 10.1001/jamaneurol.2020.2273.

Pandharipande P, et al. Long-term cognitive impairment after critical illness. N Engl J Med. 2014. doi: 10.1056/NEJMc1313886. PMID: 24401069.



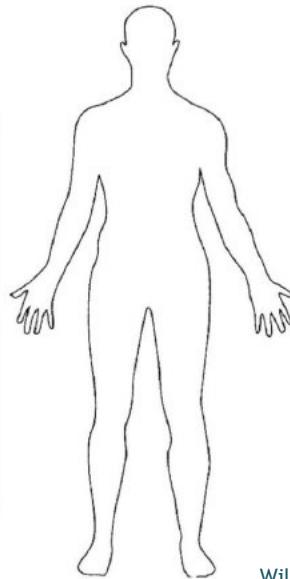
Fattori di Rischio

- Advanced age,
- Dementia
- Low education
- High comorbidity
- Frailty
- Visual and hearing impairment
- Depression
- Alcohol abuse
- Illicit drug, opioid or benzodiazepines use
- Poor nutrition
- History of delirium

- Premorbid factors
- Postoperative
- Intensive care
- Ventilated
- General hospital

Factors relating to presenting illness

- | | |
|---|---|
| <ul style="list-style-type: none"> • Surgical stress • Cardiovascular • Major abdominal • Aortic surgery • General • Major joint • Emergency operation • Comorbid diseases • Cigarette smoking | <ul style="list-style-type: none"> • Acute infections • Surgery • Dehydration • Electrolyte imbalance • Acute kidney injury • Liver dysfunction • Drug withdrawal • Seizures and heart failure • High alcohol intake |
| <ul style="list-style-type: none"> • Severity of illness • Unplanned admission • Medical admission • Prior education level • Multiple comorbidities • Sepsis • hours | <ul style="list-style-type: none"> • Failure of non-invasive ventilation • Ventilation longer than 96 hours |



Post-admission factors

- | | | |
|--|---|--|
| <ul style="list-style-type: none"> • Pain • Infection • Invasive devices • Immobility • Metabolic abnormalities • Prolonged ileus • Blood transfusion | <ul style="list-style-type: none"> • All hospital and postoperative factors • Opioids • Polypharmacy • Sleep deprivation • Environmental factors • Day night orientation • Communication • Family visits • Deep sedation | <ul style="list-style-type: none"> • Invasive devices • Physical restraints • Poor sleep • Opioids • Psychoactive drugs • Benzodiazepines • Anticholinergics • Family visit • Mobility • Fall risk |
| | | <ul style="list-style-type: none"> • Longer duration of ventilation • Infusions of benzodiazepines and opioids • Antipsychotics • Tracheostomy • Physical restraints |



Diagnosi

Più di 50 strumenti per la valutazione del delirio. Fino al 75% di mancate diagnosi in assenza di tool diagnostici.

In terapia intensiva i più usati sono il Confusion Assessment Method for Intensive Care Unit (CAM-ICU) e l'Intensive Care Delirium Screening Checklist (ICDSC) ☺ 2-5 min max. [Gélinas C. et al. Critical care nurse 38, 38-49 (2018)]

La valutazione andrebbe effettuata più volte al giorno (andamento fluttuante)

Necessaria valutazione preliminare dello stato di coscienza ☺ Richmond Agitation Screening Scale (RASS).



STEP 1 ☾ Valutazione dello stato di coscienza

Richmond Agitation-Sedation Scale

Target RASS Value		RASS Description
-4	Combative	Combative, Violent, Immediate Danger to Staff
-3	Very Agitated	Pulls or Removes Tube(s) or Catheter(s); Aggressive
-2	Agitated	Frequent non-Purposeful Movement, Fights Ventilator
-1	Restless	Anxious, Apprehensive but Movements are not Aggressive or Vigorous
0	Alert and Calm	
-1	Drowsy	Not Fully Alert, but has Sustained Awakening to Voice (Eye Opening & Contact >10sec)
-2	Light Sedation	Briefly Awakens to Voice (Eye Opening & Contact <10sec)
-3	Moderate Sedation	Movements or Eye Opening to Voice (BUT NO Eye Contact)
-4	Deep Sedation	No Response to Voice, BUT has Movement or Eye Opening to Physical Stimulation
-5	Unarousable	No Response to Voice or Physical Stimulation

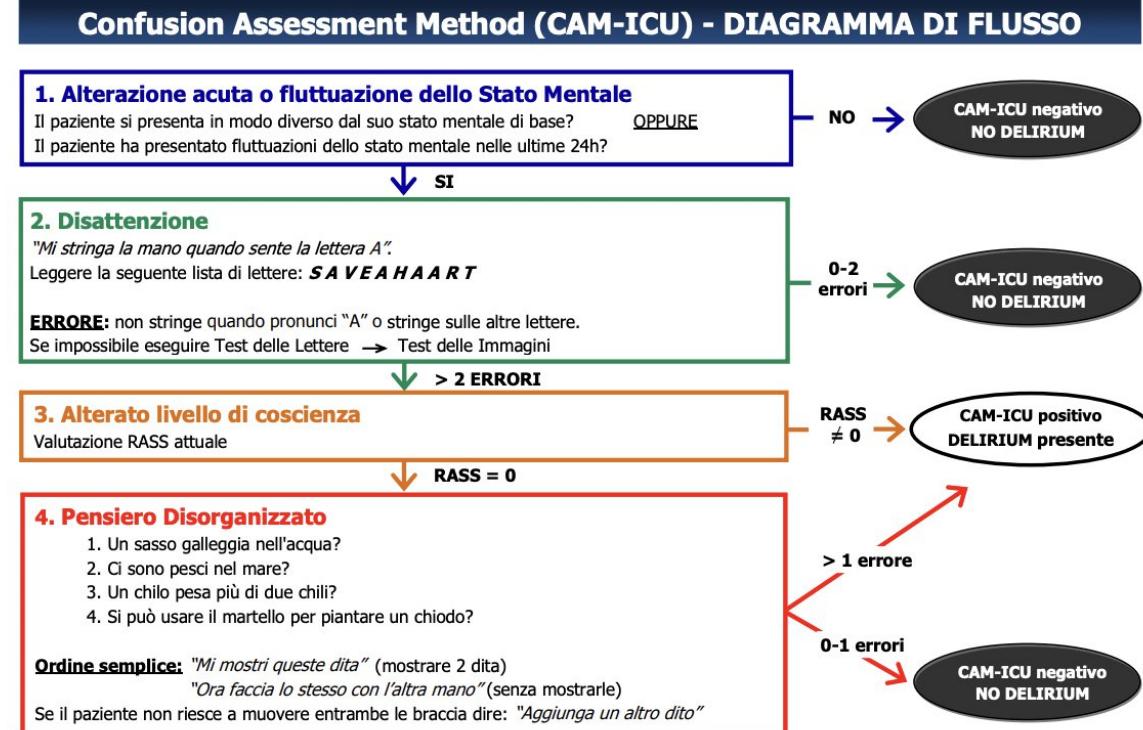
RASS ≤ -4? Rivalutazione a distanza
il paziente non è responsivo

RASS ≥ -3? Somministrare CAM-ICU
per diagnosi delirio



STEP 2 ☾

Valutazione del contenuto della coscienza





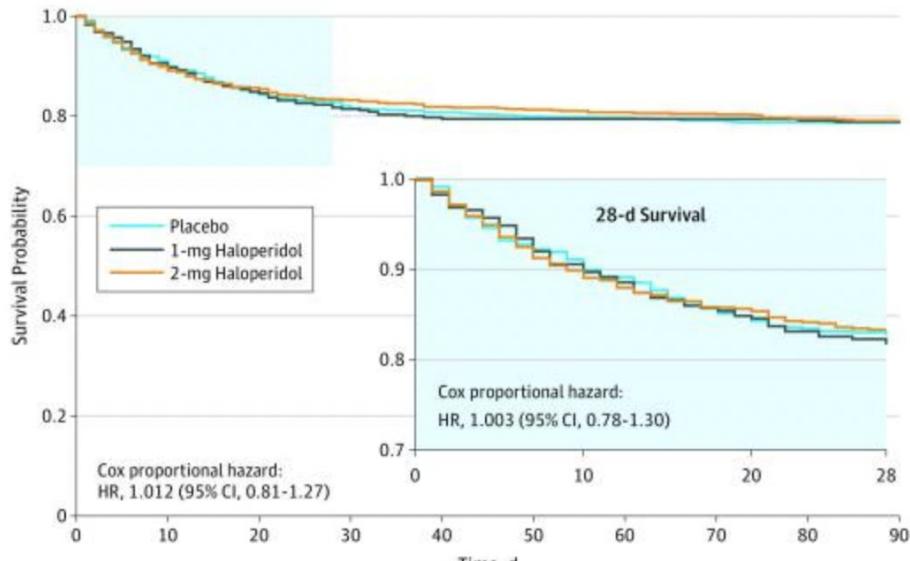
Prevenzione e Management

Nessuna evidenza sull'uso di farmaci nella prevenzione del delirium ☺

alooperidolo, inibitori colinesterasi (donepezil, rivastigmina), statine, melatonina

Van den Boogaard M, et al. Effect of Haloperidol on Survival Among Critically Ill Adults With a High Risk of Delirium: The REDUCE Randomized Clinical Trial. JAMA. 2018 doi: 10.1001/jama.2018.0160.

Raccomandato approccio multimodale non farmacologico, focalizzato a ridurre i fattori di rischio modificabili per delirium



2018 SCCM, Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU



Prevenzione e Management

l'ABCDEF bundle

ABCDEF multi-intervention approach					
A	B	C	D	E	F
Assessment, prevention, and management of pain	Both spontaneous awakening trials and spontaneous breathing trials	Choice of sedation and analgesia	Delirium assessment, prevention, and management	Early mobility and exercise	Family engagement and empowerment
					
NRS - BPS	RASS - SAS			CAM-ICU	

Barnes-Daly MA, Phillips G, Ely EW. Improving Hospital Survival and Reducing Brain Dysfunction at Seven California Community Hospitals: Implementing PAD Guidelines Via the ABCDEF Bundle in 6,064 Patients. Crit Care Med. 2017. doi: 10.1097/CCM.0000000000002149.

Trattamento Farmacologico ANTIIPSICOTICI



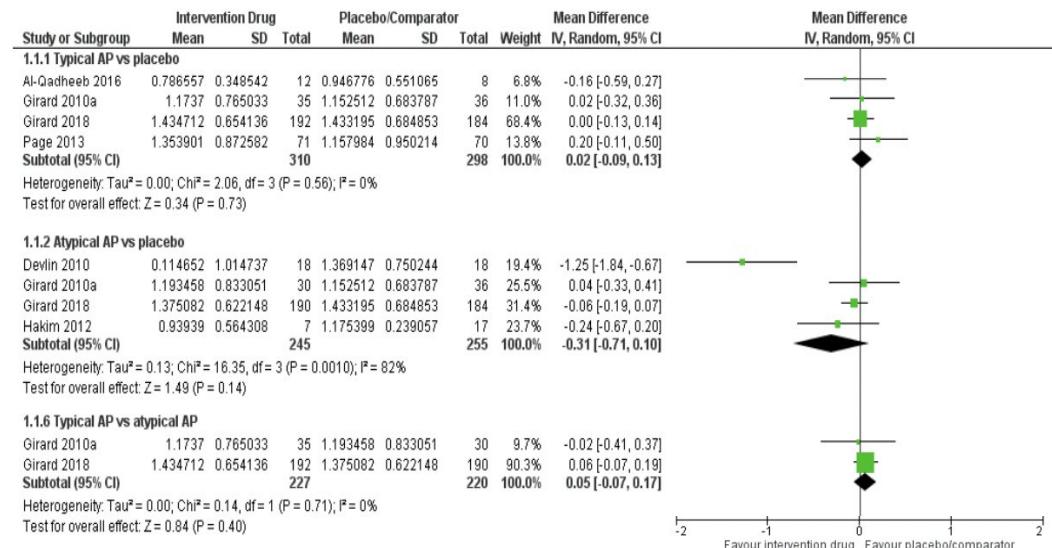
Cochrane Database of Systematic Reviews

Pharmacological interventions for the treatment of delirium in critically ill adults (Review)

Burry L, Hutton B, Williamson DR, Mehta S, Adhikari NKJ, Cheng W, Ely EW, Egerod I, Fergusson DA, Rose L

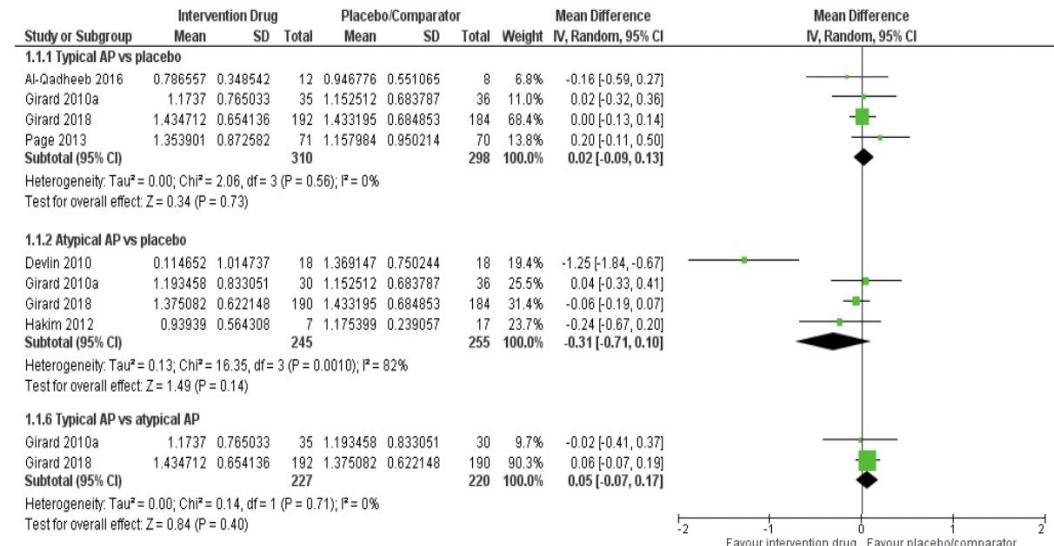
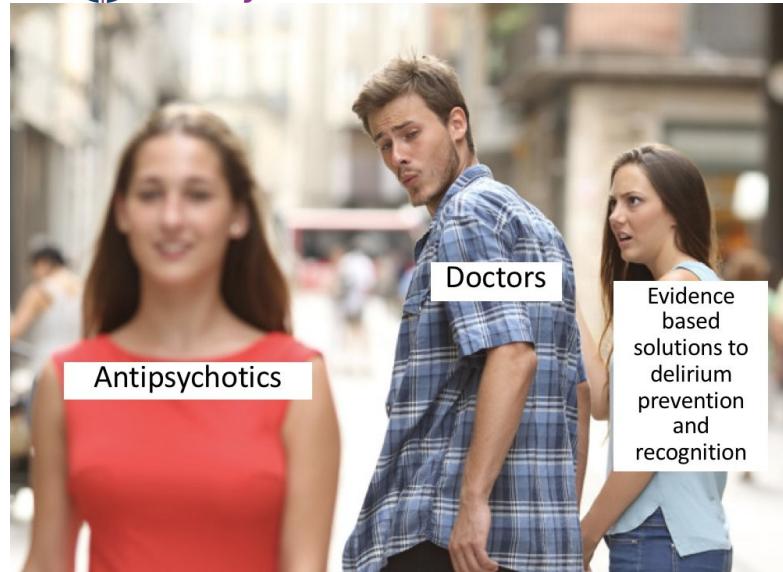
Raccommodation

We suggest not routinely using haloperidol and atypical antipsychotic to treat delirium (conditional raccommodation, low quality of evidence)



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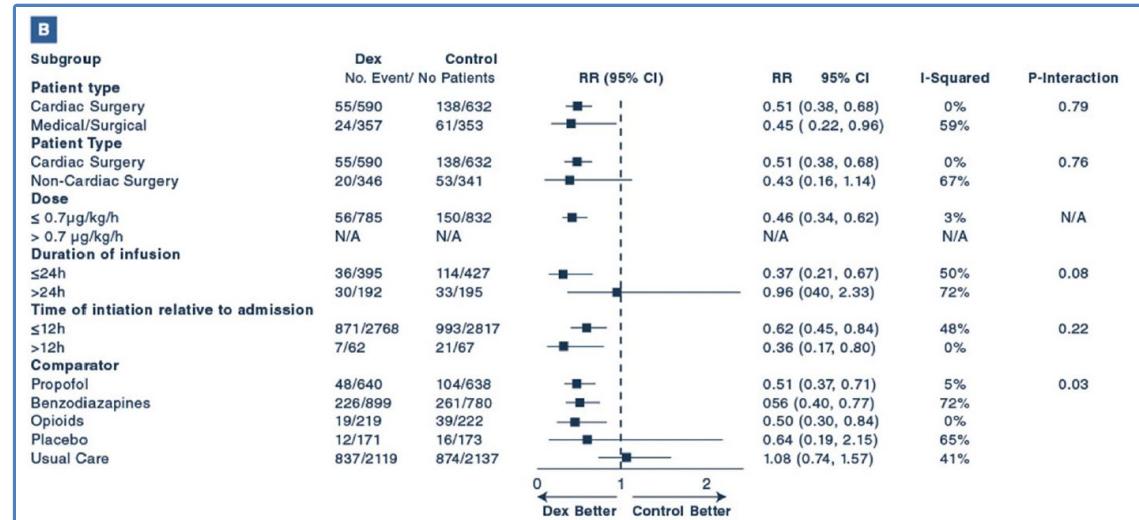


Trattamento Farmacologico

DEXMEDETOMIDINA

Recommendation:

We suggest using dexmedetomidine for delirium in mechanically ventilated adults where agitation is precluding weaning/extubation (conditional recommendation, low quality of evidence).



Lewis K, et al. GUIDE group. Dexmedetomidine vs other sedatives in critically ill mechanically ventilated adults: a systematic review and meta-analysis of randomized trials. Intensive Care Med. 2022 Jul;48(7):811-840. doi: 10.1007/s00134-022-06712-2. Epub 2022 Jun 1. PMID: 35648198.



CONCLUSIONI

Delirium complicanza acuta nei pazienti critici, fino al 50% dei ricoveri in UTIC.

Mancata diagnosi fino al 75% dei casi, se non si usano scale validate (RASS, CAM-ICU)

Rivalutazione quotidiana dello stato cognitivo (+ scale dolore, SAT e SBT se ventilato)

Prevenzione con approcci multimodali non farmacologici come il bundle ABCDEF

Se necessita' di sedare target RASS ☿ -2 1

Preferire Propofol e Dexmedetomidina

Evitare l'uso di benzodiazepine e di sedativi oppioidi

GRAZIE