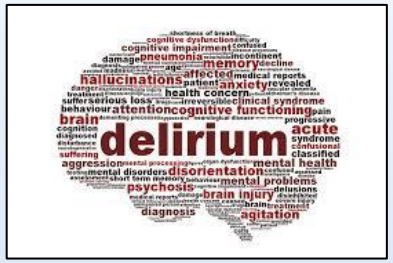


Delirium en réanimation: Stratégie diagnostique et thérapeutique

Takoua Merhabene

Réanimation Zaghouan, Novembre 2024

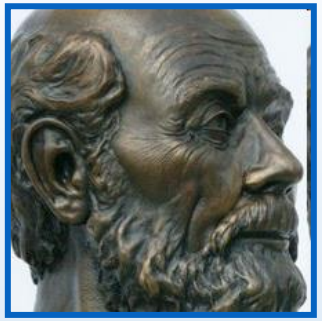
UR22SP01 « Insuffisance respiratoire et Ventilation artificielle »

WHAT'S NEW IN INTENSIVE CARE

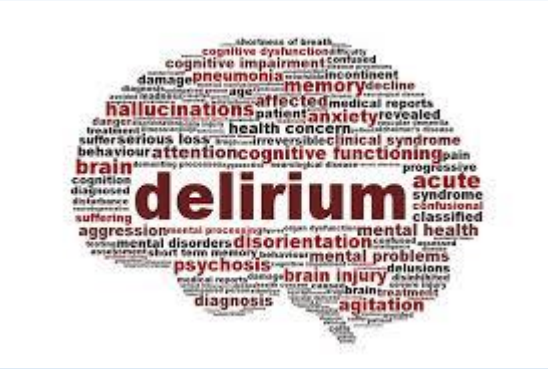
Intensive Care Med
https://doi.org/10.1007/s00134-019-05907-4

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

Arjen J. C. Slooter[1*], Wim M. Otte[2], John W. Devlin[3,4], Rakesh C. Arora[5,6], Thomas P. Bleck[7], Jan Claassen[8], Matthew S. Duprey[3,4], E. Wesley Ely[9,10], Peter W. Kaplan[11], Nicola Latronico[12], Alessandro Morandi[13,14], Karin J. Neufeld[15], Tarek Sharshar[16], Alasdair M. J. MacLullich[17] and Robert D. Stevens[18]



Delirare

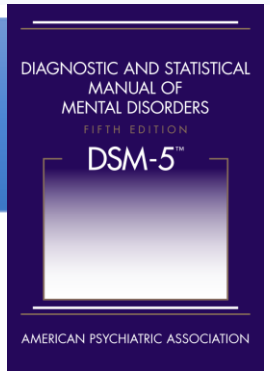


Signe Clinique	
Delirium	Syndrome confusionnel
ATTENTION faux-ami	
Delusion	Délire
Substrat physiopathologique	
Encéphalopathie aiguë	

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**

Delirium Diagnostic criteria

DSM V : Diagnostic Statistical Manual (of American Psychiatric Association)



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** (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. The disturbance is a **direct physiological 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

Outcome of delirium in critically ill patients: systematic review and meta-analysis

Jorge I F Salluh,[1] Han Wang,[2] Eric B Schneider,[2] Neeraja Nagaraja,[2] Gayane Yenokyan,[3] Abdulla Damluji,[4] Rodrigo B Serafim,[1,5] Robert D Stevens[6]

BMJ 2015

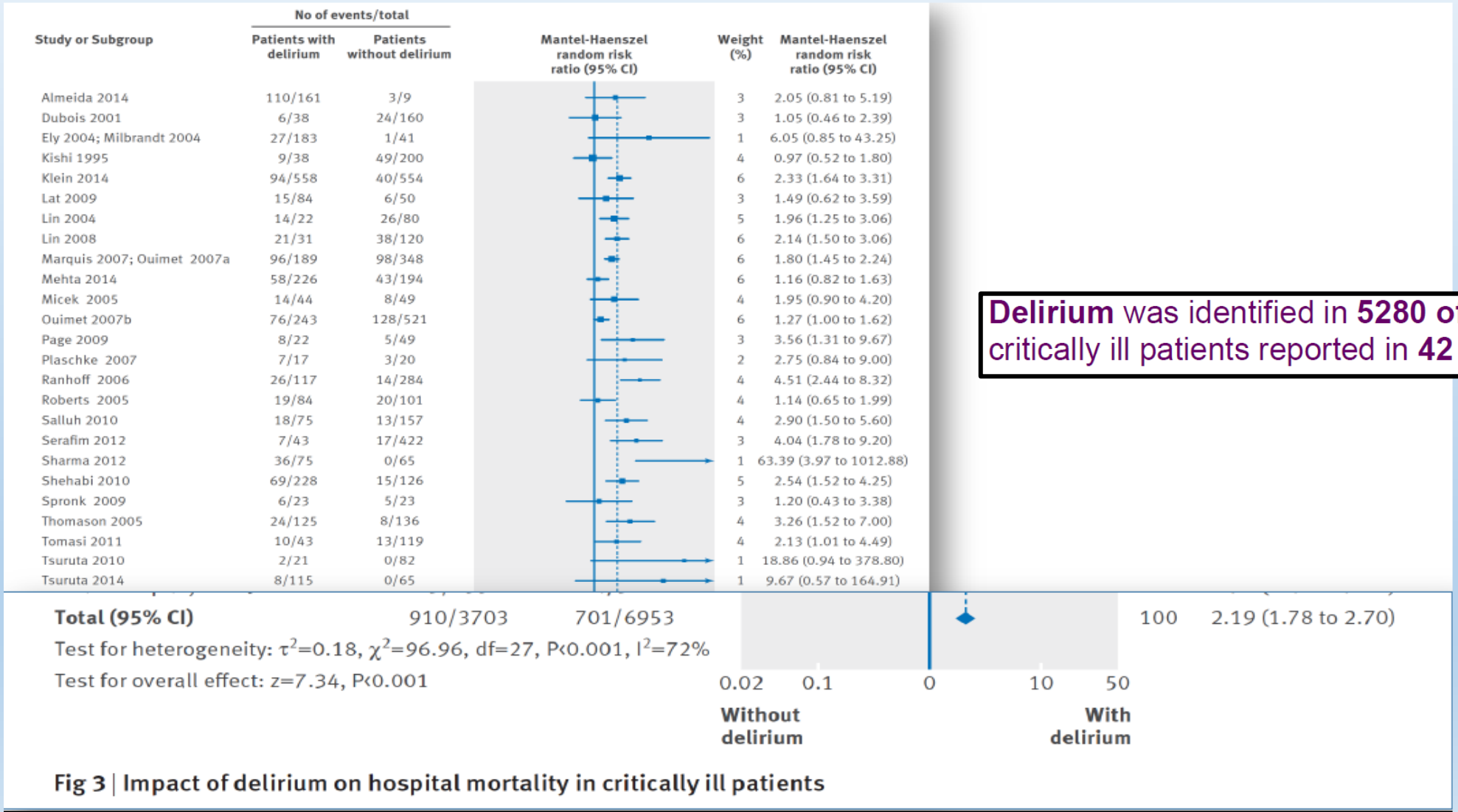
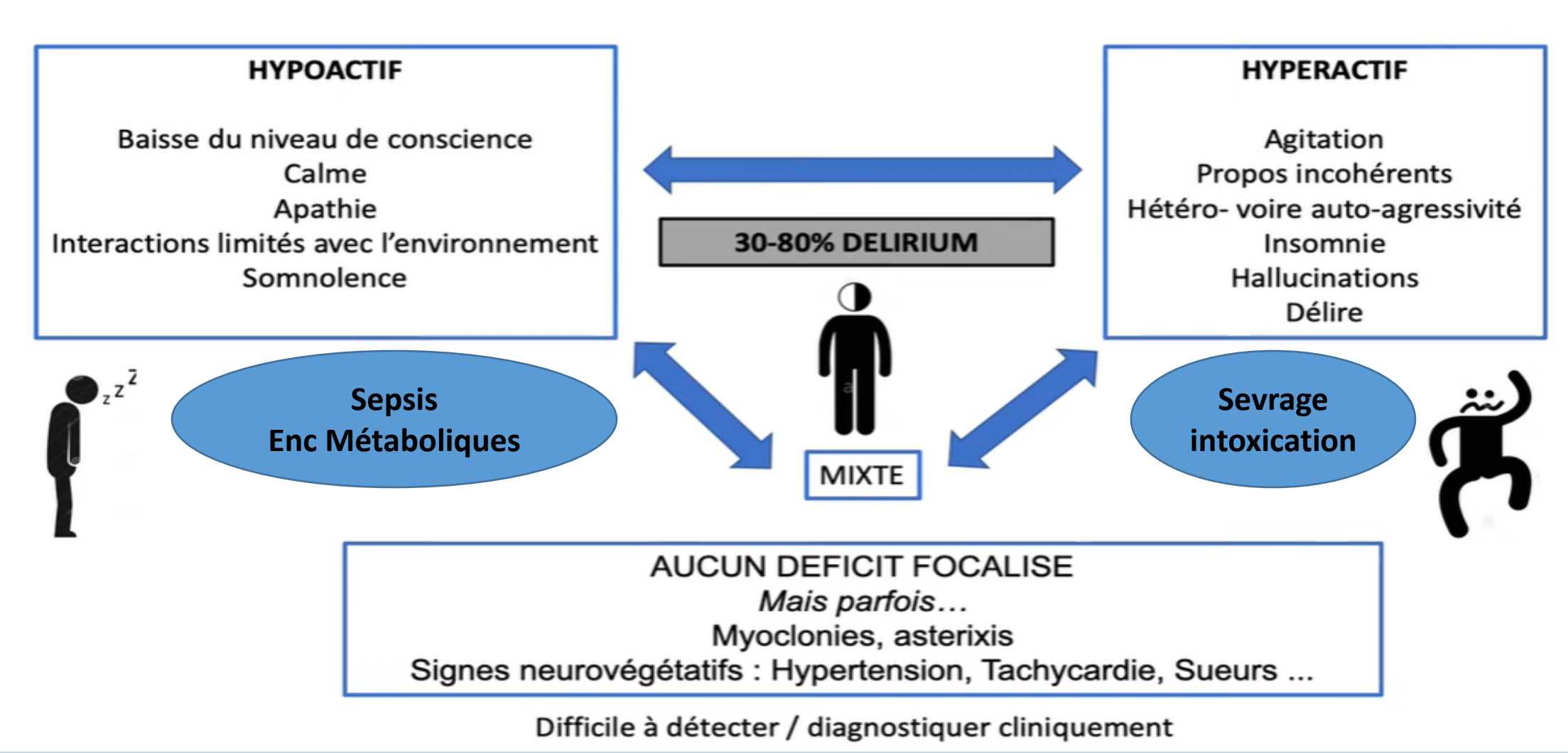


Fig 3 | Impact of delirium on hospital mortality in critically ill patients

Delirium was identified in **5280 of 16 595 (31.8%)** critically ill patients reported in **42 studies.**

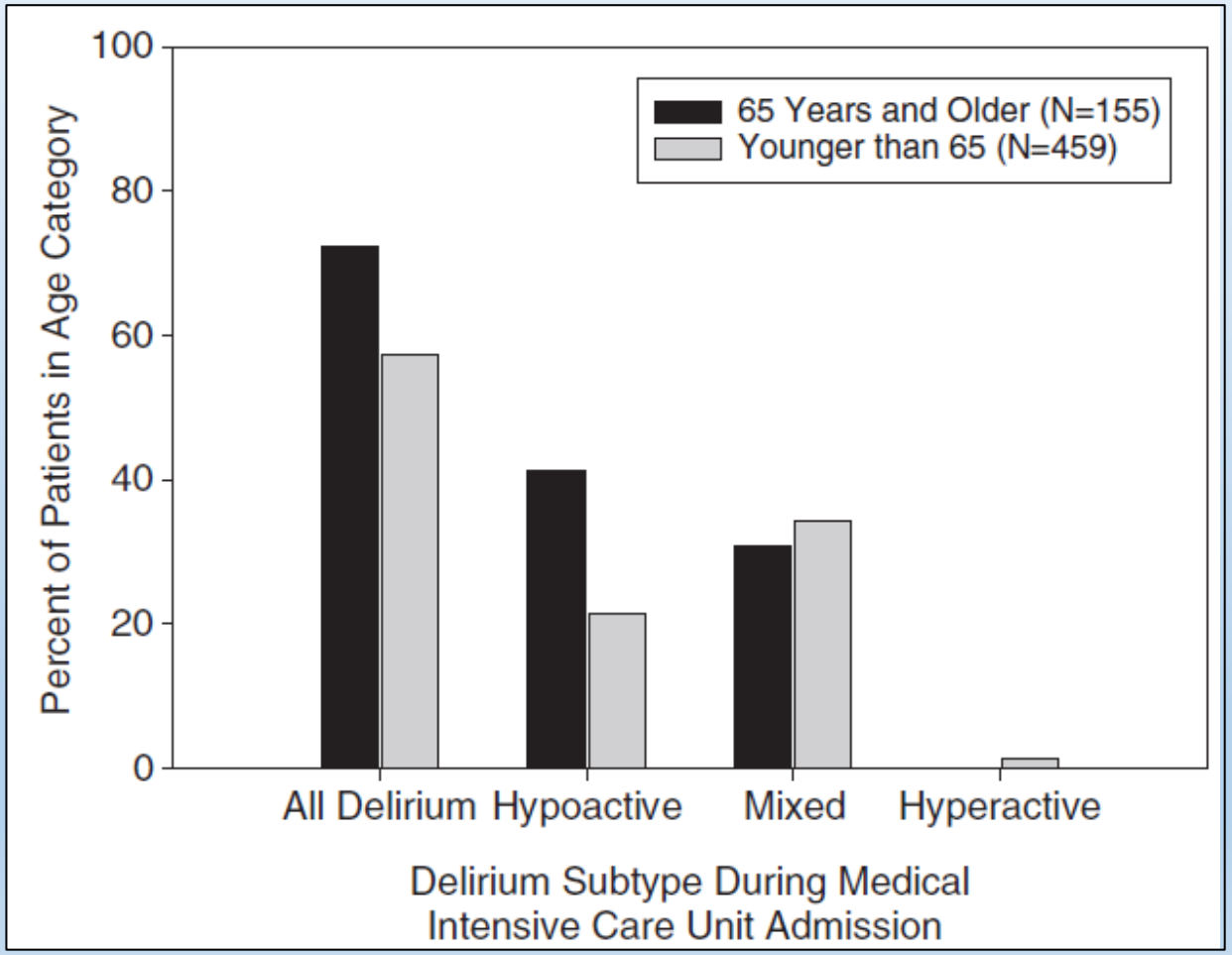
Présentations cliniques



Delirium and Its Motoric Subtypes: A Study of 614 Critically Ill Patients

Josh F. Peterson, MD, MPH,[*†] *Brenda T. Pun, RN, MSN, ACNP,*[*†‡]
Robert S. Dittus, MD, MPH,[*†‡] *Jason W. W. Thomason, MD,*[‡]
James C. Jackson, PsyD, MSc,[*†] *Ayumi K. Shintani, MPH, PhD,*[*§] *and*
E. Wesley Ely, MD, MPH[*†‡‖]

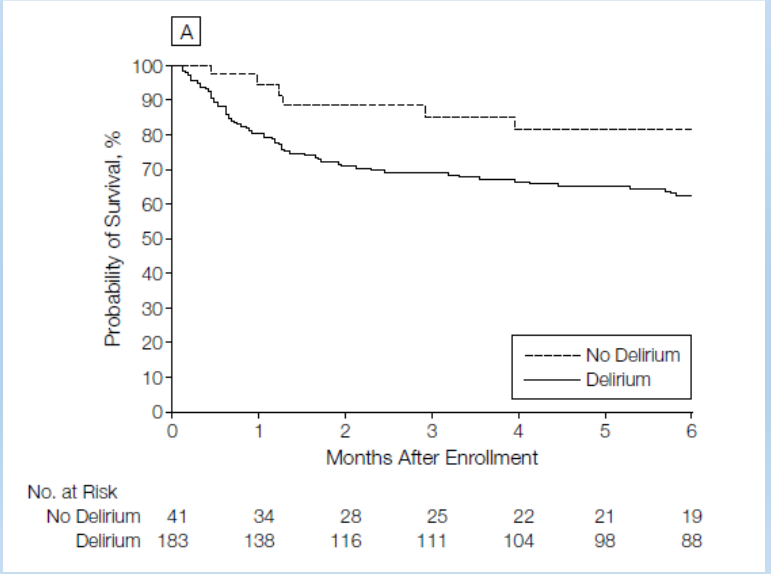
. J Am Geriatr Soc 54:479–484, 2006.



Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit

JAMA. 2004;291:1753-1762

- 275 patients, ICU/VMI
- Suivi moyen de 6 mois
- Prévalence délirium=72%
- Début précoce du délirium : 2 jours (IQR 1-3)après arrêt de la sédation
- Durée moyenne 3,4± 1,9j
- Tout au long du séjour:
  - 21% séjour normal
  - 35,3% comateux
  - 43,1% délirant
- J 7-J10: délirium est le 1er signe d'alerte
  - D'une complication
  - Sepsis nosocomial



Conséquences sur le pronostic

Immédiat

- Dépense énergétique accrue
- Iatrogénie: auto-extubation, désinsertion de KTC
- Ischémie myocardique
- Méconnaissance d'une pathologie aigue

• Jaber et al, Chest 2005

A court terme

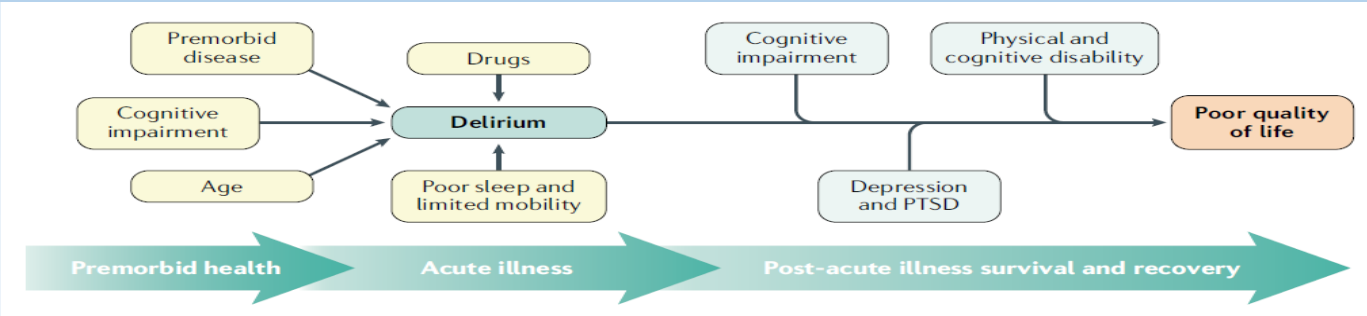
- Echec de sevrage de la VMI
- Prolongation durée de VM (OR= 1,79), durée de séjour en ICU (21 vs 7j) et hospitalière
- Surmortalité en réanimation (adjusted hazard ratio [HR],2,19; 95% confidence interval [CI], 1.78–2,7; p< 0.001)
- Infections associées aux soins
- Majoration du coût (34,000 **$** vs 15,000 **$)**

• JAMA 2004, BMJ 2015

A moyen terme

- Baisse des performances cognitives (47%,persistante jusqu'à 1 an)
- Dépendance physique et fonctionnelle
- PTSD

• NEJM 2013, Lancer Respiratory Medecine 2010



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

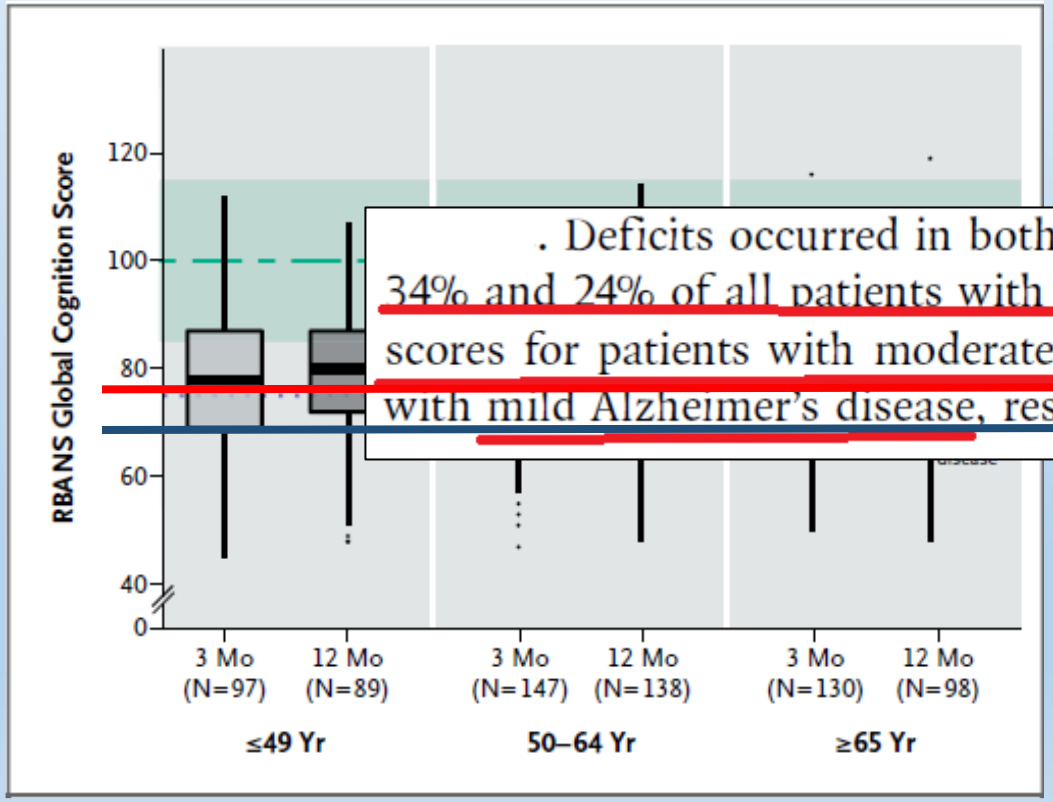
N ENGL J MED 369;14 NEJM.ORG OCTOBER 3, 2013

Long-Term Cognitive Impairment after Critical Illness

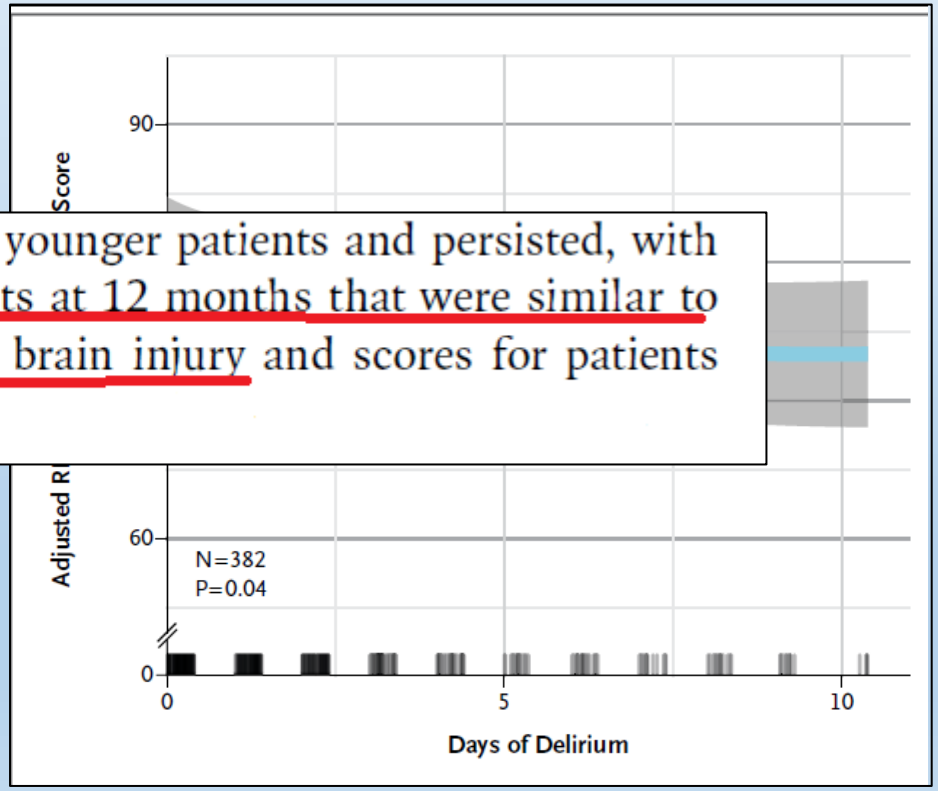
P.P. Pandharipande, T.D. Girard, J.C. Jackson, A. Morandi, J.L. Thompson, B.T. Pun, N.E. Brummel, C.G. Hughes, E.E. Vasilevskis, A.K. Shintani, K.G. Moons, S.K. Geevarghese, A. Canonico, R.O. Hopkins, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the BRAIN-ICU Study Investigators*

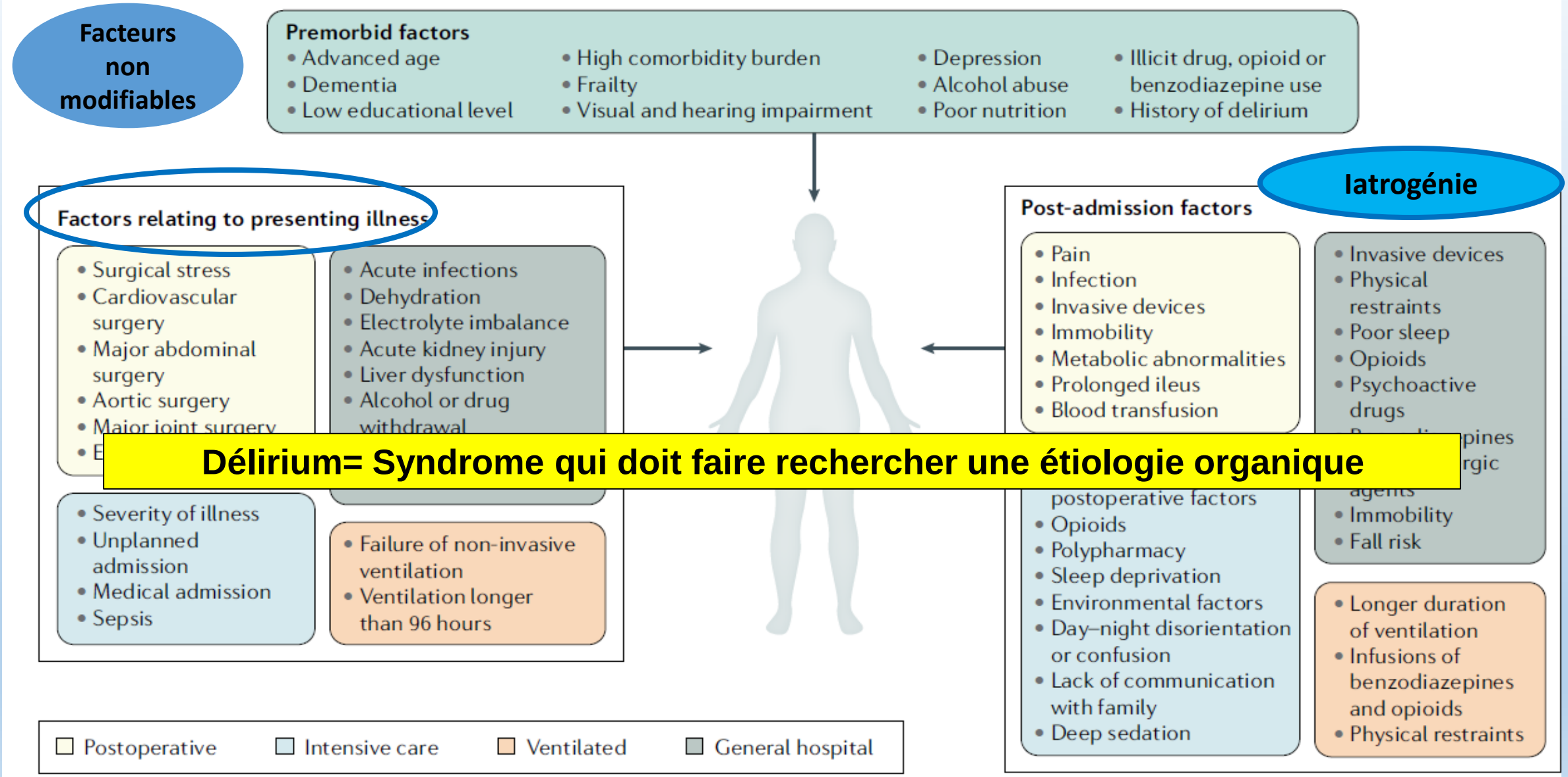
ABSTRACT

821 patients/cohorte prospective
ICU mixed
Delirium =75%



. Deficits occurred in both older and younger patients and persisted, with 34% and 24% of all patients with assessments at 12 months that were similar to scores for patients with moderate traumatic brain injury and scores for patients with mild Alzheimer's disease, respectively.

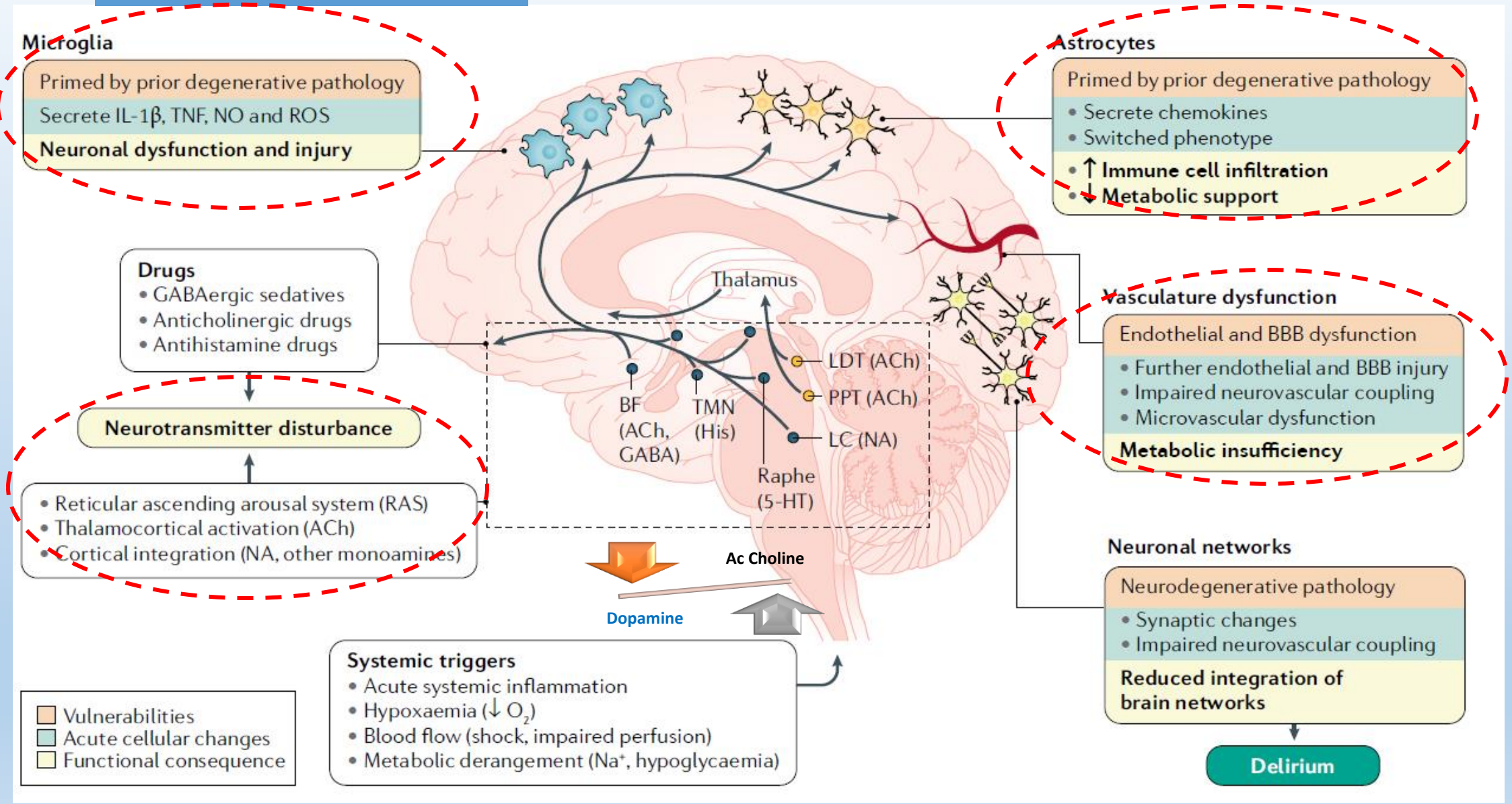




Délirium= Syndrome qui doit faire rechercher une étiologie organique

Nature, 2020

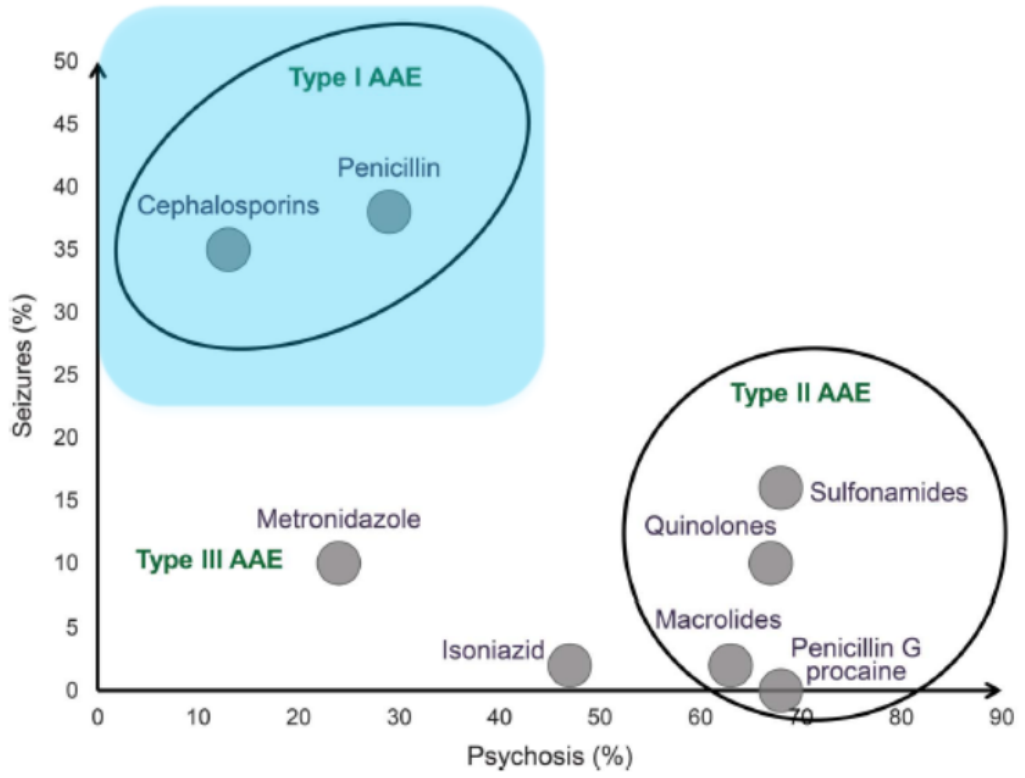
Physiopathologie



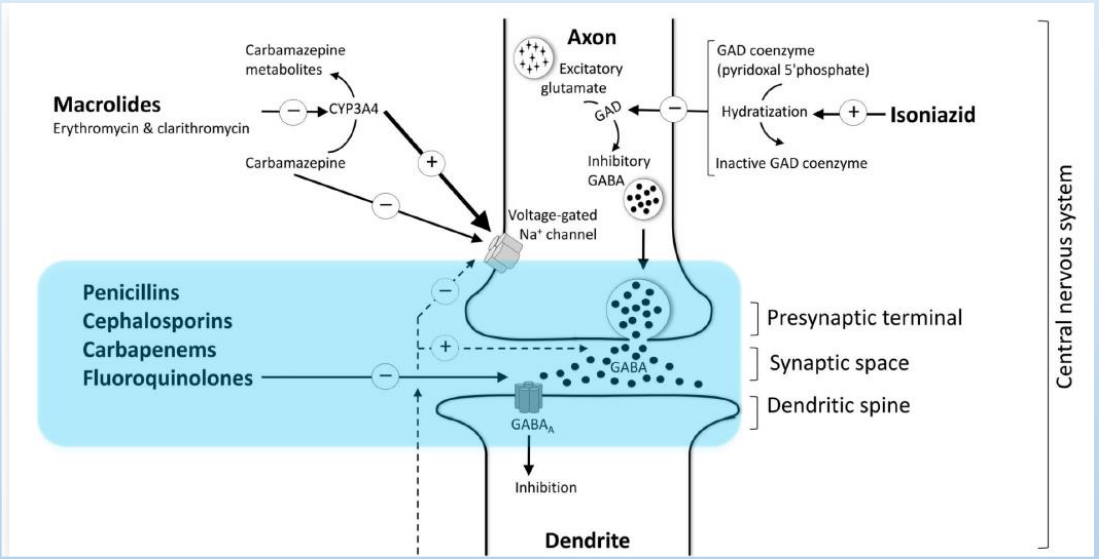
Nature, 2020

Antibiotic-associated encephalopathy

Figure 2 Types of antibiotic-associated encephalopathy



Neurology 2016



Intensive Care Med (2015) 41:2130–2137
DOI 10.1007/s00134-015-4063-z

ORIGINAL

Irene J. Zaal
John W. Devlin
Marijn Hazelbag
Peter M. C. Klein Klouwenberg
Arendina W. van der Kooi
David S. Y. Ong
Olaf L. Cremer
Rolf H. Groenwold
Arjen J. C. Slooter

Benzodiazepine-associated delirium in critically ill adults

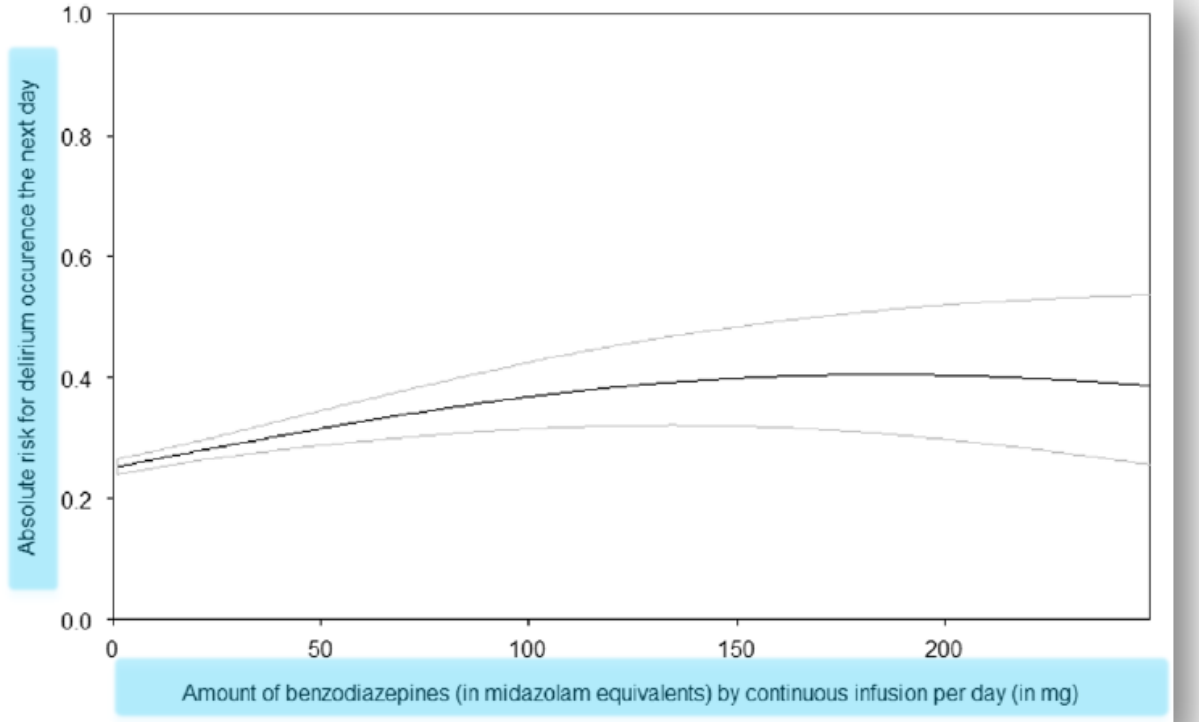


Fig. 2 Continuous infusion of benzodiazepines and the risk for delirium the next day. Among patients awake and without delirium with mean/median values for all other covariables, the absolute risk is plotted for delirium occurring the next day (*y-axis*) conditional on continuously infused IV benzodiazepine (*x-axis*). The 95 % confidence interval is plotted in *gray*

GENETIQUE

Table 3. Clinical outcomes (bivariate analysis)[a]

Variable	APOE4 Present (n = 12)	APOE4 Absent (n = 41)	*p* Values[b]
Days of delirium	4 (3, 4.5)	2 (1, 4)	.05
Coma days	1 (0, 4.5)	2 (0, 5)	.45
ICU length of stay	9.5 (6, 14)	7 (5, 11)	.37
Hospital length of stay	12 (8.5, 17.5)	10 (7, 15)	.53
Ventilator-free days	21.1 (15, 24)	22 (0, 26)	.72
Days on ventilator	5.5 (3.9, 8.9)	4 (2, 8)	.49
Mortality, % (n)	8.3 (1/12)	24.4 (10/41)	.42

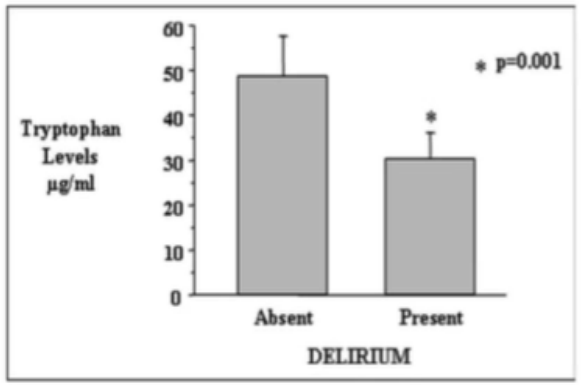
APOE4, apolipoprotein E4; ICU, intensive care unit.

[a]All data are presented as median with interquartile ranges with the exception of mortality, which is % (n); [b]unadjusted *p* values were obtained using Wilcoxon rank-sum tests for all except for mortality, where Fisher's exact test was used.

APOE: rôle dans l'amyloïdogenese/Alzheimer

Ely et al – CCM - 2007

Intérêt des biomarqueurs



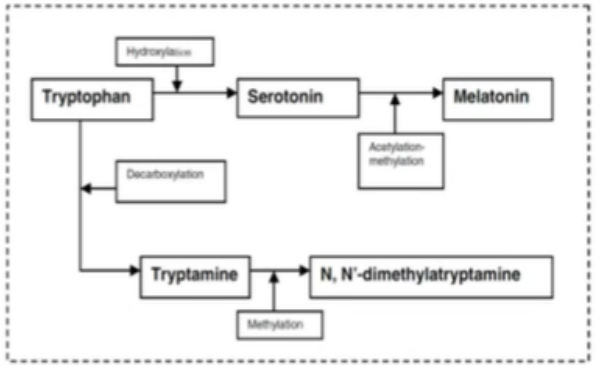
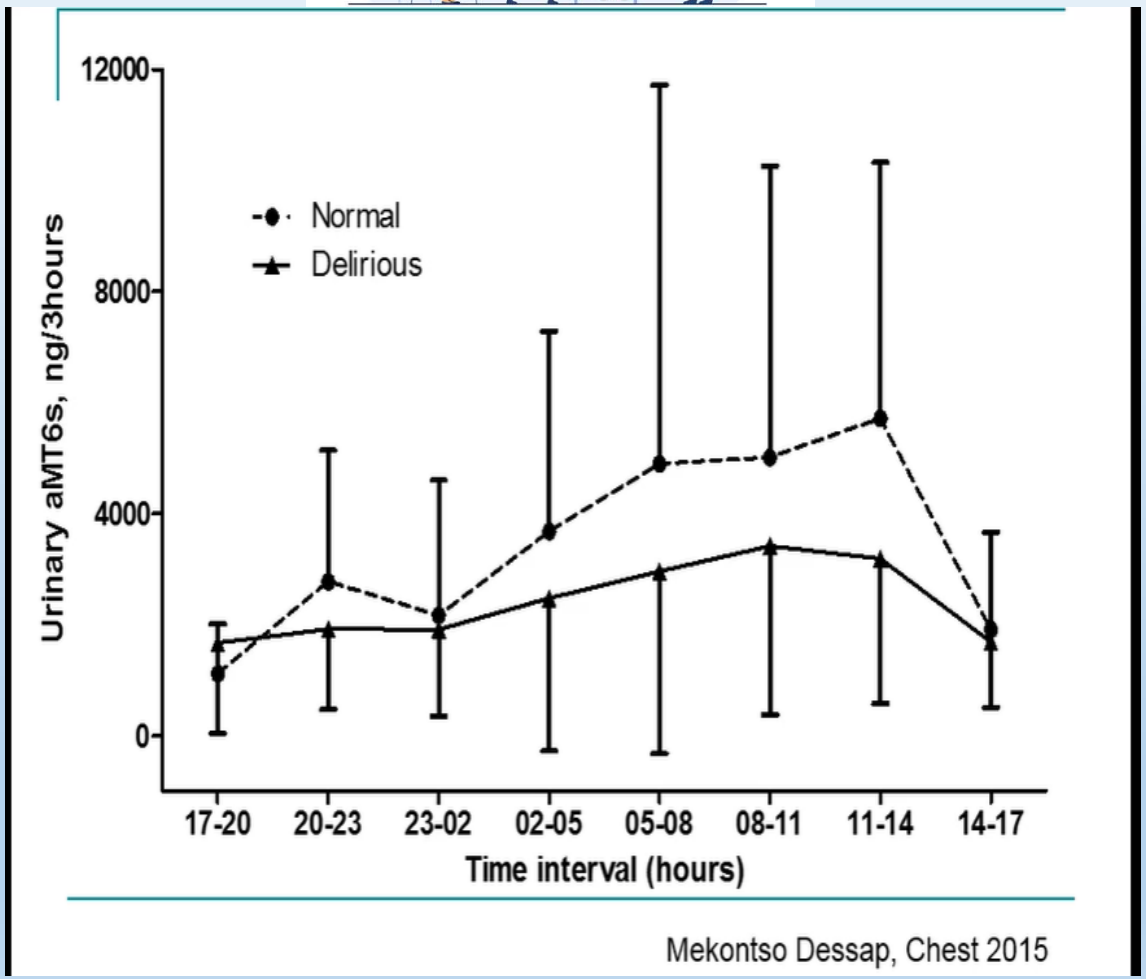


Figure 2 Metabolism of the indoleamines.

Robinson, AJS 2008

Lewis, Med Hyp 2004



Mekontso Dessap, Chest 2015

BMJ 2012;344:e420 doi: 10.1136/bmj.e420 (Published 9 February 2012)

RESEARCH

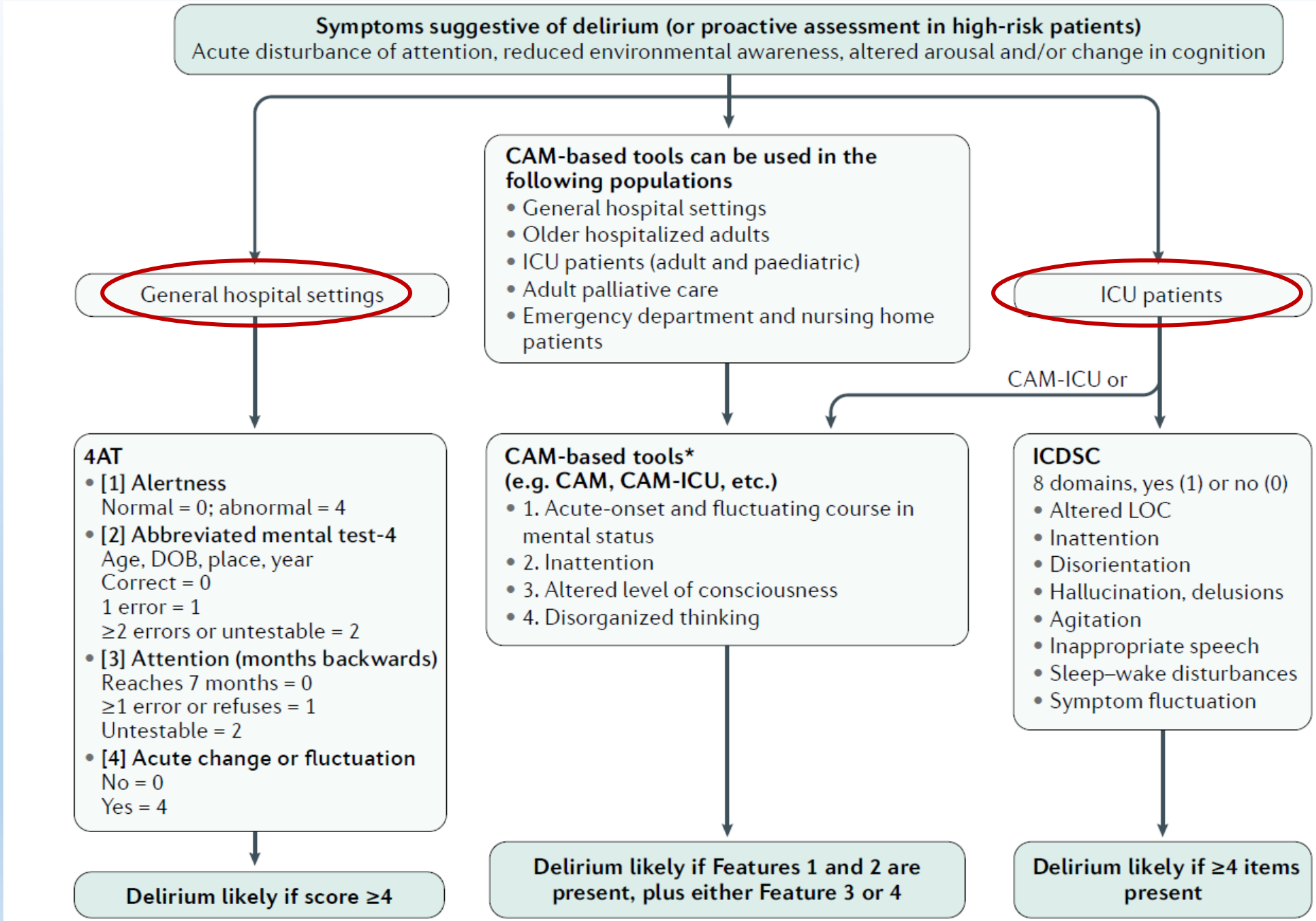
Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study

3056 intensive care patients
5 medical ICUS in the Netherlands

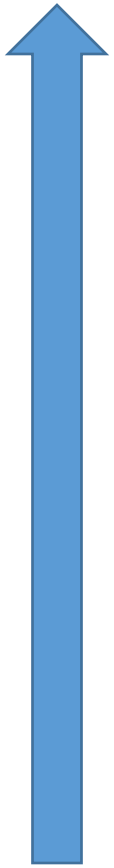
The **PRE-DELIRIC** model for intensive care patients consists of **10 risk factors** that are **readily available within 24 hours after intensive care admission** and has a **high predictive value.**

	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio
Low risk	80.7	74.7	3.19	0.26
Moderate risk	62.0	88.8	5.54	0.43
High risk	46.3	94.6	8.57	0.57
Very high risk	30.0	97.7	13.0	0.72

Variable	Regression coefficient	Odds ratio (95% CI)
Age (years)	0.04	1.04 (1.03 to 1.06)
APACHE-II score (per point)	0.06	1.06 (1.03 to 2.0)
Coma:		
Drug induced	0.59	1.8 (1.1 to 3.1)
Miscellaneous	2.92	18.5 (4.6 to 73.8)
Combination	3.06	21.3 (5.9 to 77.1)
Admission category:		
Surgery	Reference	Reference
Medical	0.33	1.4 (0.9 to 2.2)
Trauma	1.22	3.4 (1.7 to 6.8)
Neurology/neurosurgery	1.49	4.5 (2.6 to 7.5)
Infection (yes)	1.14	3.1 (2.0 to 4.8)
Metabolic acidosis (yes)	0.32	1.4 (1.0 to 2.0)
Morphine use:		
0.01-7.1 mg/day	0.44	1.6 (0.8 to 3.1)
7.2-18.6 mg/day	0.14	1.2 (0.8 to 1.8)
>18.6 mg/day	0.55	1.8 (1.1 to 2.7)
Sedation (yes)	1.51	4.5 (2.8 to 7.4)
Urea (mmol/L)	0.03	1.03 (1.0 to 1.1)
Urgent admission (%)	0.43	1.5 (1.1 to 2.3)
Intercept	−6.76	


Symptoms suggestive of delirium (or proactive assessment in high-risk patients)
Acute disturbance of attention, reduced environmental awareness, altered arousal and/or change in cognition
CAM-based tools can be used in the following populations
• General hospital settings
• Older hospitalized adults
• ICU patients (adult and paediatric)
• Adult palliative care
• Emergency department and nursing home patients
General hospital settings
ICU patients
CAM-ICU or
4AT
• [1] Alertness
Normal = 0; abnormal = 4
• [2] Abbreviated mental test-4
Age, DOB, place, year
Correct = 0
1 error = 1
≥2 errors or untestable = 2
• [3] Attention (months backwards)
Reaches 7 months = 0
≥1 error or refuses = 1
Untestable = 2
• [4] Acute change or fluctuation
No = 0
Yes = 4
CAM-based tools*
(e.g. CAM, CAM-ICU, etc.)
• 1. Acute-onset and fluctuating course in mental status
• 2. Inattention
• 3. Altered level of consciousness
• 4. Disorganized thinking
ICDSC
8 domains, yes (1) or no (0)
• Altered LOC
• Inattention
• Disorientation
• Hallucination, delusions
• Agitation
• Inappropriate speech
• Sleep–wake disturbances
• Symptom fluctuation
Delirium likely if score ≥4
Delirium likely if Features 1 and 2 are present, plus either Feature 3 or 4
Delirium likely if ≥4 items present

RASS : Richmond Agitation Sedation Scale



Score	Définition	Description
+ 4	Violent	Danger immédiat pour personnel soignant
+ 3	Très agité	Agressif, arrache cathéters, sondes…
+ 2	Agité	Lutte contre ventilateur, mouvements fréquents sans but
+ 1	Sans repos	Anxieux, sans mouvements vifs ou agressifs
0	Calme, éveillé	
- 1	Somnolent	Ouvre les yeux à l'appel (contact visuel soutenu, > 10s)
- 2	Sédation légère	Réveil bref à l'appel (contact visuel < 10s)
- 3	Sédation modérée	Ouvre les yeux ou bouge à l'appel (contact visuel : 0)
- 4	Sédation profonde	Pas de réponse à l'appel, réactif aux stim. douloureuses
- 5	Non réveillable	Pas de réponse à l'appel ou aux stim. douloureuses

Confusion Assessment Method for the ICU (CAM-ICU)

1. Modification de l'état neurologique par rapport à l'état habituel ?
Début brutal, fluctuations

et

2. inattention, distractibilité

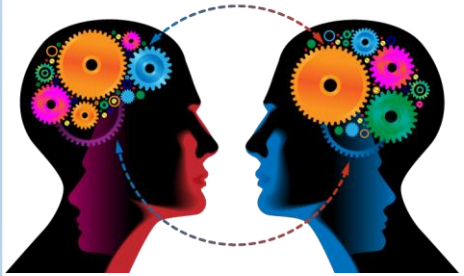
et

3. Altération du niveau de conscience

ou

4. Altération du « jugement »

ABRACADABRA



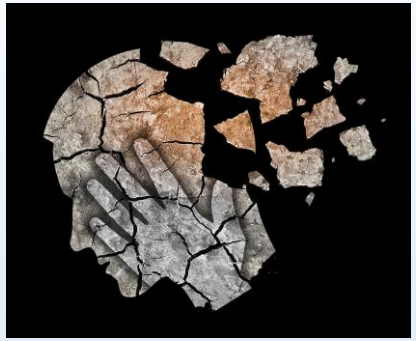
=

DELIRIUM

Sensibilité 93-100%
Spécificité 89-100%

Ely, JAMA 2001

DÉSORGANISATION DE LA PENSÉE



Existe-t-il des signes de pensée désorganisée ou incohérente mis en évidence par au moins 3 réponses incorrectes sur 4 et/ou l'incapacité à exécuter les ordres ?

Questions (alterner les jeux de questions A et B) :

Jeu A :
1. Une pierre flotte-t-elle sur l'eau ?
2. Y a-t-il des poissons dans la mer ?
3. Un kilogramme pèse-t-il plus que 2 k
4. Pouvez-vous utiliser un marteau pour

Jeu B :
1. Une feuille flotte-t-elle sur l'eau ?
2. Y a-t-il des éléphants dans la mer ?
3. Deux kilogrammes pèsent-t-ils plus q
4. Pouvez-vous utiliser un marteau pour

NIVEAU DE CONSCIENCE

Le niveau de conscience du patient est-il différent de « éveillé »
- **Eveillé** = spontanément attentif à son environnement avec des interactions appropriées
- **Hyper vigilant**
- **Obnubilé** =endormi mais facilement réveillé, ignorant certains éléments de son environnement, ou n'interagissant pas spontanément de façon appropriée avec l'examinateur; devenant complètement attentif et approprié avec une stimulation minimale.
- **Stuporeux** =pas complètement attentif malgré une forte stimulation ; peut seulement être réveillé par des stimulations vigoureuses et répétées, et dès qu'elles cessent, le patient tombe de nouveau dans un état stuporeux
- **Comateux** = que l'on peut réveiller ; pas d'interaction spontanée ou conscience de la présence de l'examinateur (meme après stimulation maximale)

Ben Saida *et al. BMC Psychiatry* (2020) 20:206
https://doi.org/10.1186/s12888-020-02622-z

BMC Psychiatry

RESEARCH ARTICLE Open Access

A Tunisian version of the confusion assessment method for the intensive care unit (CAM-ICU): translation and validation

أداة تقييم الهذيان في وحدة العناية المرّكزّة : ورقة توضيحية اللهجة التونسية

1. **تغيير حاد أو تقلّب في سير الحالة الذهنية المعتادة للمريض**
   - هل أن الحالة الذهنية غير مطابقة لحالته المعتادة عند الدخول ؟ أو
   - هل أن الحالة الذهنية تغيرت خلال 24 ساعة الماضية.

لا ← **لا يوجد هذيان**
اداة تقييم الهذيان في وحدة العناية المركزة سلبية

نعم ↓

2. **فحص الانتباه:**

كل ما تسمع حرف "م" اكبسلي على يدي، وتقرالو مجموعة الحروف بنفس نبرة الصوت :
" م ح م ود م ا ط ري "

الأخطاء : احتساب خطأ كلما غفل المريض عن الضغط عند مرور الحرف المذكور "م" أو كلما ضغط في الحرف غير المناسب.
إذا كان المريض غير قادر على استكمال الحروف ← استعمل دليل الصور

2-0 خطأ ← **لا يوجد هذيان**
اداة تقييم الهذيان في وحدة العناية المركزة سلبية

2< خطأ ↓


3. اختلال درجة الوعي
مجموع اختبار مقياس درجة التخدير (مقياس ريتشموند RASS) الحالي
RASS
مخالف للصفر
يوجد هذيان
أداة تقييم
الهذيان في وحدة
العناية المركزة
إيجابية
RASS =0
4. اختلال تنظيم التفكير
الأسئلة
" الحجرة تعوم عل الماء "؟
" فما حوت في البحر"؟
"أناهو الي يوزن أكثر؟ الكيلو ولا زوز كيلو "؟
"انجمو نستعملو مطرقة بش ندقو مسمار"؟
الأوامر
وريني العدد هذا بصوابعك " (المقيّم يشير بإصبعين للمريض) ثم اطلب منه
" توة وريني العدد هذا بيدك لخرى " (لا تكرر نفس العدد)
أو "أضف إصبعا اخر " إذا كان المريض غير قادر على تحريك ذراعيه
1< خطأ
1-0 خطأ
لا يوجد هذيان
أداة تقييم
الهذيان في وحدة
العناية المركزة
سلبية

Intensive Care Delirium Screening Checklist (ICDSC)

8 items, côtés 0 ou 1

Réalisée une fois par 8 heures

Si total > ou = 4 : DELIRIUM

1. Conscience altérée (Si A ou B, ne pas poursuivre évaluation)
   - A. Pas de réponse à stimulation : ne pas coter
   - B. Réponse à une stimulation intense et répétée (voix, douleur) : idem
   - C. Réponse à une stimulation modérée : 1
   - D. Patient normalement éveillé : 0
   - E. Réponse exagérée à la stimulation : 1
2. Inattention (0 ou 1)
3. Désorientation (0 ou 1)
4. Hallucinations (0 ou 1)
5. Agitation ou ralentissement psychomoteur (0 ou 1)
6. Discours ou humeur inappropriés (0 ou 1)
7. Troubles du cycle veille-sommeil (0 ou 1)
8. Fluctuations des symptômes (0 ou 1)

Bergeron ICM, 2001

Chanques et al. Ann. Intensive Care (2018) 8:33
https://doi.org/10.1186/s13613-018-0377-7

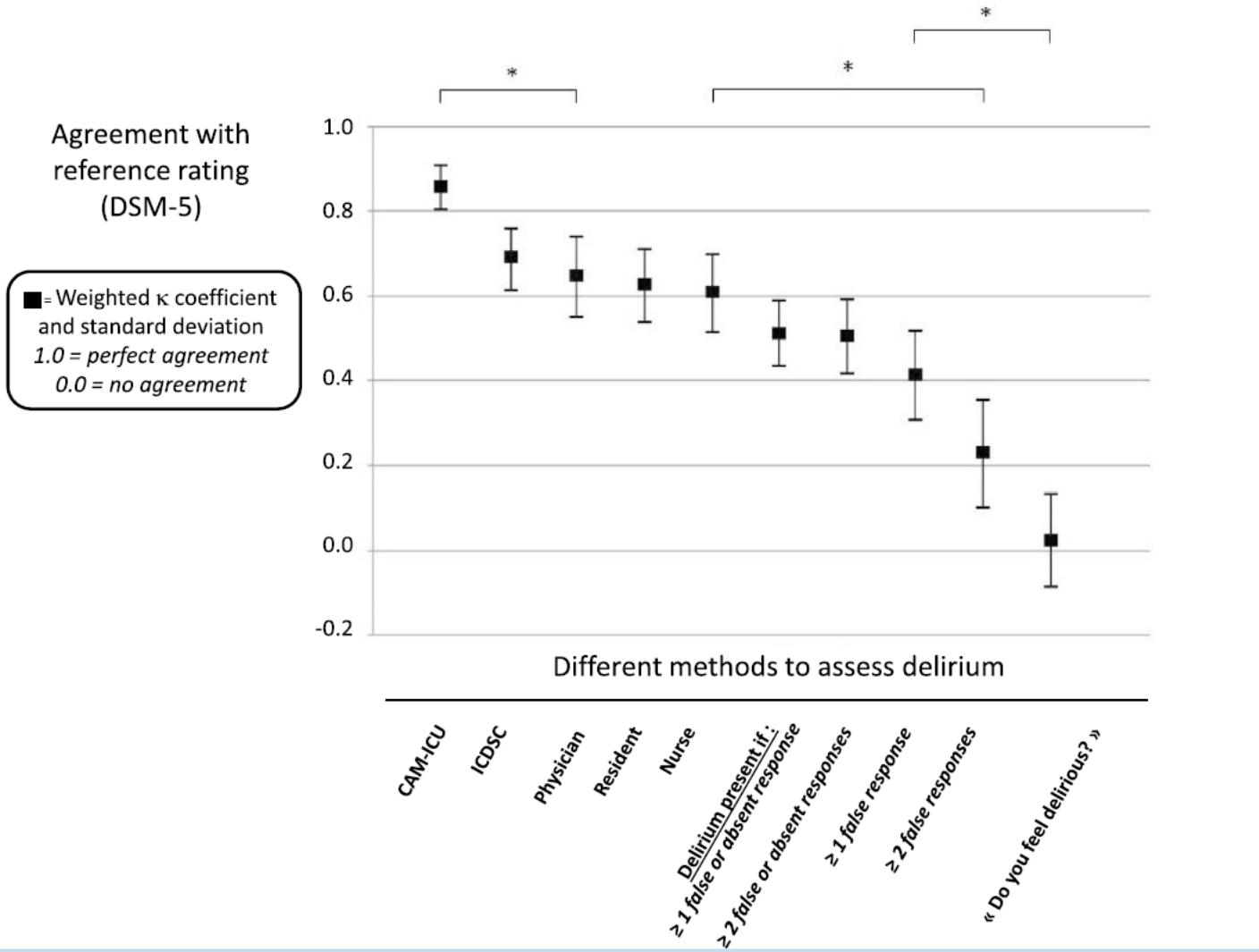
Annals of Intensive Care

RESEARCH Open Access

The 2014 updated version of the Confusion Assessment Method for the Intensive Care Unit compared to the 5th version of the Diagnostic and Statistical Manual of Mental Disorders and other current methods used by intensivists

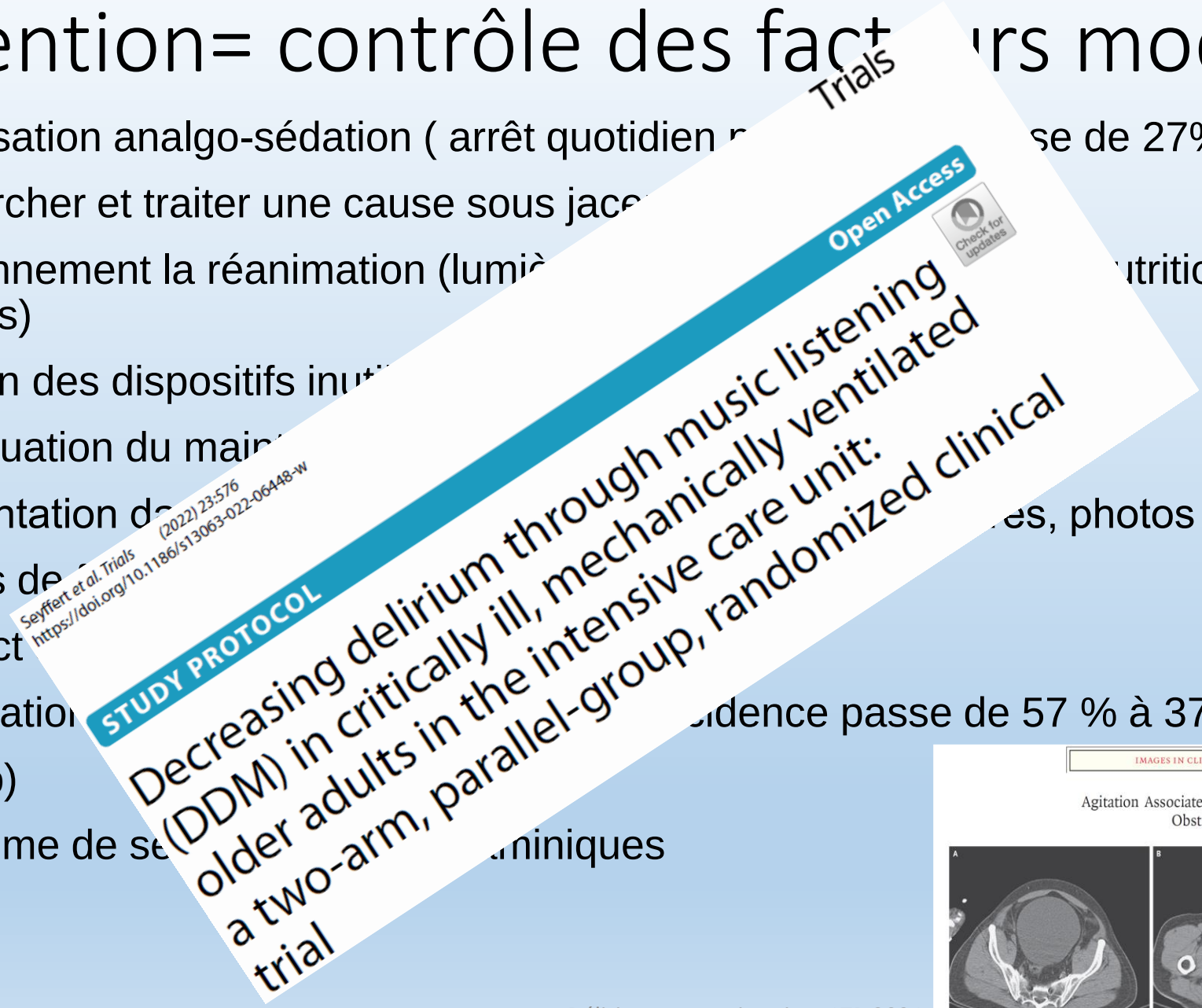
Gérald Chanques[1,2*†], E. Wesley Ely[3,4†], Océane Garnier[1], Fanny Perrigault[5], Anaïs Eloi[5], Julie Carr[1], Christine M. Rowan[3], Albert Prades[1], Audrey de Jong[1,2], Sylvie Moritz-Gasser[5,6], Nicolas Molinari[7] and Samir Jaber[1,2]

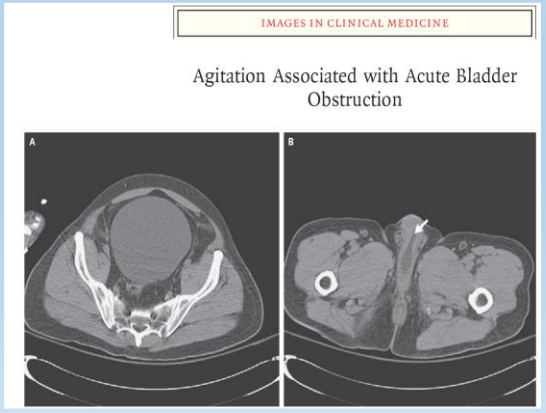
Étude prospective
psychomotrice
108 patients
Delirium=38%
RASS≥ -3



Prévention= contrôle des fact urs modifiables

- Optimisation analgo-sédation (arrêt quotidien r se de 27% à 9% ,NEJM 2001)
- Rechercher et traiter une cause sous jace
- Environnement la réanimation (lumi utrition, intensité des alarmes)
- Ablation des dispositifs inu
- Réévaluation du mai
- Réorientation d es, photos des membres de
- Respect
- Mobilisatio idence passe de 57 % à 37%, Lancet 2009)
- Syndrome de se niniques





Approche **ABCDEF**

ABCDEF bundle component[267]	Approach	D
A	Assess, prevent pain	
B	Be	
C		caused by es; over-sedation sed by sedatives; exposure to deliriogenic sedatives (for example, benzodiazepines)
D	prevent and	Disordered sleep–wake cycle; vision and hearing impairment; other unrecognized delirium risk factors
	Early mobility and exercise	Immobility
	Family engagement and empowerment	Disorientation

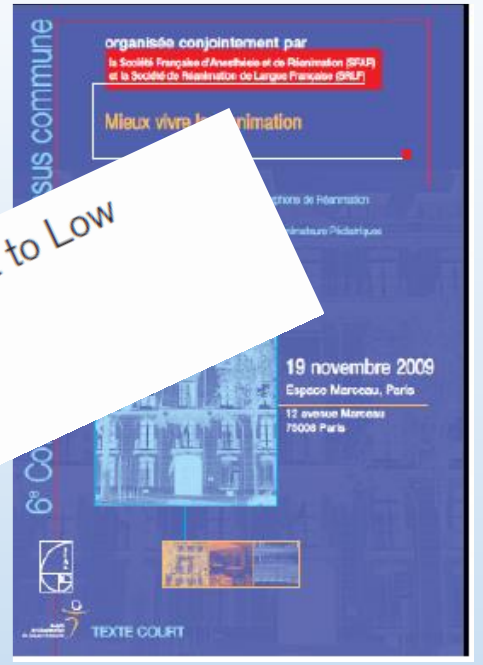
Executive Summary: Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

Conditional

VL to Low

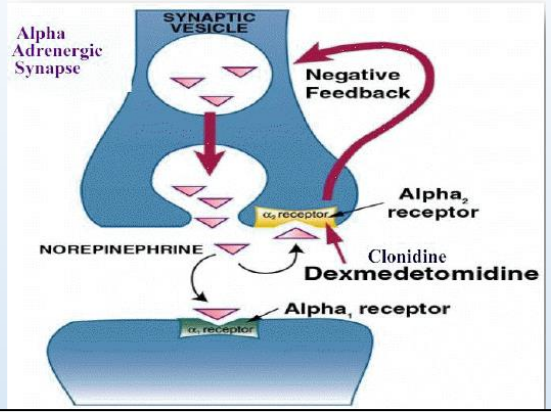
We suggest not using haloperidol, an atypical antipsychotic, dexmedetomidine, a HMG-CoA reductase inhibitor (i.e., statin), or ketamine to prevent delirium in all critically ill adults.

Should a pharmacologic agent (vs no use of this agent) be used to "prevent" delirium in critically ill adults?

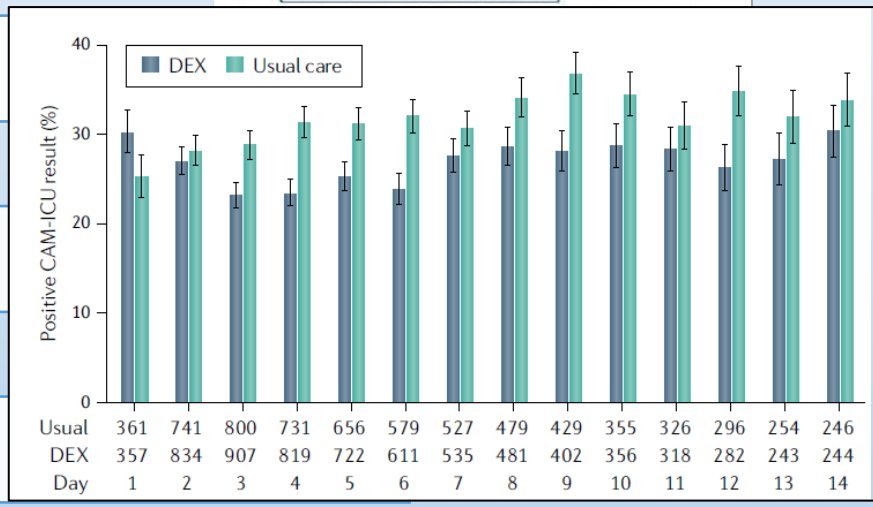


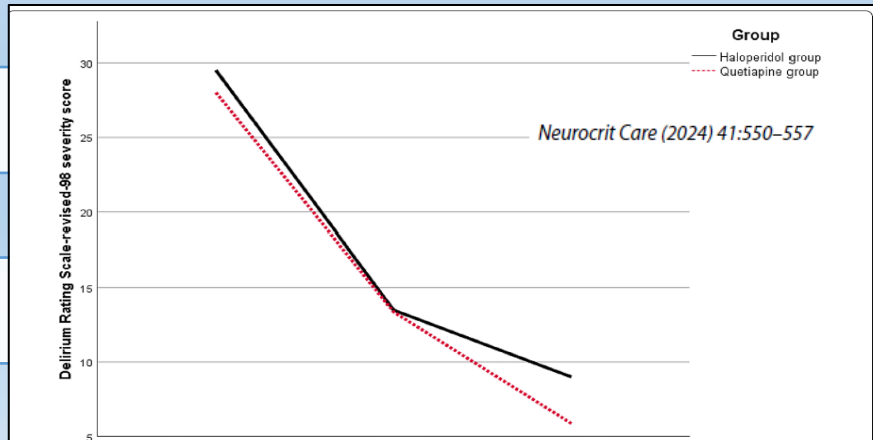
PADIS guidelines, CCM 2018

Traitement = Antipsychotique/NLP



- **Dexmedetomidine/Clonidine = α2-agonistes**
- **Halopéridol= Neuroleptique antagoniste des récepteurs dopaminergiques D2**
- **Loxapine**
- **Antipsychotiques atypiques: Quetiapine, Ziprasidone, Olanzapine**
- **Statines: Inhibiteurs HMG-CoA reductase (Rosuvastatin, Simvastatine)**





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

Should a pharmacologic agent (vs no use of this agent) be used to treat delirium in all critically ill adults with delirium?	We suggest not routinely using haloperidol, an atypical antipsychotic, or a HMG-CoA reductase inhibitor (i.e., a statin) to treat delirium. We suggest using dexmedetomidine for delirium in mechanically ventilated adults where agitation is precluding weaning/extubation.	Conditional Conditional	Low Low

Durée la plus courte, dose minimale nécessaire

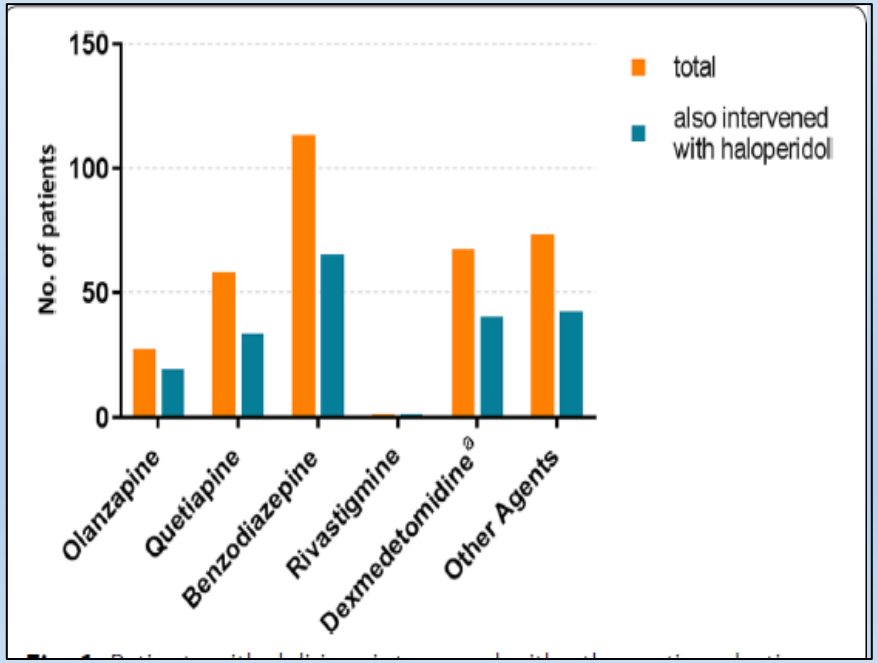
(*Crit Care Med* 2018; 46:1532–1548)

Intensive Care Med (2018) 44:1081–1089
https://doi.org/10.1007/s00134-018-5204-y

ORIGINAL

Prevalence and risk factors related to haloperidol use for delirium in adult intensive care patients: the multinational AID-ICU inception cohort study

99 ICU, 1260 patients, 14 j d'inclusion, delirium à 25%, 46% des patients délirants ont reçu Halopéridol



	All patients (*N* = 1260)	No haloperidol (*N* = 1094)	Haloperidol (*N* = 166)	*p*-value[b]
First 24-h in ICU admission				
In coma, *n* (%)	479 (38.0)	390 (35.7)	89 (53.6)	< 0.01
Delirium[b], *n* (%)	125 (9.9)	71 (6.5)	54 (32.5)	< 0.01
Mechanical ventilation, *n* (%)	702 (55.7)	581 (53.1)	121 (72.9)	< 0.01
Circulatory support, *n* (%)	569 (45.2)	453 (41.4)	116 (70.1)	< 0.01
Renal replacement therapy, *n* (%)	105 (8.3)	86 (7.9)	19 (11.5)	0.12

Table 1 Haloperidol use in milligram presented as the cumulative dose received during ICU stay and median administrated daily dose

	% Of the 1260 patients (95% CI)	Median cum. dose (in mg) (IQR)	Median daily dose (in mg) (IQR)
Haloperidol (*n* = 166)	13.2 (11.4–15.2)	18 (6–55)	10 (5–15)
As fixed dose	9.8 (8.2–11.5)	12 (5–46)	5 (3–10)
As per needed dose	12.4 (10.6–14.3)	10 (5–30)	5 (3–10)

Conclusions

- Délirium: sous diagnostiqué/traduit une souffrance cérébrale aigue
- Impact sur le pronostic
- Stratégie multifacette:
  - Identification des patients à risque
  - Moyens non pharmacologique (environnement/gestion de la sédation/ immobilisation)
  - Humanisation de la réanimation
  - Diminuer la prescription des opioïdes/benzodiazépines
  - Moyens pharmacologiques de dernier recours (agitation++,hallucination, anxiété)
- Benzodiazépine= Délirium Tremens