Y-a-t-il une alternative aux morphinomimétiques pour la prise en charge de la douleur en réanimation

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La 4ème Journée COmmune de Réanimation
Hammamet 31 mai 2025

Douleur en USI et réanimation

Douleur en réanimation: Fréquente, Intense, Délétère

Determinants of Procedural Pain Intensity in the Intensive Care Unit

The Europain® Study

Am J Respir Crit Care Med 2014, Vol 189, Iss 1, pp 39–47

ences in Pain Intensity from before the Procedure to during the Procedure

cedure	N (%)	Preprocedural Pain Intensity Median (IQR)	Pain Intensity During the Procedure Median (IQR)	Difference Median (IQR)	V
tube removal	292 (6.1)	2 (0–4)	5 (3–7)	2.5 (0.5–4)	<0
d drain removal	75 (1.6)	2 (0–4)	4.5 (2–7)	2 (0–4.5)	<0
l line insertion	199 (4.1)	1 (0–2.5)	4 (2–6)	2.75 (0–5)	<0
racheal suctioning	767 (15.9)	1 (0–4)	4 (1–6)	1.5 (0–4)	<0
eal suctioning	302 (6.3)	1 (0–3.5)	4 (1–6)	1 (0–4)	<0
eral intravenous rtion	315 (6.5)	1 (0–3)	3 (1–5.5)	1 (0–3)	<0
eral blood draw	328 (6.8)	0.5 (0–3)	3 (1–5)	1 (0–3)	<0
g	873 (18.1)	1.75 (0–4)	3 (0.25–6)	1 (0–2.5)	<0
ratory exercises	439 (9.1)	2 (0–4)	3 (1–5)	1 (0–2)	<0
oning	371 (7.7)	1 (0–4)	3 (0–5)	1 (0–2)	<0
d care	301 (6.3)	2 (0–4)	3 (1–6)	0.5 (0–2)	<0
zation	526 (10.9)	1 (0–3)	2 (0–5)	0 (0–2)	<0

Analgésie (Sédation) en USI et réanimation

Concepts en évolution

SPECIAL ARTICLE Mars 2025 - Volume 53 - Numéro 3

A Focused Update to the Clinical Practice Guidelines for the Prevention Management of Pain, Anxiety, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

2000	Sedation target						
2008	Sedation goal confort (not coma) in most patients	Analgesia target					
2013	Pain top priority if present	Agitation	Delirium				
2018	**P**ain mutimodal approach	**A**gitation	**D**elirium	**I**mmobility	**S**leep disruption	**PADIS**	
2025	**P**ain mutimodal approach	**A**gitation	**D**elirium	**I**mmobility	**S**leep disruption	ANXIETE	

Analgésie (Sédation) en USI et réanimation

A2F global bundle : concepts intriqués

Assess = prévention et gestion de la douleur (priorité)

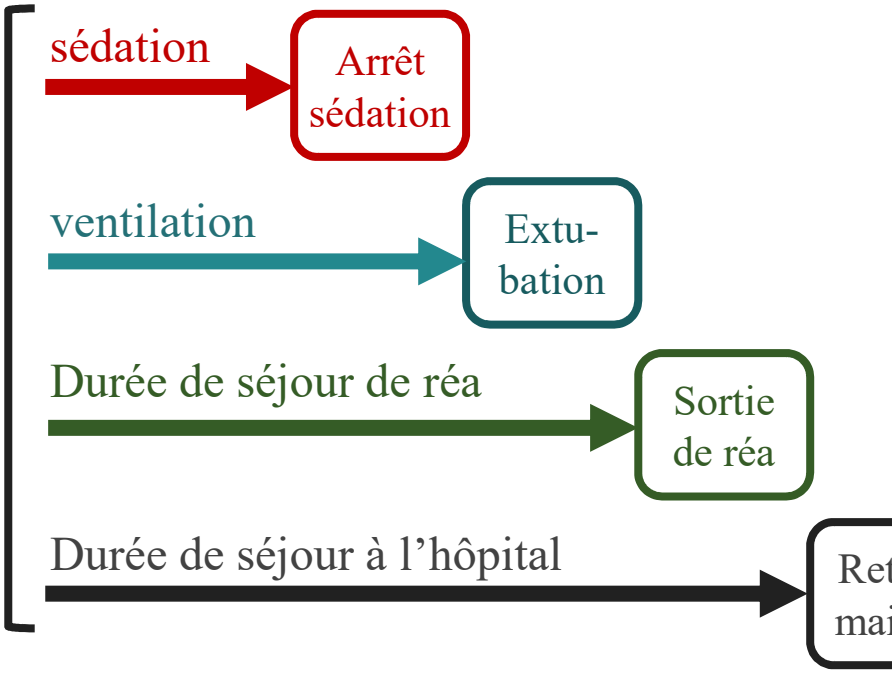
Both = combiner épreuves d'arrêt sédation/ventilation

Choice = choix des médicaments, adaptation posologique

Delirium = dépistage et gestion (diagnostic++)

Early = exercice, mobilisation, réhabilitation précoce

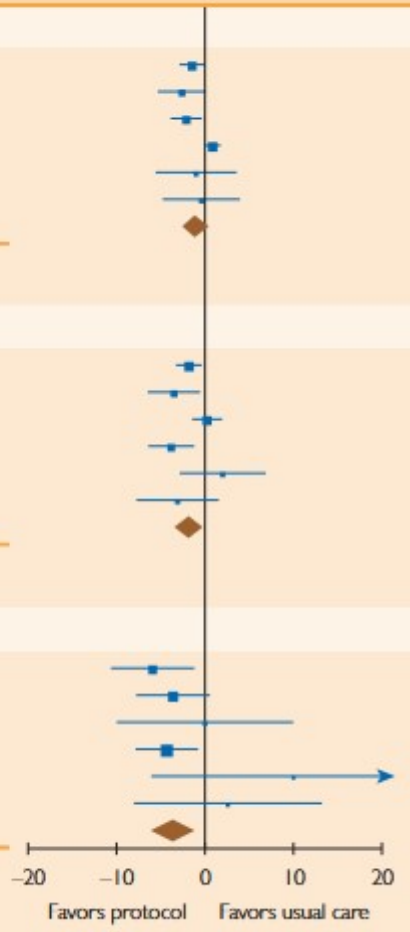
Family = famille impliquée, autonome



Effect of Protocolized Sedation on Clinical Outcomes in Mechanically Ventilated Intensive Care Unit Patients: A Systematic Review and Meta-analysis of Randomized Controlled Trials

2015 Mayo Foundation for Medical Education and Research ■ Mayo Clin Proc. 2015;■■(■):1-11

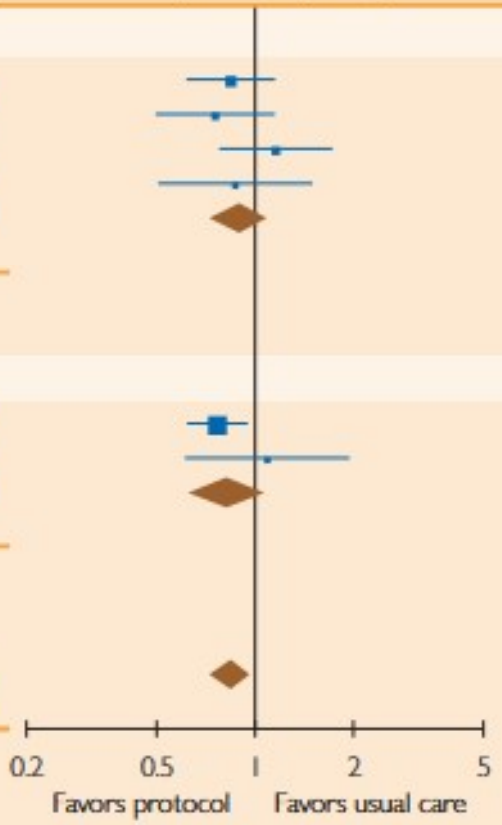
Study	Protocolized sedation Mean	SD	Total	Usual care Mean	SD	Total	Weight (%)	Mean difference IV, random (95% CI)
Duration of mechanical ventilation								
Brook et al,[7] 1999	3.71	5.56	162	5.16	6.4	159	22.6	−1.45 (−2.76 to −0.14)
Kress et al,[8] 2000	4.7	4.52	68	7.3	9.41	60	15.0	−2.60 (−5.21 to 0.01)
Girard et al,[11] 2008	7.1	7	167	9.2	8.4	168	20.5	−2.10 (−3.76 to −0.44)
Bucknall et al,[12] 2008	3.29	3.61	153	2.41	3.45	159	25.4	0.88 (0.10 to 1.66)
Anifantaki et al,[10] 2009	7.7	13.5	49	8.7	8.35	48	8.0	−1.00 (−5.46 to 3.46)
Weisbrodt et al,[9] 2011	8	8.08	26	8.4	7.3	24	8.5	−0.40 (−4.66 to 3.86)
Subtotal (95% CI)			**625**			**618**	**100.0**	**−1.04 (−2.54 to 0.47)**
Heterogeneity: τ^2=2.16; χ^2=19.20, *df*=5 (*P*=.002); I^2=74%								
Test for overall effect: *z*=1.35 (*P*=.18)								
ICU LOS								
Brook et al,[7] 1999	5.7	5.9	162	7.5	6.5	159	25.6	−1.80 (−3.16 to −0.44)
Kress et al,[8] 2000	6.4	6.01	68	9.9	9.78	60	15.6	−3.50 (−6.36 to −0.64)
Bucknall et al,[12] 2008	3.92	7.66	153	3.67	6.58	159	23.9	0.25 (−1.34 to 1.84)
Girard et al,[11] 2008	9.1	9.41	167	12.9	13.49	168	17.8	−3.80 (−6.29 to −1.31)
Anifantaki et al,[10] 2009	14	13.5	49	12	10.17	48	8.3	2.00 (−2.75 to 6.75)
Weisbrodt et al,[9] 2011	8.2	8.08	26	11.3	8.3	24	8.8	−3.10 (−7.65 to 1.45)
Subtotal (95% CI)			**625**			**618**	**100.0**	**−1.73 (−3.32 to −0.14)**
Heterogeneity: τ^2=2.10; χ^2=12.58, *df*=5 (*P*=.03); I^2=60%								
Test for overall effect: *z*=2.13 (*P*=.03)								
Hospital LOS								
Brook et al,[7] 1999	14	17.3	162	19.9	24.2	159	22.8	−5.90 (−10.51 to −1.29)
Kress et al,[8] 2000	13.3	9.41	68	16.9	13.42	60	27.9	−3.60 (−7.67 to 0.47)
Bucknall et al,[12] 2008	13	18.6	153	13	60.6	159	5.8	0.00 (−9.87 to 9.87)
Girard et al,[11] 2008	14.9	13.26	167	19.2	18.3	168	36.1	−4.30 (−7.72 to −0.88)
Anifantaki et al,[10] 2009	31	47.6	49	21	31.6	48	2.3	10.00 (−6.05 to 26.05)
Weisbrodt et al,[9] 2011	21.1	22.76	26	18.5	14.6	24	5.1	2.60 (−7.92 to 13.12)
Subtotal (95% CI)			**625**			**618**	**100.0**	**−3.55 (−5.98 to −1.12)**
Heterogeneity: τ^2=1.20; χ^2=5.71, *df*=5 (*P*=.34); I^2=12%								
Test for overall effect: *z*=2.86 (*P*=.004)								



Effect of Protocolized Sedation on Clinical Outcomes in Mechanically Ventilated Intensive Care Unit Patients: A Systematic Review and Meta-analysis of Randomized Controlled Trials

2015 Mayo Foundation for Medical Education and Research ■ Mayo Clin Proc. 2015;■■(■):1-11

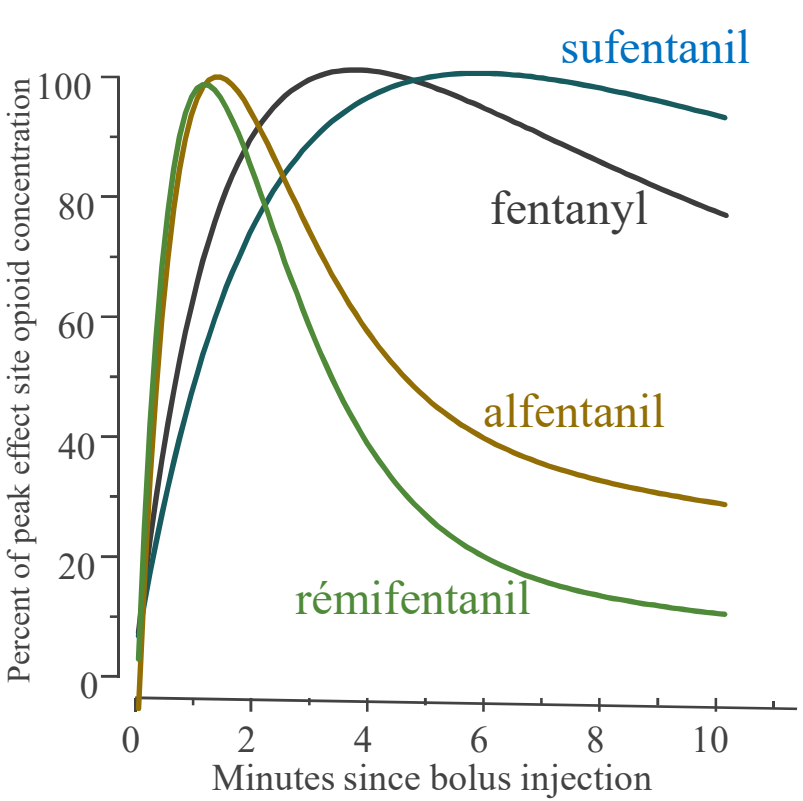
Study	Protocolized sedation Events	Protocolized sedation Total	Usual care Events	Usual care Total	Weight (%)	Risk ratio M-H, random (95% CI)
Hospital mortality						
Brook et al,[7] 1999	49	162	57	159	20.3	0.84 (0.62-1.15)
Kress et al,[8] 2000	24	68	28	60	11.2	0.76 (0.50-1.15)
Bucknall et al,[12] 2008	39	153	35	159	12.5	1.16 (0.78-1.73)
Anifantaki et al,[10] 2009	16	49	18	48	6.7	0.87 (0.51-1.50)
Subtotal (95% CI)		**432**		**426**	**50.7**	**0.89 (0.73-1.09)**
Total events	128		138			
Heterogeneity: τ^2=0.00; χ^2=2.38, *df*=3 (*P*=.50); I^2=0%						
Test for overall effect: *z*=1.11 (*P*=.27)						
6- to 12-month mortality						
Girard et al,[11] 2008	74	167	97	168	43.4	0.77 (0.62-0.95)
Weisbrodt et al,[9] 2011	13	26	11	24	5.9	1.09 (0.61-1.95)
Subtotal (95% CI)		**193**		**192**	**49.3**	**0.82 (0.63-1.08)**
Total events	87		108			
Heterogeneity: τ^2=0.01 χ^2=1.24, *df*=1 (*P*=.27); I^2=20%						
Test for overall effect: *z*=1.41 (*P*=.16)						
Total (95% CI)		**625**		**618**	**100.0**	**0.85 (0.74-0.97)**
Total events	215		246			
Heterogeneity: τ^2=0.00 χ^2=4.25, *df*=5 (*P*=.51); I^2=0%						
Test for overall effect: *z*=2.32 (*P*=.02)						
Test for subgroup differences: χ^2=0.24, *df*=1 (*P*=.62); I^2=0%						

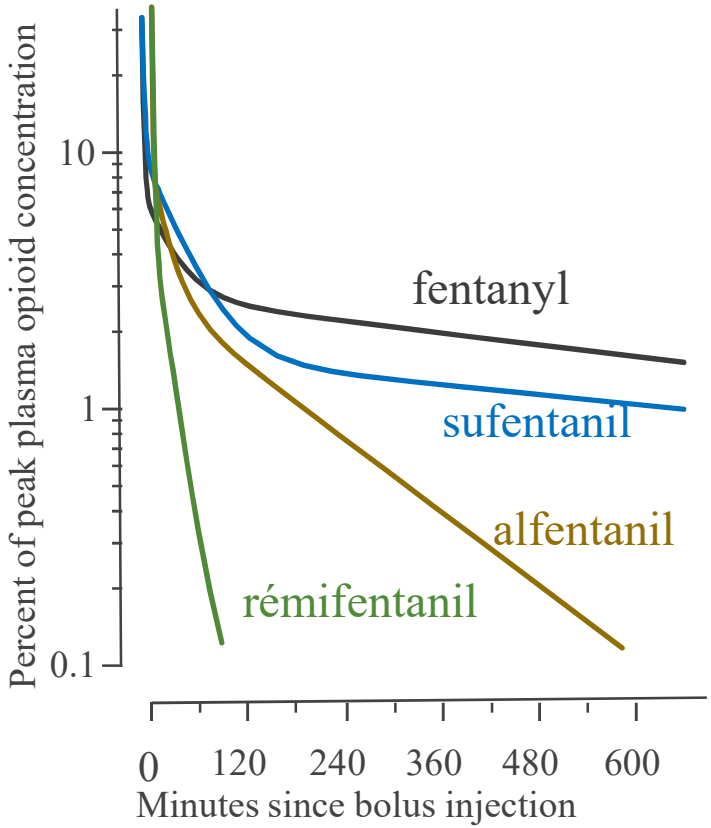


Analgésie en USI et réanimation
Choix des médicaments : Points directeurs

Analgésie en réanimation: morphiniques de 1ère intention

Morphine : Pas en continu; $T_{1/2}$ longue, métabolite actif (G6M); attention en cas d'IR





Minto et al, Anesthesiology,

Analgésie en USI et réanimation
Choix des médicaments : Points directeurs

Y-a-t-il une alternative aux morphinomimétiques?

① Pourquoi cette question ?

EI, balance bénéfice/risque

② Comment remplacer les morphiniques ?

Analgésie en USI et réanimation
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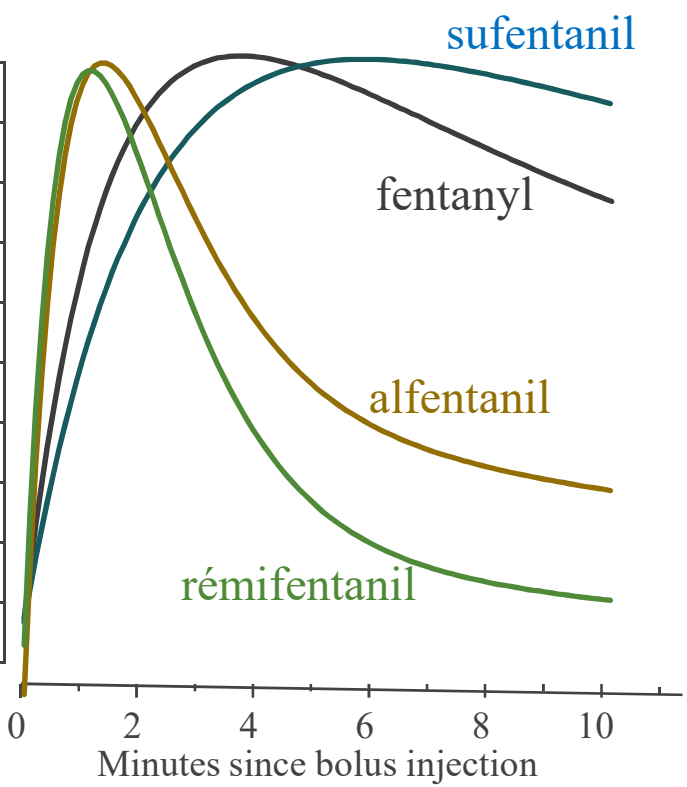
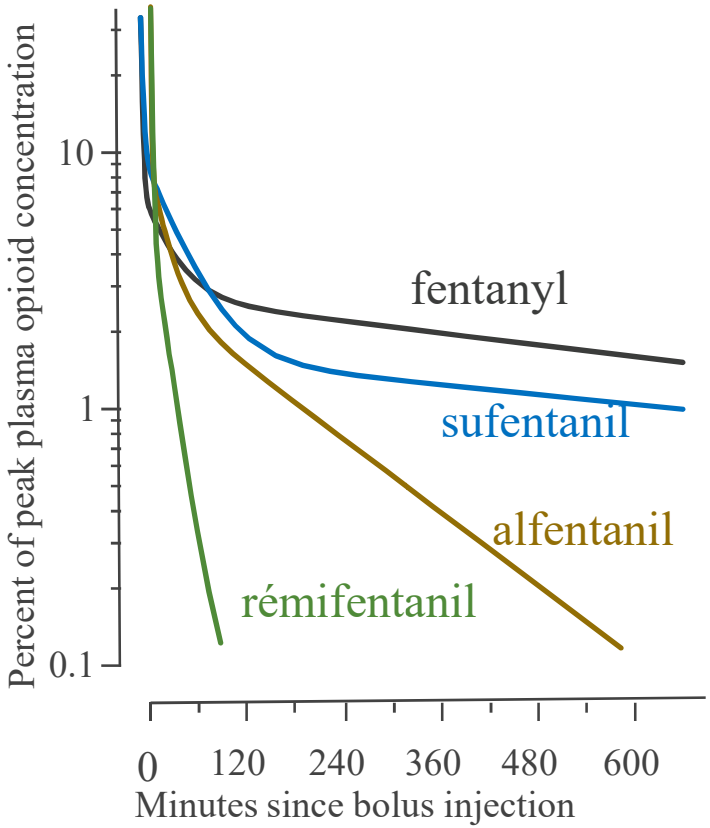
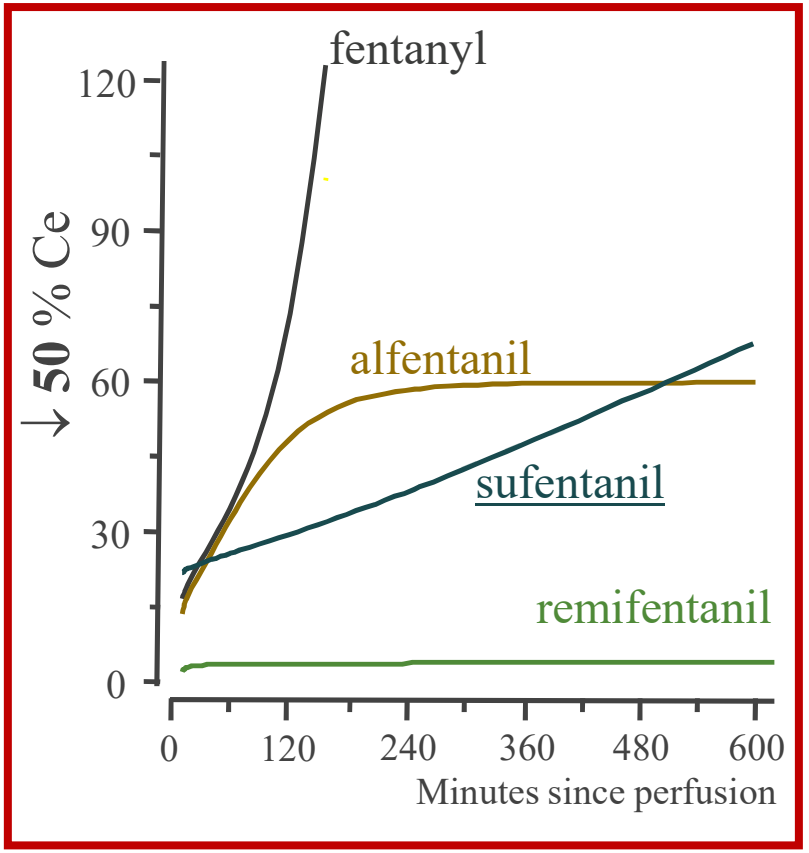


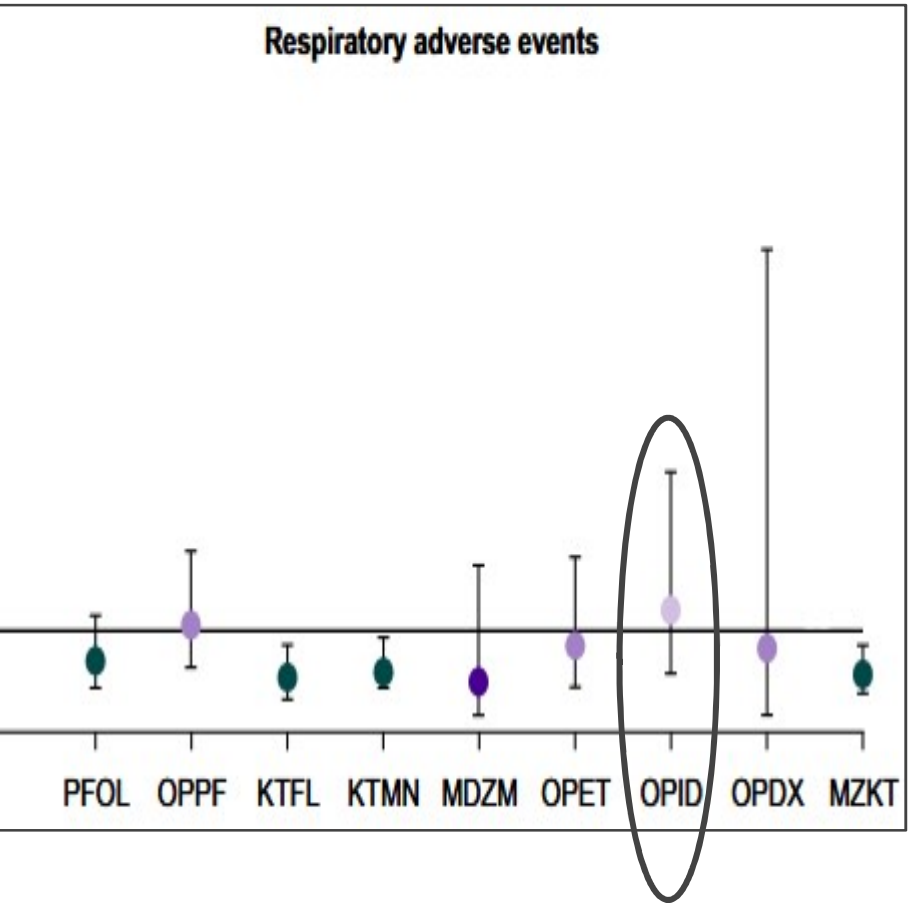


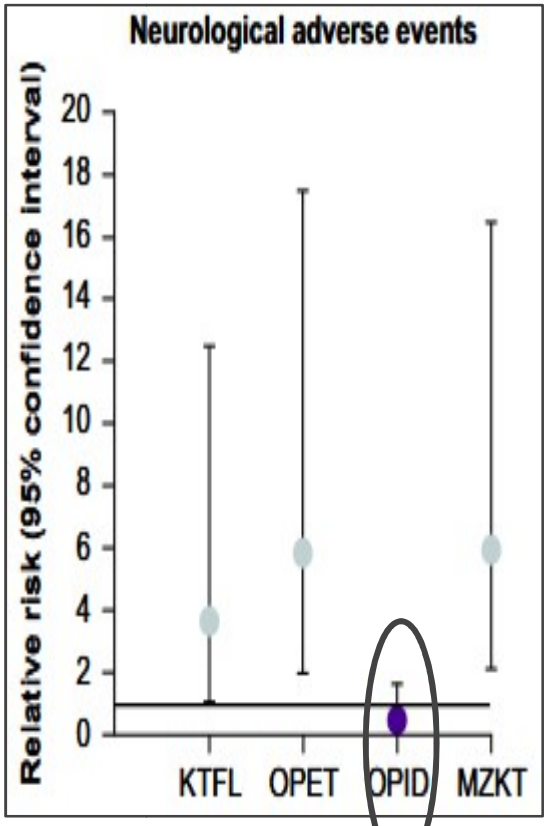


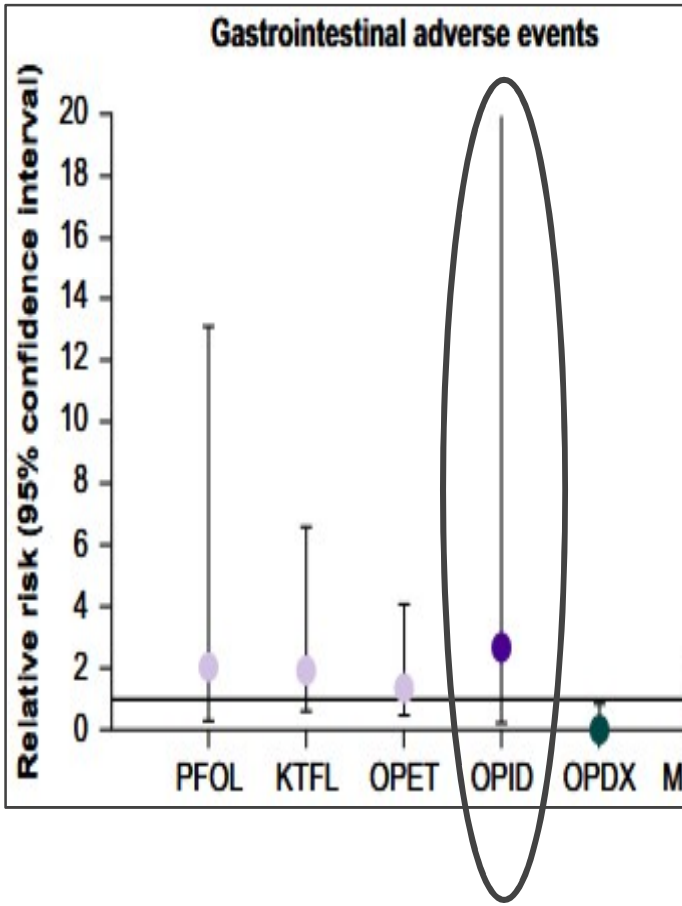
Minto et al, Anesthesiology,

Pharmacological agents for procedural sedation and analgesia in the emergency department and intensive care unit: a systematic review and network meta-analysis of randomised trials

British Journal of Anaesthesia, 132 (3): 491–506 (2024)







Risk factors for late defecation and its association with the outcomes of critically ill patients: a retrospective observational study

Fukuda *et al. Journal of Intensive Care* (2016) 4:33 DOI 10.1186/s40560-016-0156-1

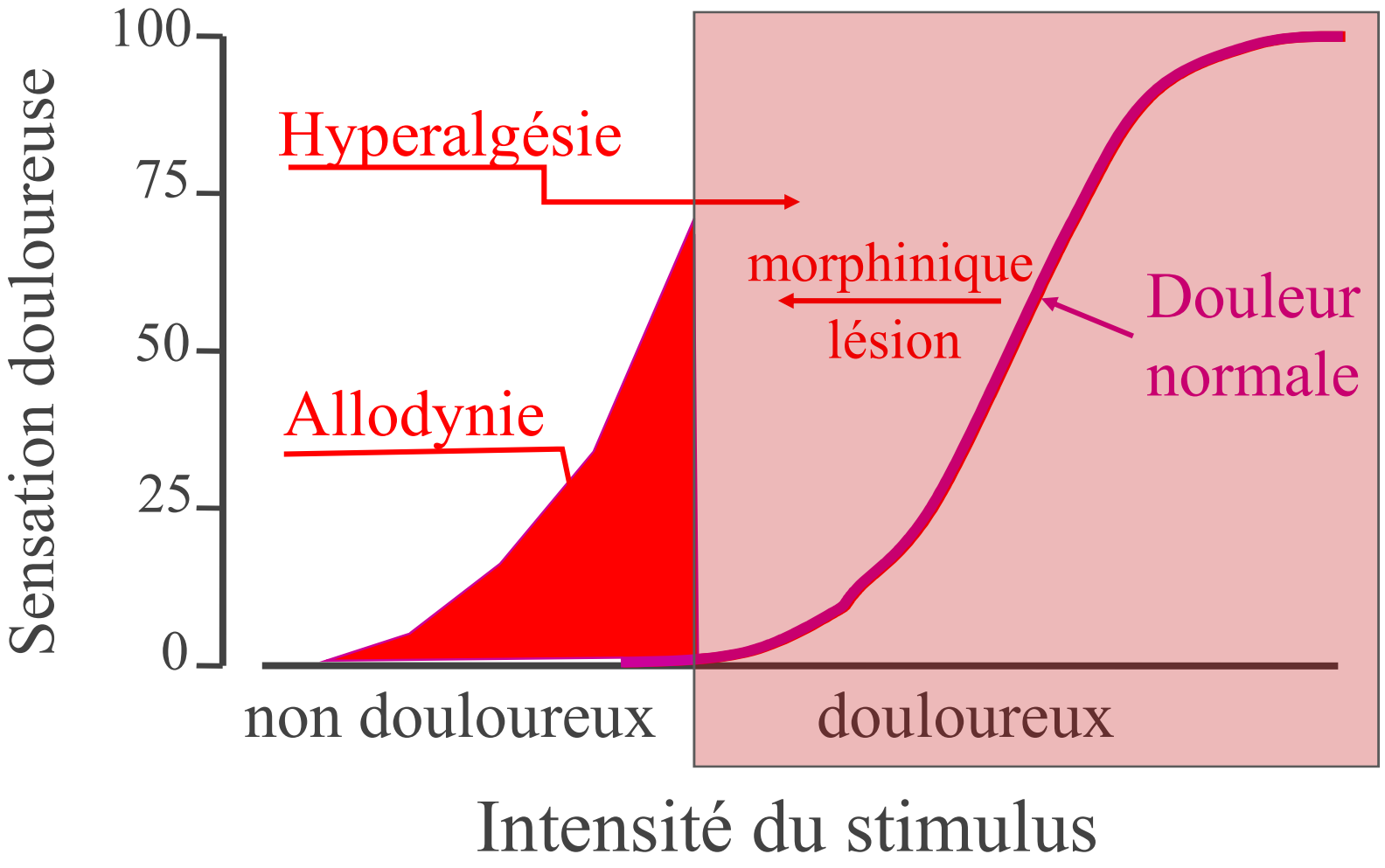
Risk factors for late defecation

	Univariate	
	OR (95 % CI)	*P* value
ge	1.00 (0.99–1.01)	0.94
ale sex	0.84 (0.51–1.37)	0.48
MI	1.01 (0.97–1.06)	0.61
erum CRP	0.97 (0.93–1.00)	0.063
PACHE II score	1.00 (0.98–1.03)	0.76
OFA score	0.93 (0.85–1.02)	0.108
iagnosis on admission		0.090
te enteral nutrition	4.52 (2.55–7.99)	<0.001
echanical ventilation	2.36 (1.43–3.91)	0.001
edative use	4.40 (2.56–7.56)	<0.001
entanyl use	2.78 (1.50–5.14)	0.001
urgery	3.33 (1.92–5.77)	<0.001

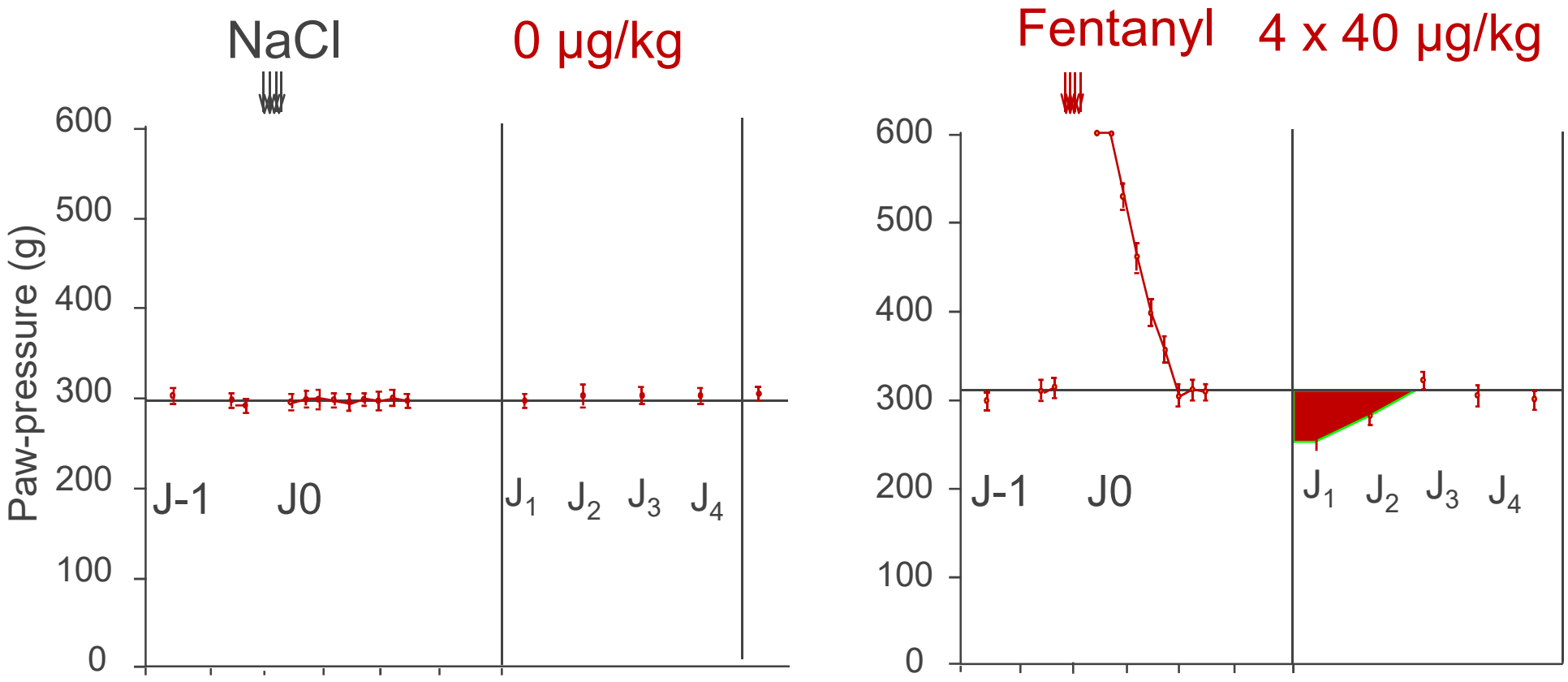
Clinical outcomes

	Early defecation group		Late defecation group		*P* va
ICU mortality, *n* (%)	13	(7)	6	(6)	0.81
Length of ICU stay, days					
All patients	12	(9–19)	16	(10–23)	0.02
Survivors	12	(8–19)	15	(9–23)	0.01
Non-survivors	26	(16–31)	26	(18–34)	0.42
Length of mechanical ventilation, days					
All patients	8	(4–15)	11	(4–19)	0.30
Survivors	7	(3–14)	9	(3–18)	0.39
Non-survivors	18	(11–23)	24	(17–34)	0.28

Pharmacodynamie des morphiniques
Tolérance aiguë aux morphiniques

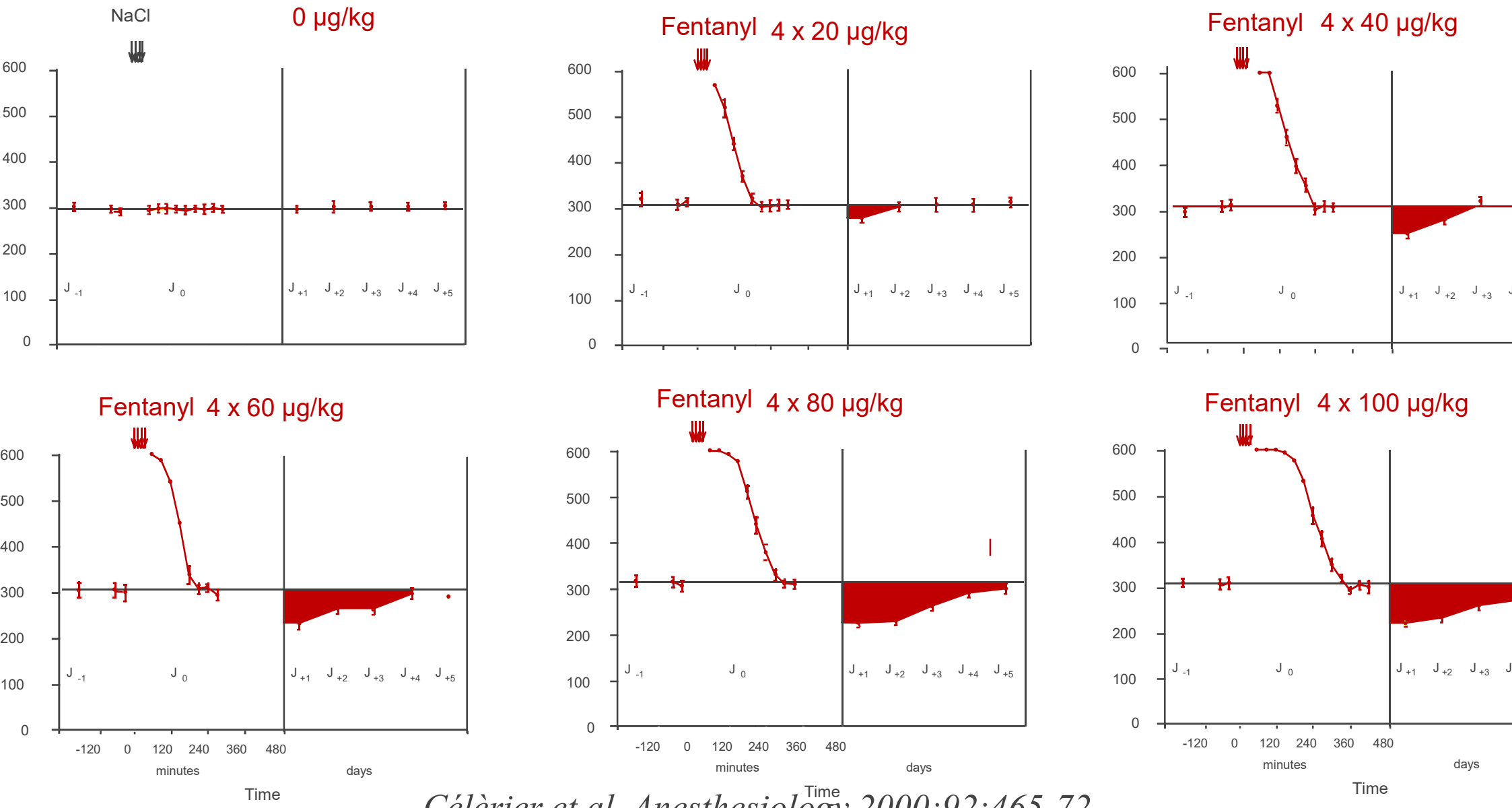


Tolérance aiguë aux morphiniques



Célèrier et al. Anesthesiology 2000;92:465-72.

Tolérance aiguë aux morphiniques



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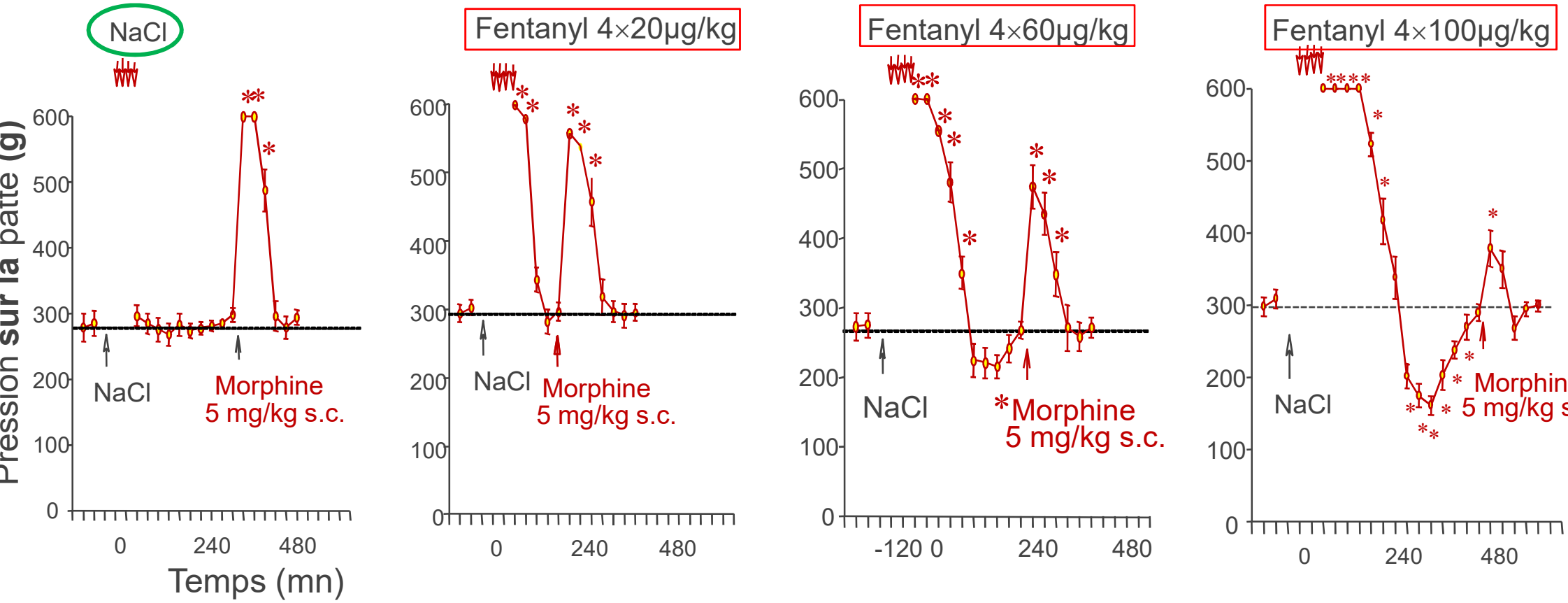
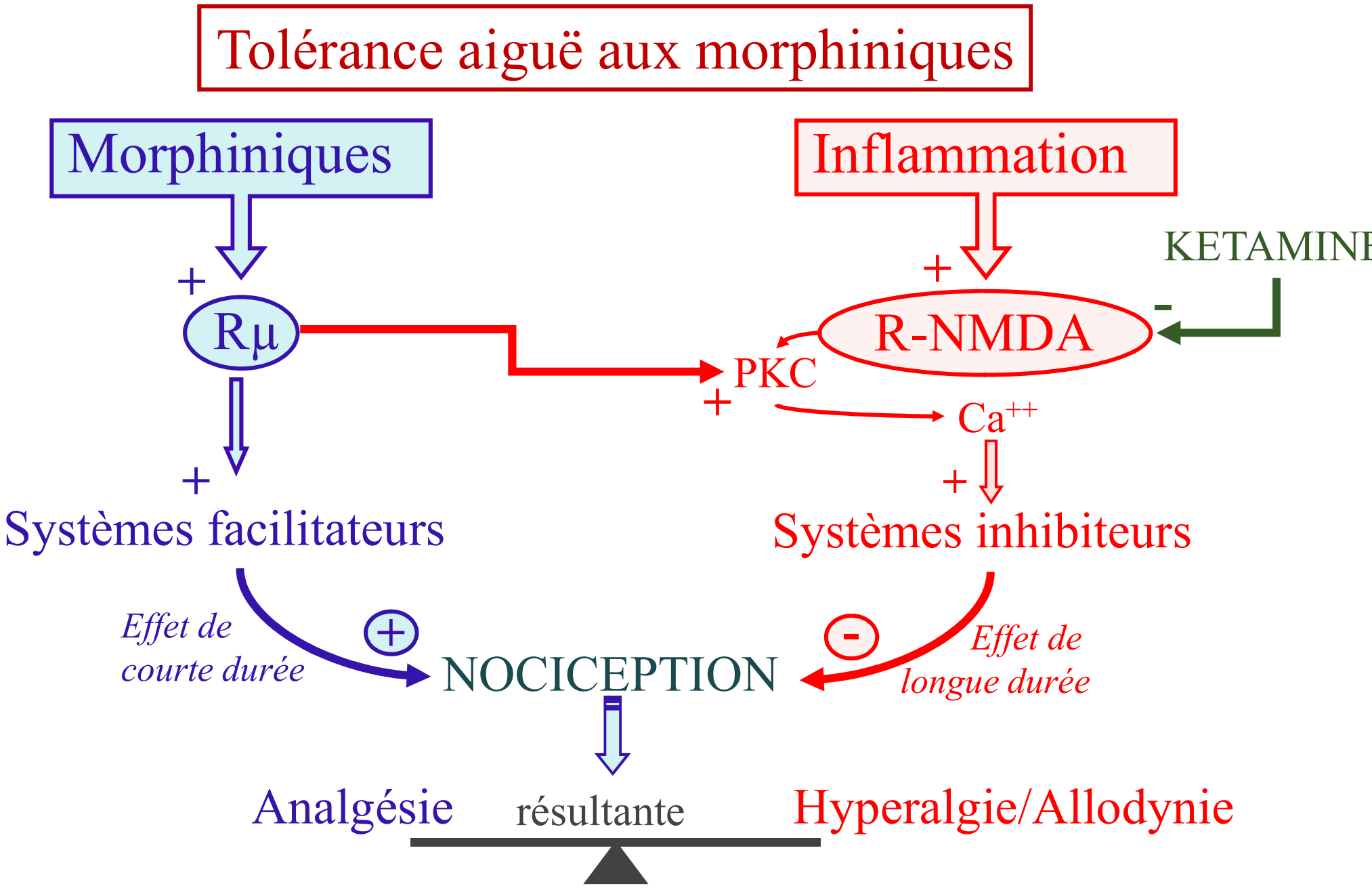
Tolérance aiguë aux morphiniques



Laulin et al. Anesth Analg 2002;94:1263-9


Tolérance aiguë aux morphiniques
Morphiniques
Inflammation
KETAMINE
+
+
-
Rμ
R-NMDA
PKC
+
Ca++
+
+
Systèmes facilitateurs
Systèmes inhibiteurs
Effet de
courte durée
+
NOCICEPTION
-
Effet de
longue durée
Analgésie
résultante
Hyperalgie/Allodynie

Tolérance aiguë aux morphiniques

Determinants of Procedural Pain Intensity in the Intensive Care Unit

The Europain® Study

Am J Respir Crit Care Med 2014, Vol 189, Iss 1, pp 39–47

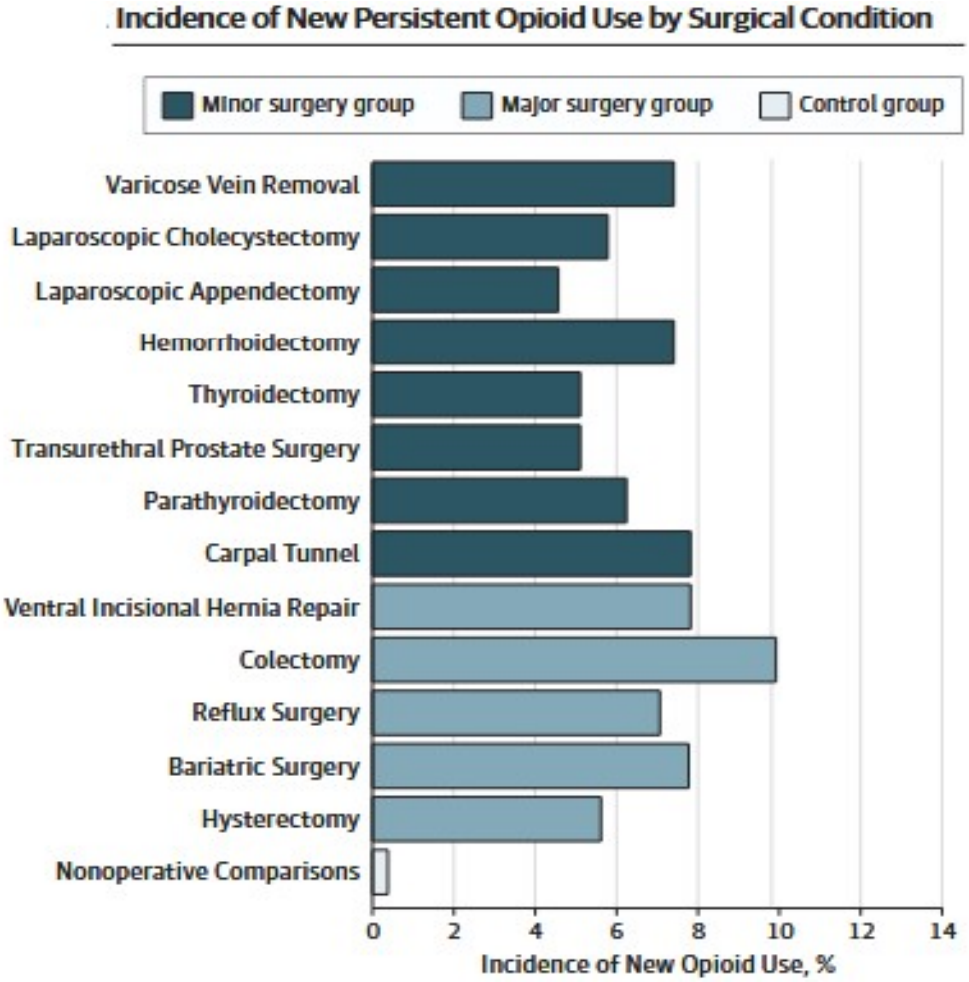
Effect of the Procedures on Pain Intensity, as Reported on a 0–10 Numeric Rating Scale When Adjusted on the Othe Cofounders in a Multivariate Hierarchical Binomial Model (N = 2,769)*

Factors	Relative Risk	95% CI Lower Limit	95% CI Upper Limit	*P* Value	Overall *P* Val
Procedure in 13 classes					
Mobilization†	1.00				
Turning	1.21	1.09	1.35	0.0006	<0.0001
Positioning	1.16	1.01	1.32	0.03	
Respiratory exercises	1.06	0.93	1.21	0.38	
Peripheral blood draw	1.28	1.12	1.46	0.0004	
Peripheral intravenous insertion	1.25	1.10	1.44	0.001	
Arterial line insertion	1.67	1.40	1.98	<0.0001	
Endotracheal suctioning	1.35	1.19	1.54	<0.0001	
Tracheal suctioning	1.16	0.99	1.36	0.06	
Chest tube removal	1.46	1.27	1.67	<0.0001	
Wound drain removal	1.52	1.24	1.86	<0.0001	
Wound care	1.15	1.00	1.32	0.05	
Other	1.15	0.64	2.08	0.63	
Worst pain intensity today (before the procedure)				<0.0001	<0.0001
Opioids specifically for the procedure	1.22	1.11	1.33	<0.0001	<0.0001
Pa				<0.0001	<0.0001
Pain intensity preprocedure				<0.0001	<0.0001
Person performing the procedure‡					
Nurse	1.00				
Physician	1.10	1.00	1.20	0.05	0.02
Respiratory therapist	1.22	1.06	1.40	0.007	
Physiotherapist	1.11	0.95	1.29	0.18	
Other	0.96	0.83	1.11	0.60	
Random variables					
Country	0				
Intensive care unit	1.06	1.03–1.08		<0.0001	<0.0001

Dépendance aux morphiniques

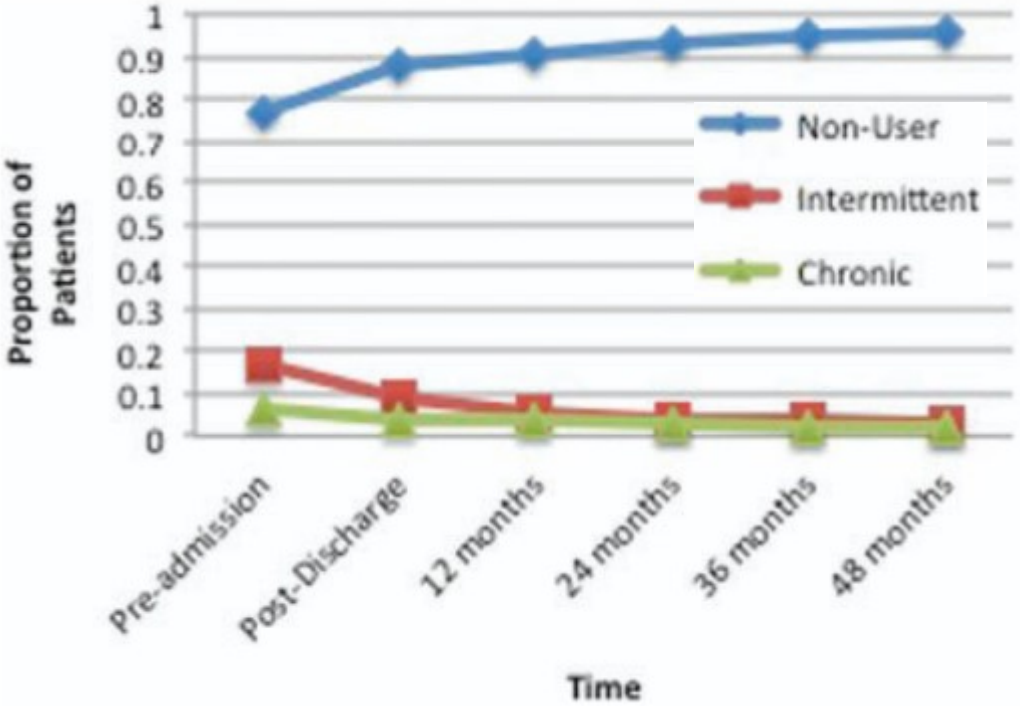
New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults

JAMA Surg. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504



Is Admission to the Intensive Care Unit Associated With Chronic Opioid Use? A 4-Year Follow-Up of Intensive Care Unit Survivors

Journal of Intensive Care Medicine October 29, 2015.



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Choix des médicaments : Points directeurs

Y-a-t-il une alternative aux morphinomimétiques?

① Pourquoi cette question ?

EI, balance bénéfice/risque

② Comment remplacer les morphiniques ?

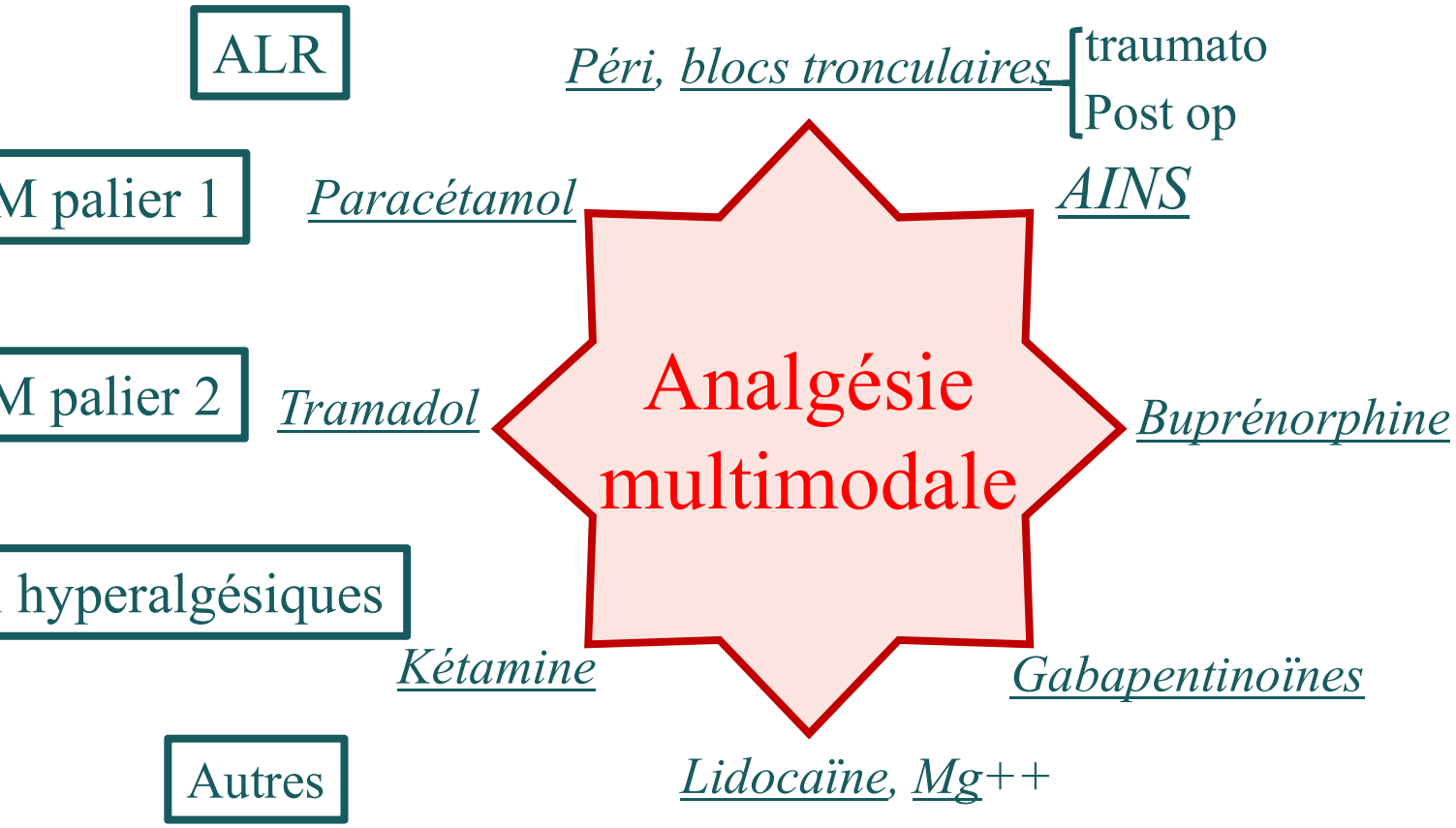
Épargne morphinique

Objectif; ↴ EI, améliorer le rapport bénéfice/risque

Analgésie en USI et réanimation
Alternatives aux morphiniques

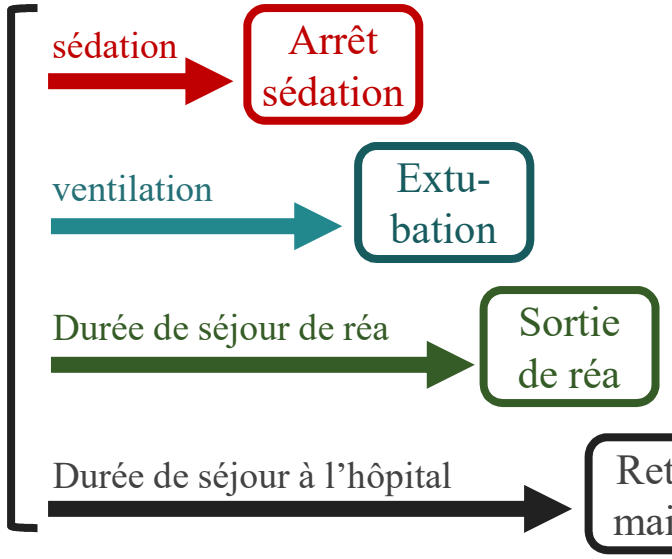
2000	Sedation target						
2008	Sedation goal confort (not coma) in most patients	Analgesia target					
2013	Pain top priority if present	Agitation	Delirium				
2018	**P**ain mutimodal approach	**A**gitation	**D**elirium	**I**mmobility	**S**leep disruption		
2025	**P**ain mutimodal approach	**A**gitation	**D**elirium	**I**mmobility	**S**leep disruption	ANXIETE	

Analgésie en USI et réanimation
Alternatives aux morphiniques



objectifs

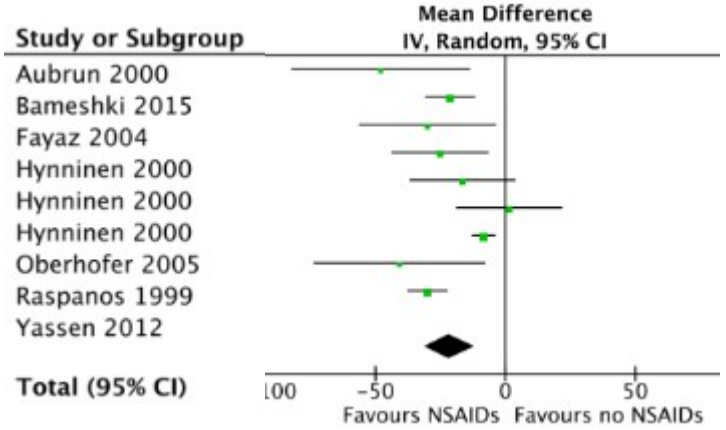
1) Épargne morphinique
2) ↴ EI des morphiniques
3) ↴ morbidité; ↴mortalité

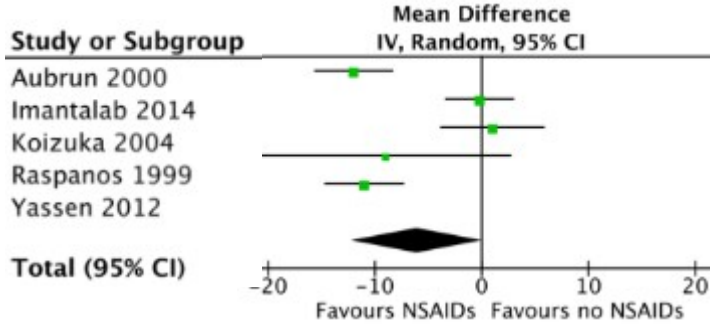


Non-steroidal anti-inflammatories for analgesia in critically ill patients: a systematic review and meta-analysis of randomized control trials

Crit Care Expl 28 juin 2023 ; 5(7):e0938. https://doi.org/10.1101/2023.01.03.23284166;

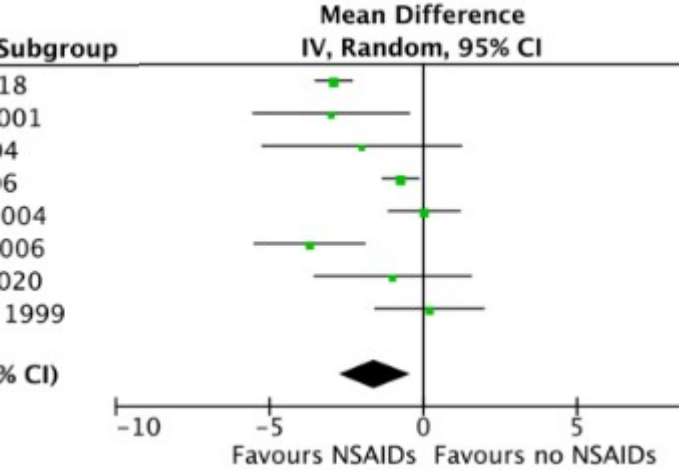
opioid consumption



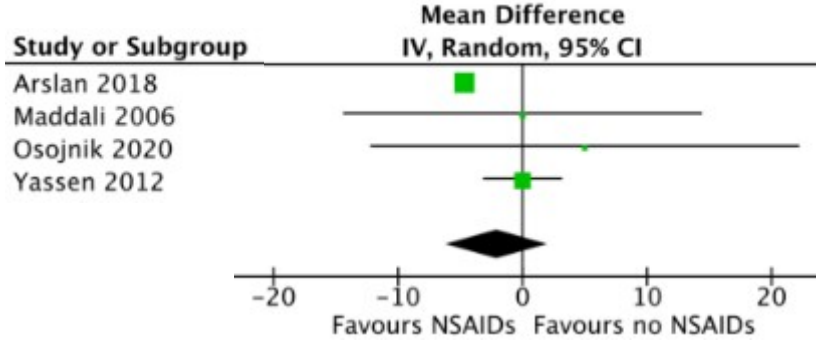


pain scores

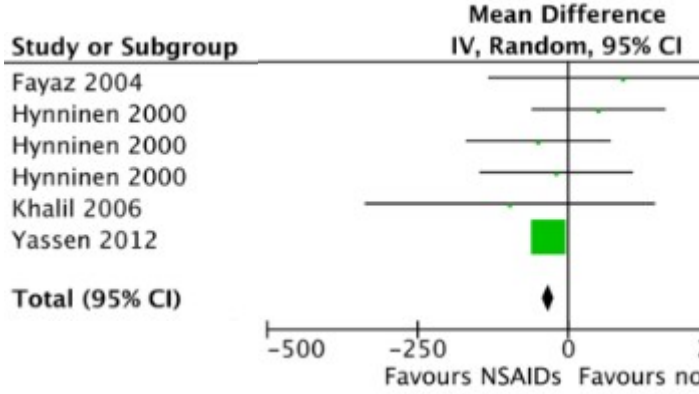
uration of mechanical ventilation



intensive care unit length of stay



bleeding



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NSAIDs.

estion: Should a COX-1–selective NSAID be used as an
ct to an opioid (vs an opioid alone) for pain management
ically ill adults?

Recommendation: We suggest not routinely using a C
1–selective NSAID as an adjunct to opioid therapy for
management in critically ill adults (conditional recomme
tion, low quality of evidence).

EI
- ✓Toxicité gastrique avec tendance au saignement (↴↴ en cas d'association IPP)
- ✓Toxicité Rénale (↴↴ si préservation du DSR : normo volémie; DC préservé)
- ✓Toxicité cardiaque (attention aux coronarien)

estion: Should an NSAID administered IV, orally, and/or
y (vs an opioid) be used for critically ill adults undergo-
rocedure?

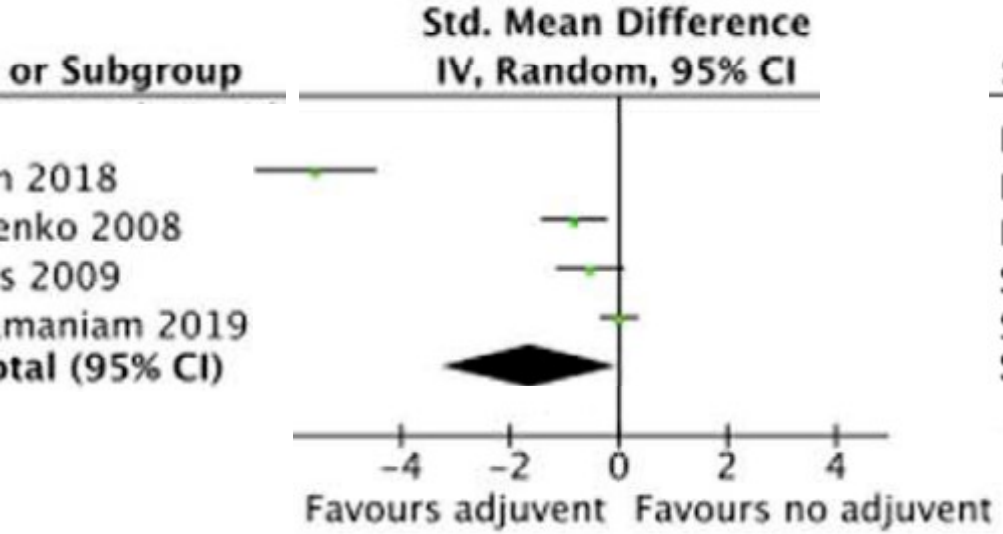
Recommendation: We suggest using an NSAID adminis
IV, orally, or rectally as an alternative to opioids for pain
agement during discrete and infrequent procedures in
cally ill adults (conditional recommendation, low quali
evidence).

Adjuvant Analgesic Use in the Critically Ill: A Systematic Review and Meta-Analysis

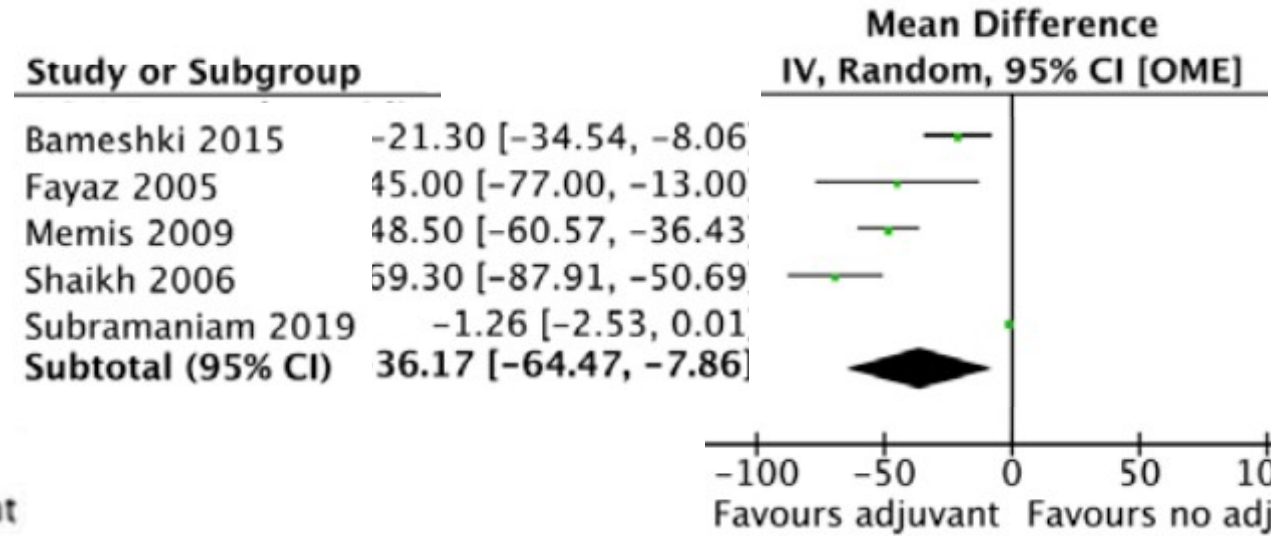
Wheeler et al *Crit Care Expl* 2020; 2:e0157 10.1097/CCE.0000000000000157

Acetaminophen

pain scores at 24 hr after intervention.



opioid consumption in first 24 hr



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Acetaminophen.

uestion: Should acetaminophen be used as an adjunct to
ioid (vs an opioid alone) for pain management in criti-
ll adults?

Recommendation: We suggest using acetaminophen
adjunct to an opioid to decrease pain intensity and opioid
sumption for pain management in critically ill adults (c
tional recommendation, very low quality of evidence).

- EI ≅ 0 (discrète ↴ PA surtout cérébrolésé et malade septique)

- élimination hépatique: 90% glucuroconjugué

  5 % CYP2E1 ⇨ NAPQI ⇨ réduit par la Glutathion synthétase (↴ dénutrie, IH, II

  ↳ toxique pour la mitochondrie

➡Dose maximale : 4g (3g si IR); CI si IH

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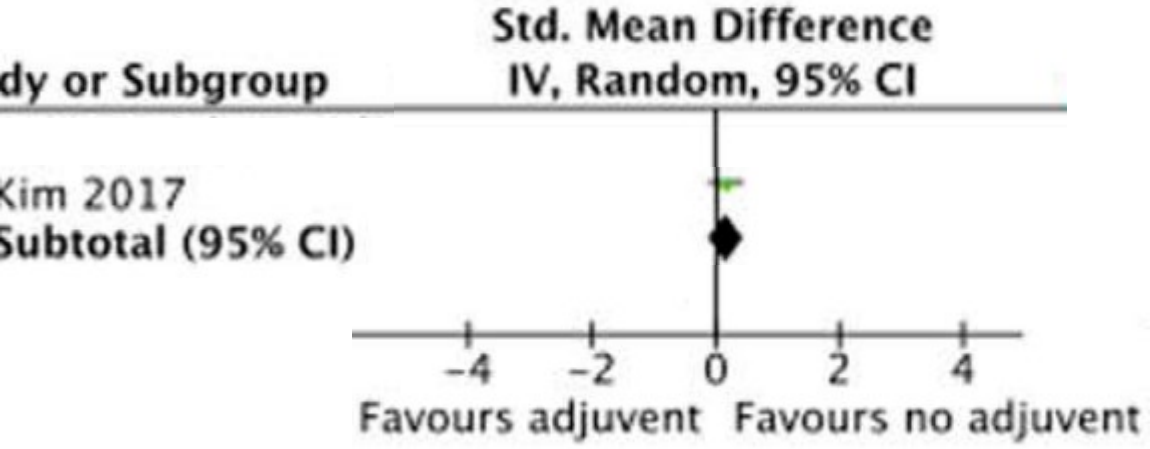
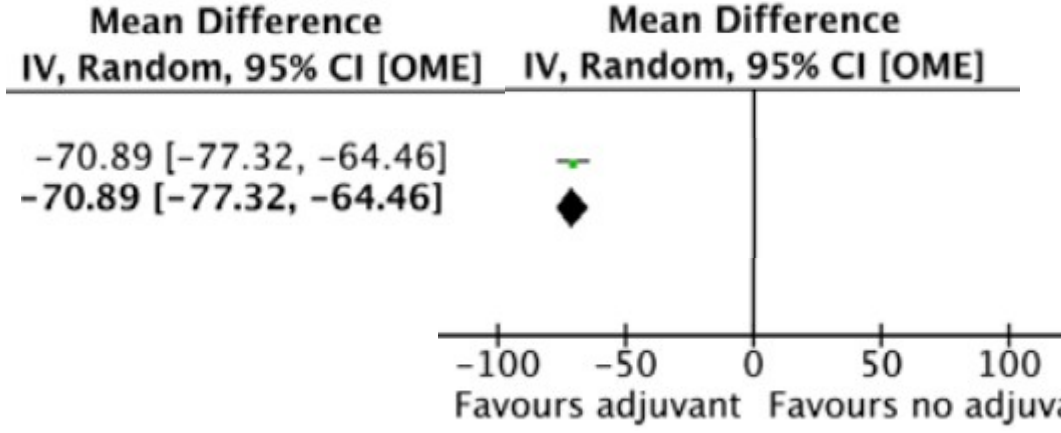
Wheeler et al *Crit Care Expl* 2020; 2:e0157 10.1097/CCE.0000000000000157

Nefopam

pain scores at 24 hr after intervention.



opioid consumption in first 24 hr



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Nefopam.

uestion: Should nefopam be used either as an adjunct or a
cement for an opioid (vs an opioid alone) for pain man-
ent in critically ill adults?

Recommendation: We suggest using nefopam (if feasi
either as an adjunct or replacement for an opioid to red
opioid use and their safety concerns for pain managem
in critically ill adults (conditional recommendation, very
quality of evidence).

EI
- ✓ ↥ FC, ↧ PA (risque ↓ en cas de perfusion continue; attention chez le coronarien)
- ✓ parfois confusion mentale (effet anti cholinergique; CI glaucome)
- ✓ peut majorer les convulsions (CI)

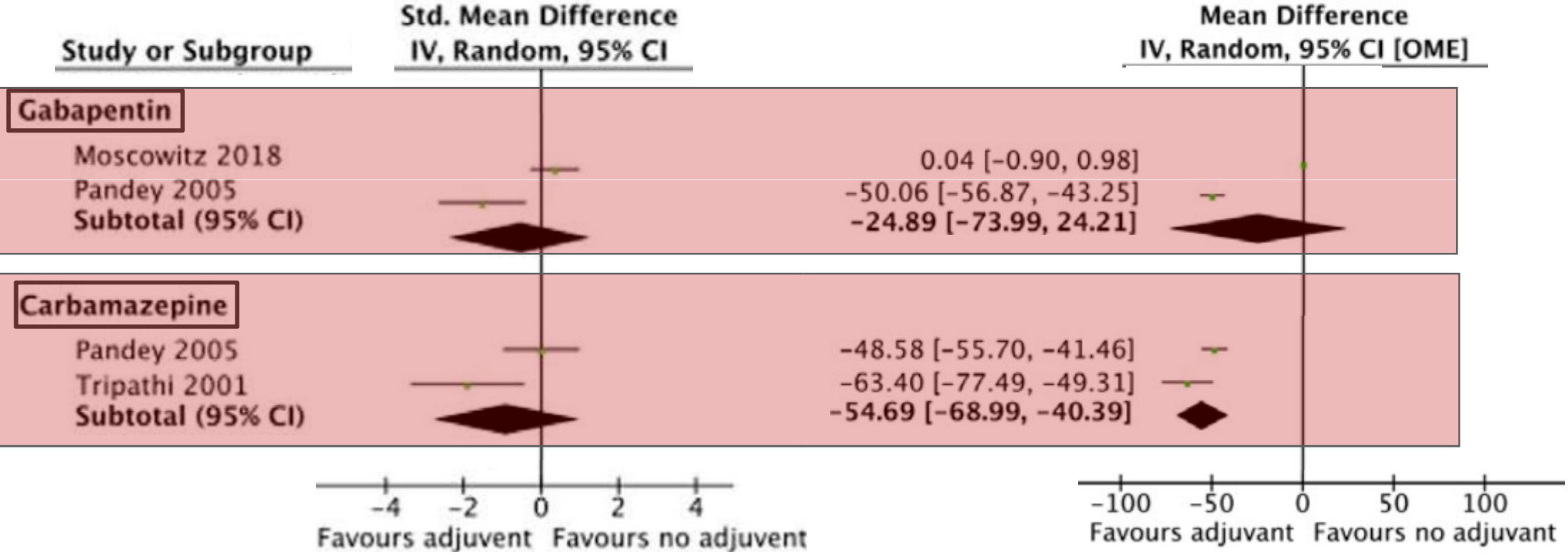
✓ élimination hépatique (95 %): ⇨ desméthyl néfopam (métabolite actif) ⇨ Éliminé par voie urinaire ↧ Doses (IH, IR)

Adjuvant Analgesic Use in the Critically Ill: A Systematic Review and Meta-Analysis

Wheeler et al *Crit Care Expl* 2020; 2:e0157 10.1097/CCE.0000000000000157

pain scores at 24 hr after intervention.

opioid consumption in first 24 hr



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Neuropathic Pain Medications.

uestion: Should a neuropathic pain medication (e.g., gab-
in, carbamazepine, and pregabalin) be used as an adjunct
opioid (vs an opioid alone) for pain management in criti-
ill adults?

Recommendations: We recommend using a neuropathic p
medication (e.g., gabapentin, carbamazepine, and pregaba
with opioids for neuropathic pain management in criticall
adults (strong recommendation, moderate quality of eviden

✓ Σd Guilland Barré; post chirurgie cardiaque: OUI

✓ Attention : IR

Adjuvant Analgesic Use in the Critically Ill: A Systematic Review and Meta-Analysis

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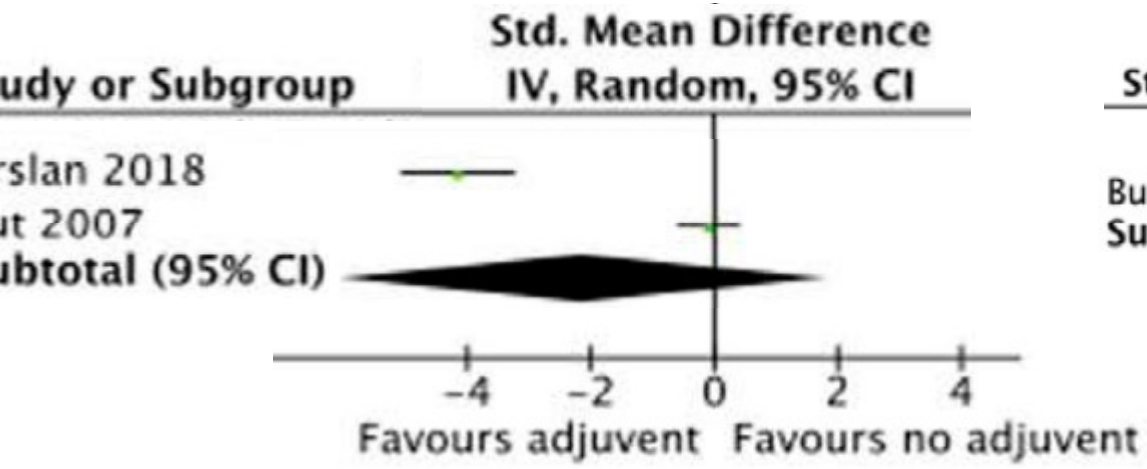
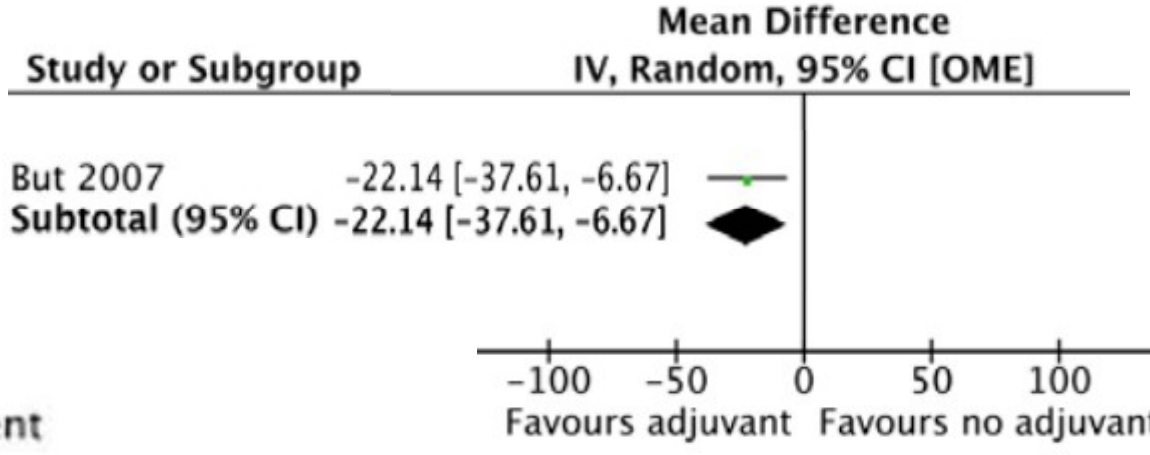
Tramadol

pain scores at 24 hr after intervention.



opioid consumption in first 24 hr



EI
- ✓ Dépression respiratoire (surtout IR)
- ✓Σd sérotoninergique (agitation, confusion, convulsion) majoré avec IRS

✓élimination hépatique (95 %): ⇨ O-desméthyl Tramadol (métabolite actif)
- Éliminé par voie urinaire

Doses
- IH (acétyleurs rapi
- IR

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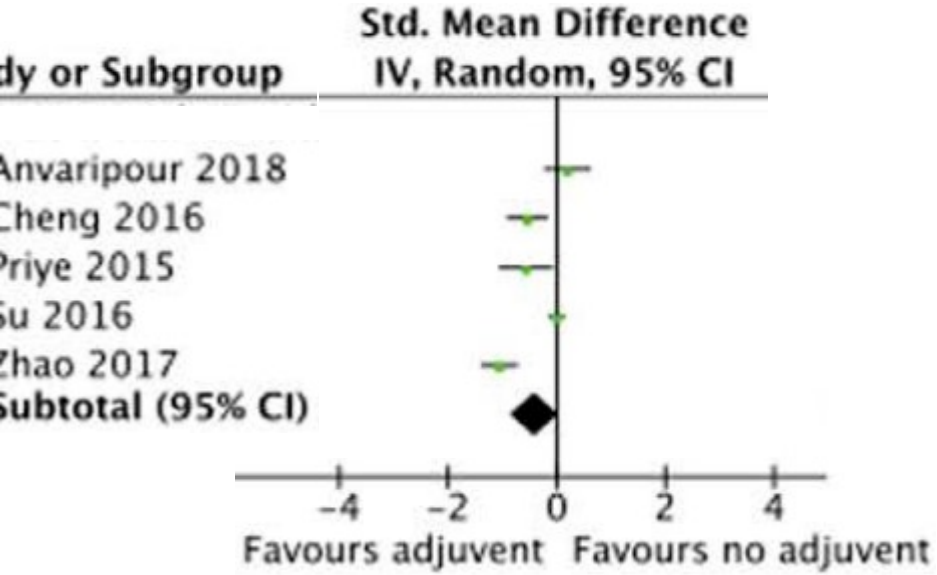
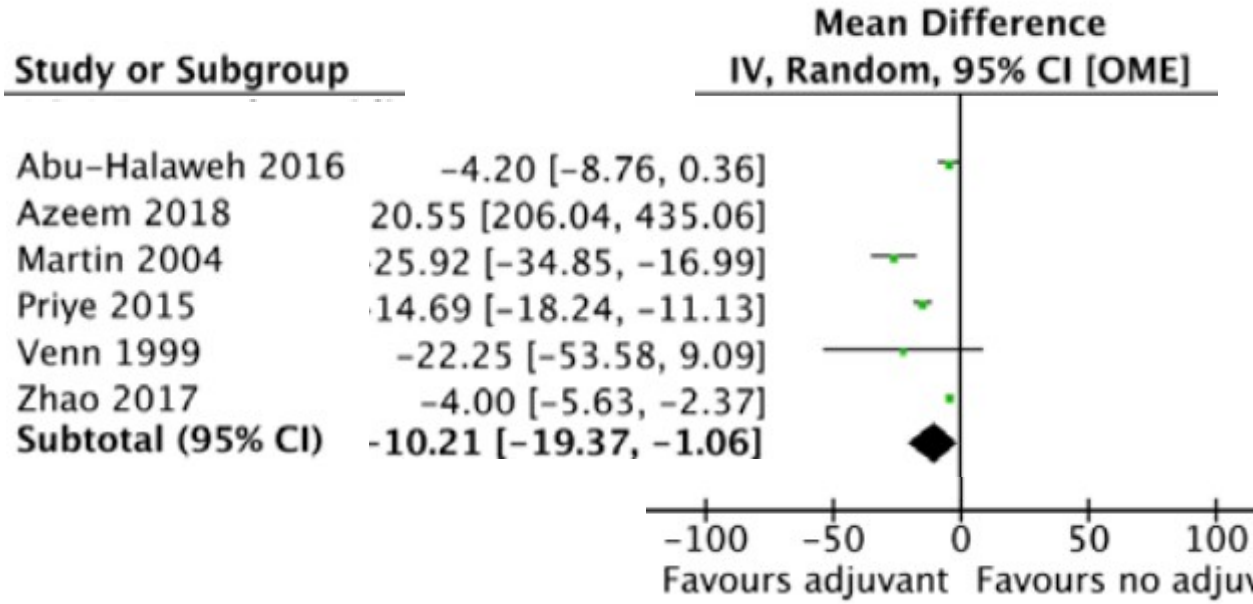
Dexmedetomidine

pain scores at 24 hr after intervention.



opioid consumption in first 24 hr



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oice of Sedative

edical and Surgical Patients Not Undergoing rdiac Surgery

commendation: We suggest using either propofol or dex-tomidine over benzodiazepines for sedation in critically echanically ventilated adults (conditional recommenda-ow quality of evidence).

Dexmedetomidine = Propofol > BZD

DEXMEDETOMIDINE FOR SEDATIO

Recommendation

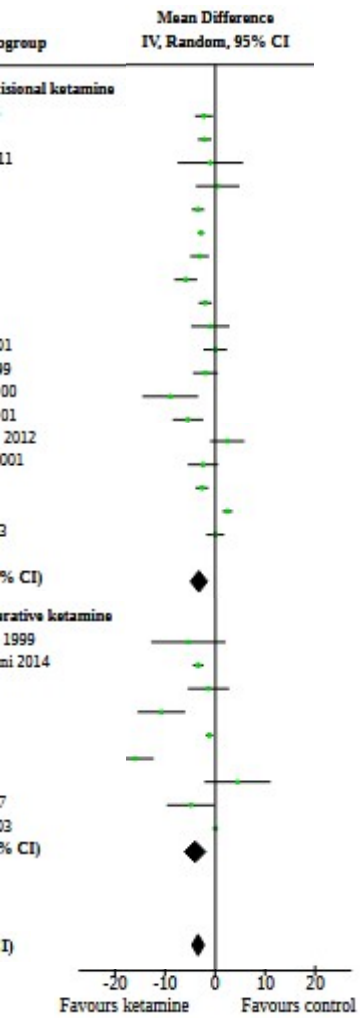
We suggest using dexmedetomidine over pro for sedation in mechanically ventilated adult pat admitted to the ICU where light sedation and reduction in delirium are of highest priorities (ditional recommendation; for intervention; mod certainty of evidence).

Dexmedetomidine > Propofol > B

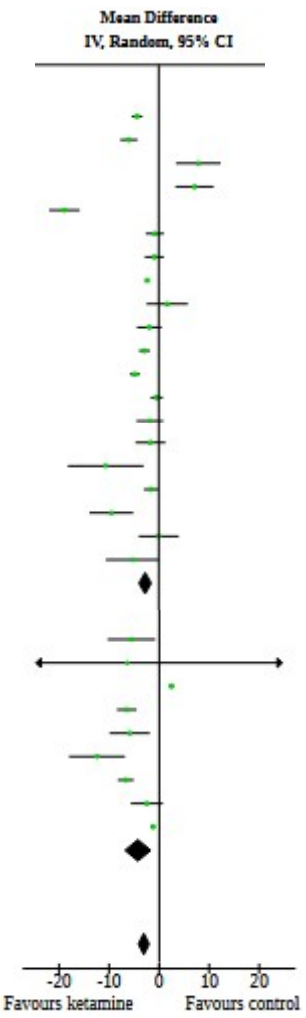
Cochrane Library

Perioperative intravenous ketamine for acute postoperative pain in adults (Review)

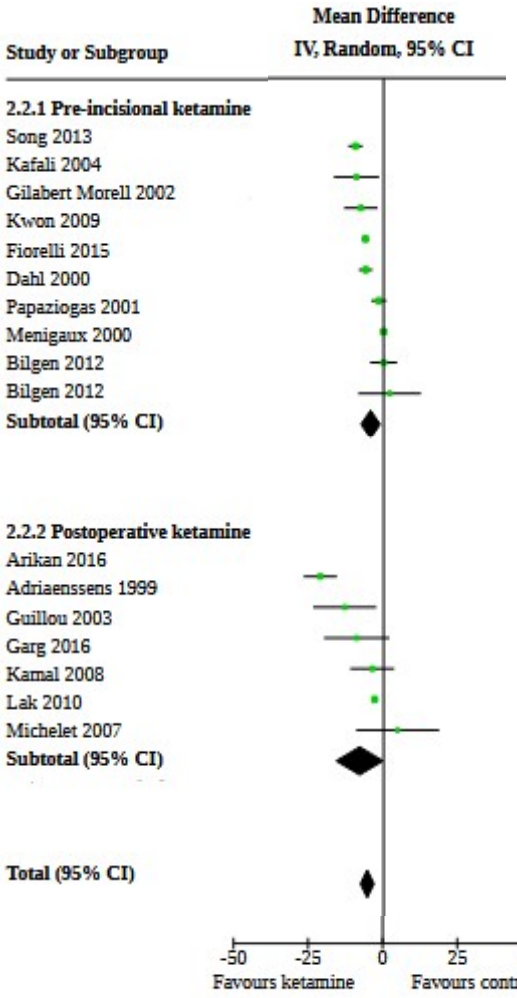
Pain Intensity at 24 hours



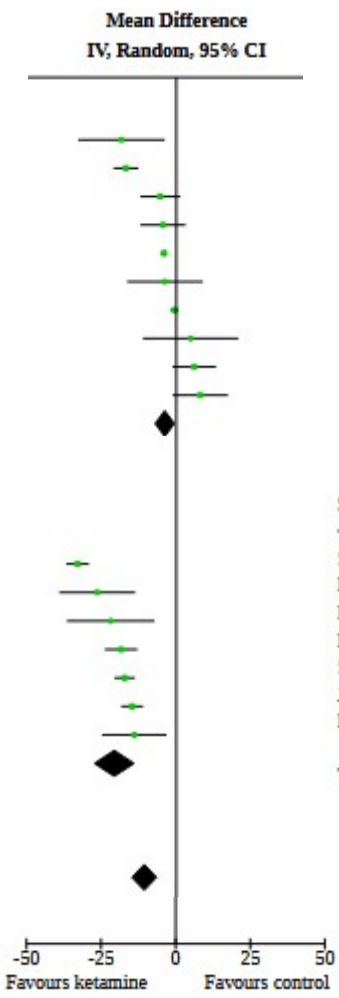
Opioid consumption at 24 hours



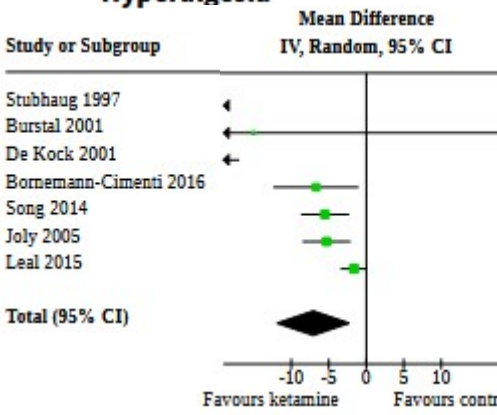
Pain Intensity at 48 hours



Opioid consumption at 48 hours



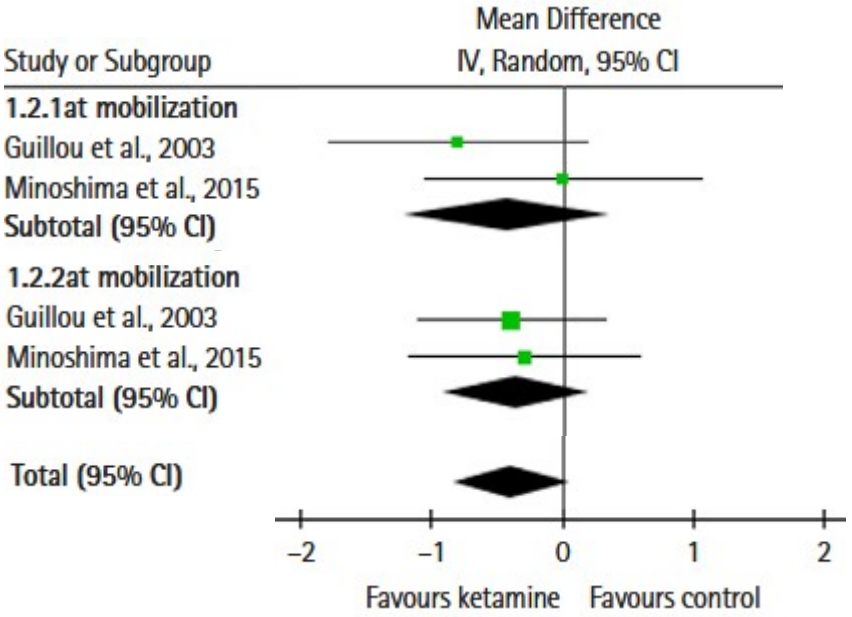
Hyperalgesia



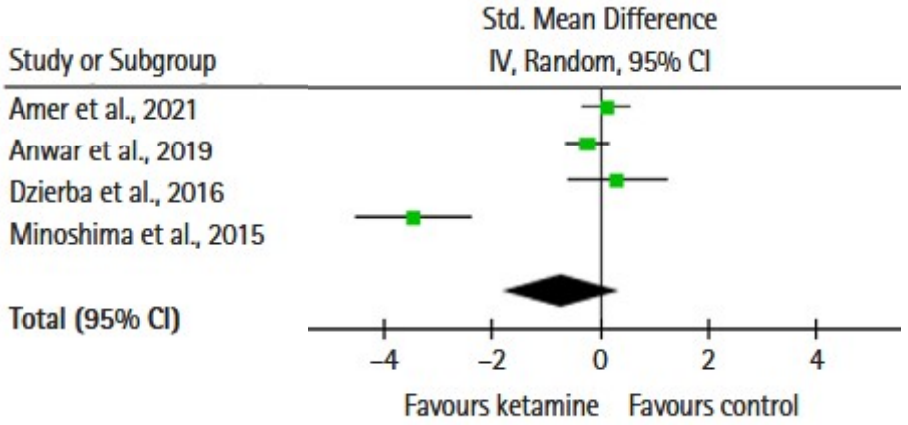
The impact of ketamine on outcomes in critically ill patients: a systematic review with meta-analysis and trial sequential analysis of randomized controlled trials

Yerkin Abdildin[1], Karina Tapinova[2], Assel Nemerenova[1], Dmitriy Viderman[3,4]

Acute and Critical Care 2024 February 39(1):34-46



Forest plot of pain intensity (0–10)



Forest plot of cumulative opioid consumption

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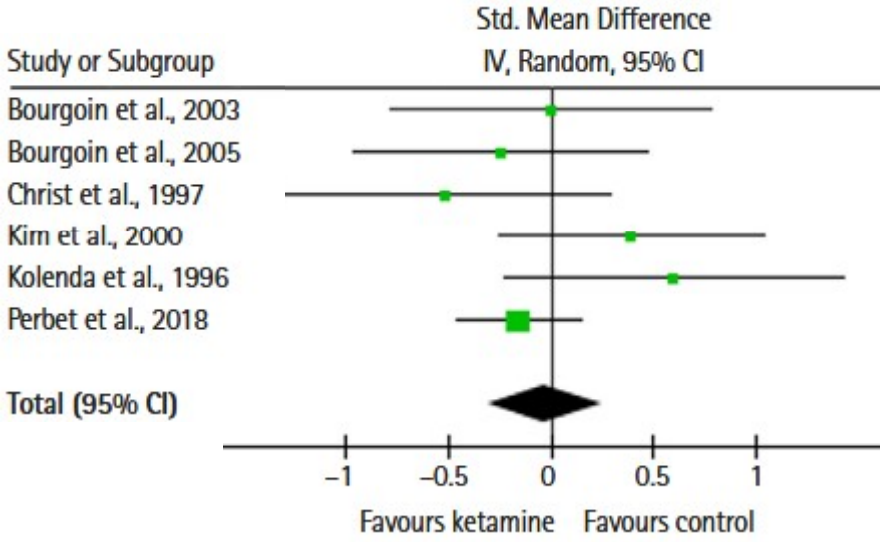
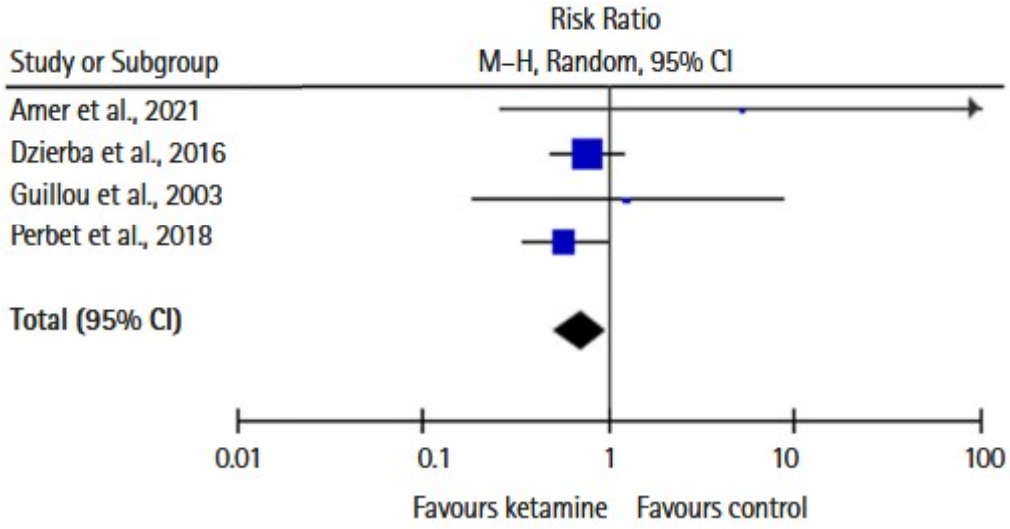


Forest plot of midazolam consumption



Forest plot of delirium.

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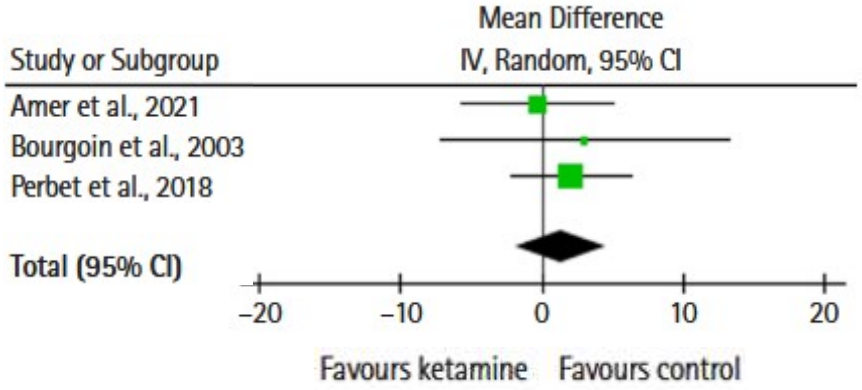
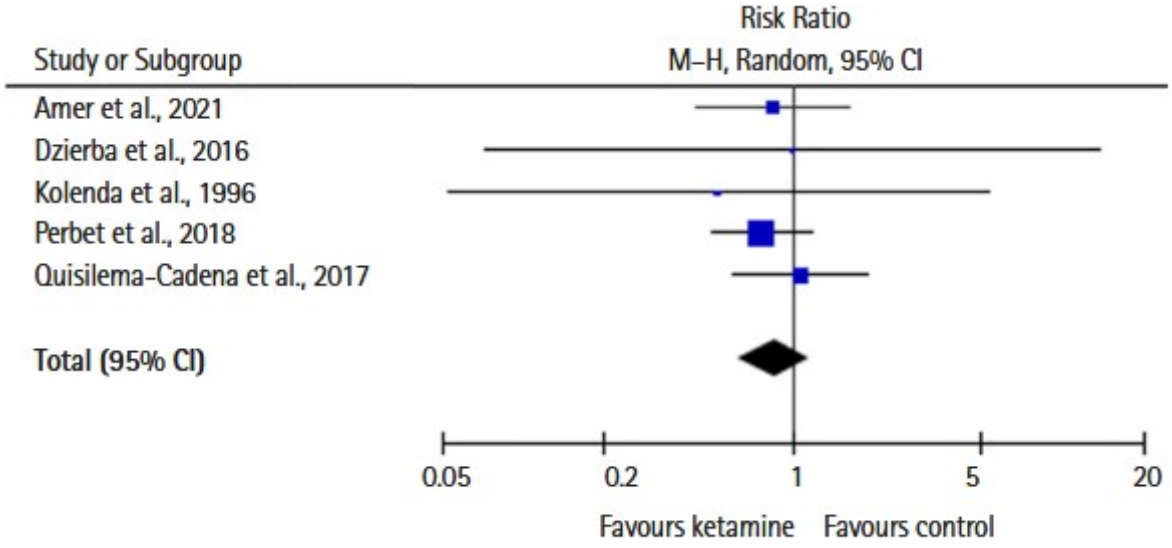


Forest plot of intensive care unit length of stay (day).



Forest plot of mortality.

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Ketamine.

estion: Should ketamine be used as an adjunct to an opi- s an opioid alone) for pain management in critically ill ?

Recommendation: We suggest using low-dose ketam (0.5 mg/kg IVP x 1 followed by 1-2 µg/kg/min infusion) as adjunct to opioid therapy when seeking to reduce opioid co sumption in postsurgical adults admitted to the ICU (con tional recommendation, very low quality of evidence).

Conclusion

- Mdes de réanimation : état douloureux (intensité modérée à sévère)
- Stratégie globale de prise en charges des symptômes (PADIS)
  douleur (**P**ain), **A**gitation, Anxiété, **D**élire, **I**mmobilisation, insomnie (**S**leep disruption
- TTT Douleur en réa : priorité, personnalisée (évaluation)
- Utilisation des morphiniques: le plus souvent oui
- Alternatives des morphiniques: toujours oui

Évaluation de nos pratiques

Analgésie multimodale

Essais cliniques, méthodologie

R

ANM palier 1

Paracétamol
AINS

ANM palier 2

Tramadol
Buprénorphine

Anti hyperalgésiques

Kétamine
Gabapentinoïnes

Autres

Clonidine, Dexmédétomidine
Carbamazépines, neuroleptiques
Lidocaïne, Mg++

Moyens n
médicamen