La 4ème Journée COmmune de Réanimation

Prophylaxie de l'ulcère de stress chez les patients en réanimation

Dr Nouira Hajer

Service de Réanimation Médicale

EPS Taher Sfar Mahdia

Introduction

CRITICAL CARE

➢ 74 à 100 % des patients en réanimation:

H24

Figure: Stress-related mucosal disease: a: Gastric antral erosions

Mark P Plummeret al; Critical care 2014

Introduction

CRITICAL CARE

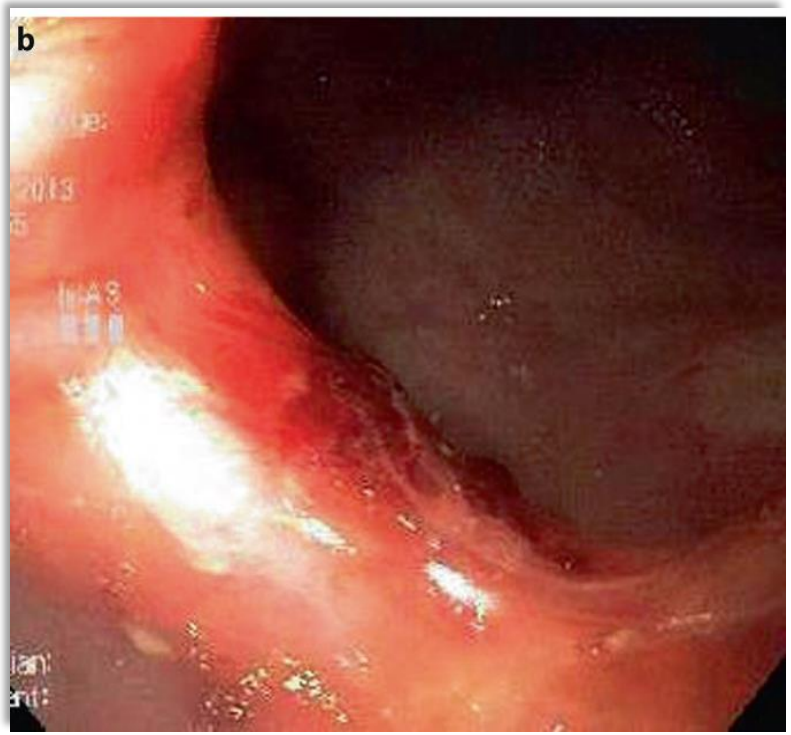


Figure: Stress-related mucosal disease. b: Pyloric ulcer with adherent clot

Mark P Plummeret al; Critical care 2014

Introduction

- Variabilité des pratiques médicales…

RESEARCH **Étude multicentrique** Open Access

2021

Physicians' knowledge, attitude, and prescribing behavior regarding stress ulcer prophylaxis in China: a multi-center study

- Participants : 1 266
- 100% taux de response .

Table 2 SUP clinical practice guideline awareness

Guideline	Institutions	No. (%) of respondents*
Consensus review for stress ulcer prophylaxis and treatment	CMASS	530 (42%)
Therapeutic guidelines on stress ulcer prophylaxis	ASHP	138 (11%)
Practice management guidelines for stress ulcer prophylaxis (2008)	EAST	109 (9%)
Guideline for stress ulcer prophylaxis in the intensive care unit	DSAICM and DSICM	
No awareness	N/A	**46%**

CMASS, Chinese Medical Association Surgery Society; ASHP, American Society of Health-System Pharmacists; EAST, Eastern Association for the DSAICM, Danish Society of Anesthesiology and Intensive Care Medicine; DSICM, Danish Society of Intensive Care Medicine; N/A, not applicable

* Some participants choose more than one option

Article

Current Practice of Stress Ulcer Prophylaxis in Surgical Departments in Mecklenburg Western Pomerania, Germany

Julia Rauch [1], Marco Franze [2], Maciej Patrzyk [1], Claus-Dieter Heidecke [1,3] and Tobias Schulze [1,*]

- Questionnaire
- Services de chirurgie des hôpitaux de soins aigus
- Allemagne.

01

02

Aucun protocole stabdardisé dans 68% des services

Dans 68 % des services chirurgicaux, aucun protocole standardisé (SOP) de prévention de l'ulcère de stress (SUP) n'a été mis en place.

47,7% des médecins ignoraient son existence

Parmi les médecins prescripteurs exerçant **dans des services disposant d'un Protocol, 47,6 % ignoraient son existence**

Survey of stress ulcer prophylaxis

Brian L Erstad*, Jeffrey F Barletta†, Judith Jacobi‡, Aaron D Killian§, Katherine M Kramer¶ and Steven J Martin#

- Une enquête
- 368 membres de la «Society of Critical Care Medicine».
- Etats unis

01

02

> 90% des patients en soins intensifs

86 % des répondants déclarent que **la SUP est administrée à la majorité des patients (>90 %)** admis en soins intensifs (ICU).

Seulement 22 % des établissements disposent de recommandations

Seulement 22 % des établissements disposent de recommandations pour la SUP à la fois en réanimation et hors réanimation.

Survey of stress u
Brian L Erstad*, Jeffr
Katherine M Kramer[¶]

Article

Current Practice of Str
Departments in Meckl

Julia Rauch [1], Marco Franze [2], Maciej Pa

RESEARCH Open Access

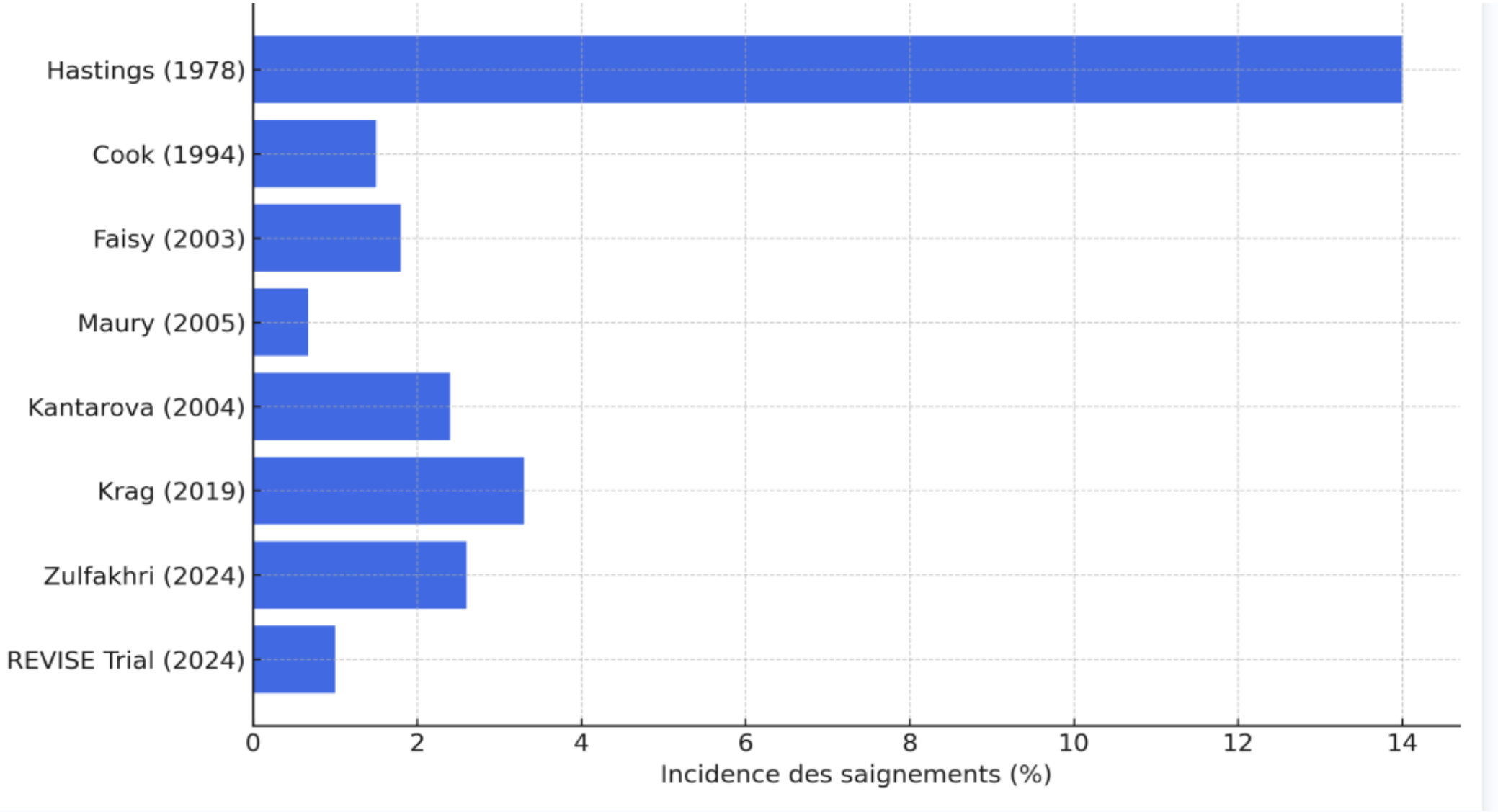
Physicians' knowledge, attitude, and prescribing behavior regarding stress ulcer prophylaxis in China: a multi-center study

Xiao Xuan Xing[1,2†], Chen Zhu[3†], Yan Qi Chu[1,2], Xiang Rong Bai[1,2], Ke Wang[1,2], Si Tao Zhang[1,2] and Su Ying Yan[1,2*]

- Pratique motivée par une perception de sécurité
- Non toujours fondée sur des preuves solides
- Manque de protocoles écrits et de réévaluation

Epidémiologie

➢ Evolution de l'incidence des saignements digestifs à travers des études publiées entre 1978 et 2024



2024

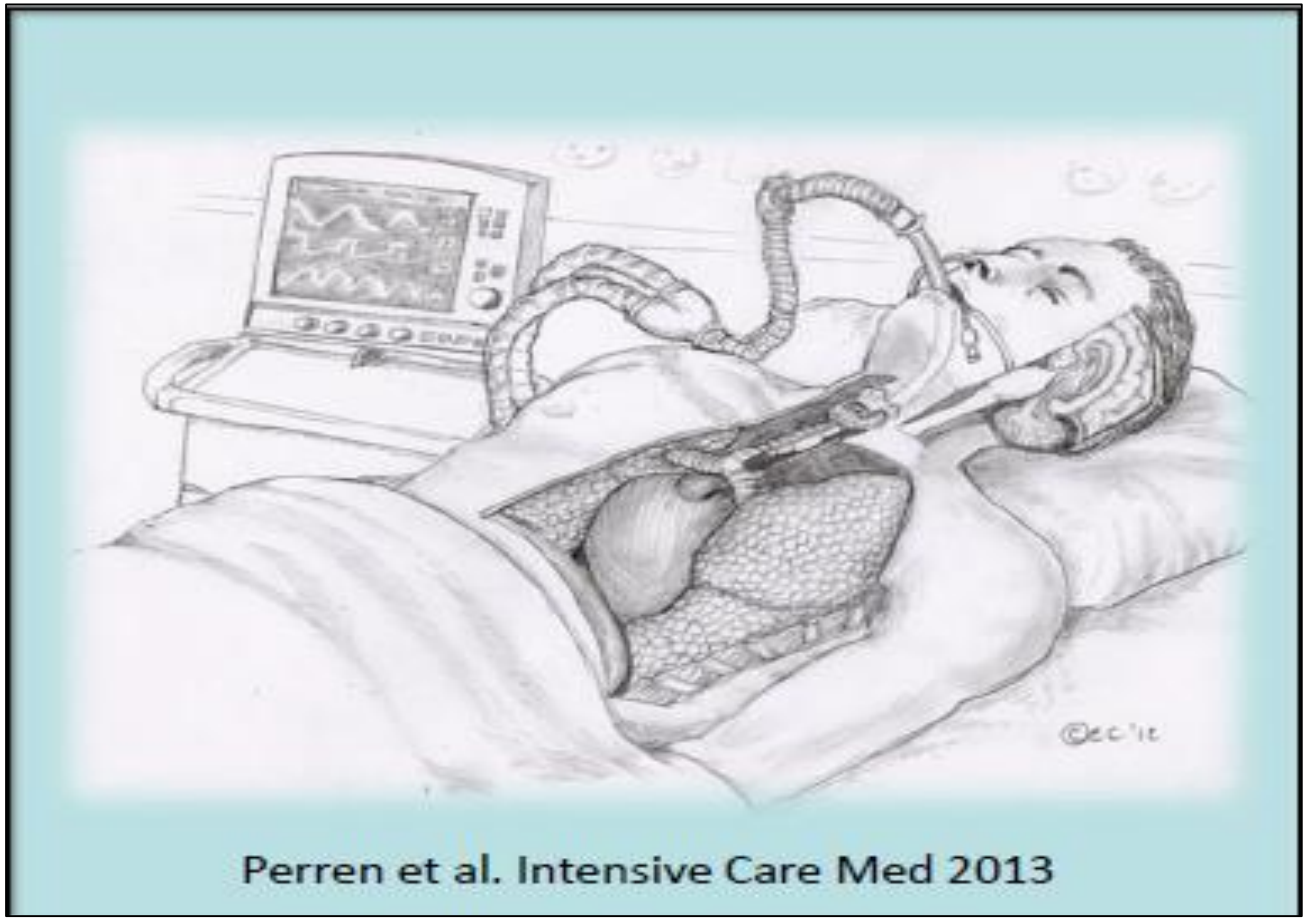
LITERATURE REVIEW

Prevention and Management of Stress Ulcers in Critically ill Patients

Zulfakhri✉, Akhmad Yun Jufan, Calcarina Fitriani Retno Wisudarti

An international prevalence study reported that 27 of 1,034 critically ill patients (2.6%) experienced a significant gastrointestinal bleeding, and 49 of 1,034 critically ill patients (4.7%) experienced at least one event of overt gastrointestinal bleeding in the ICU.

Altération des défenses en réanimation



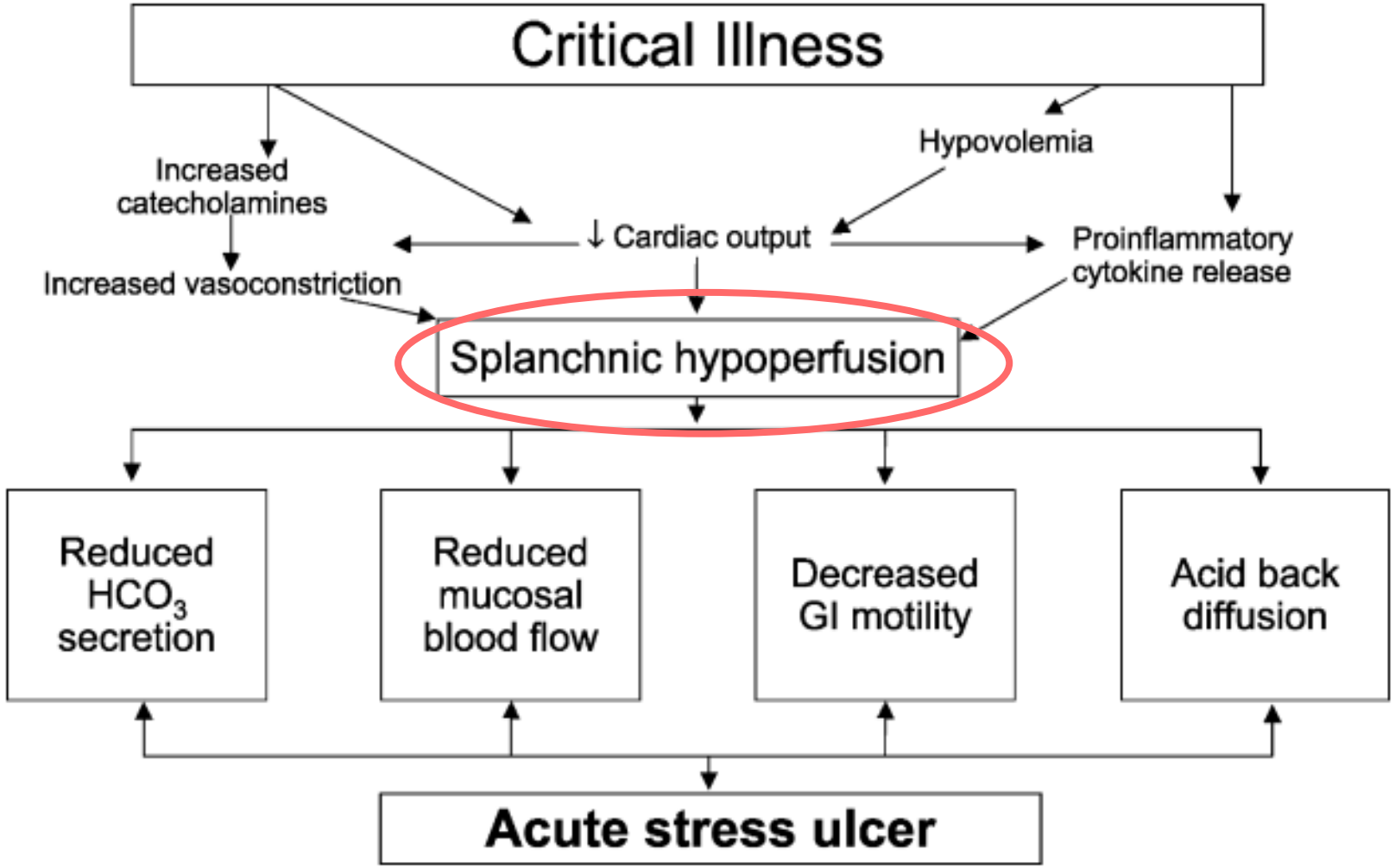
Perren et al. Intensive Care Med 2013

ELSEVIER

Journal of Critical Care

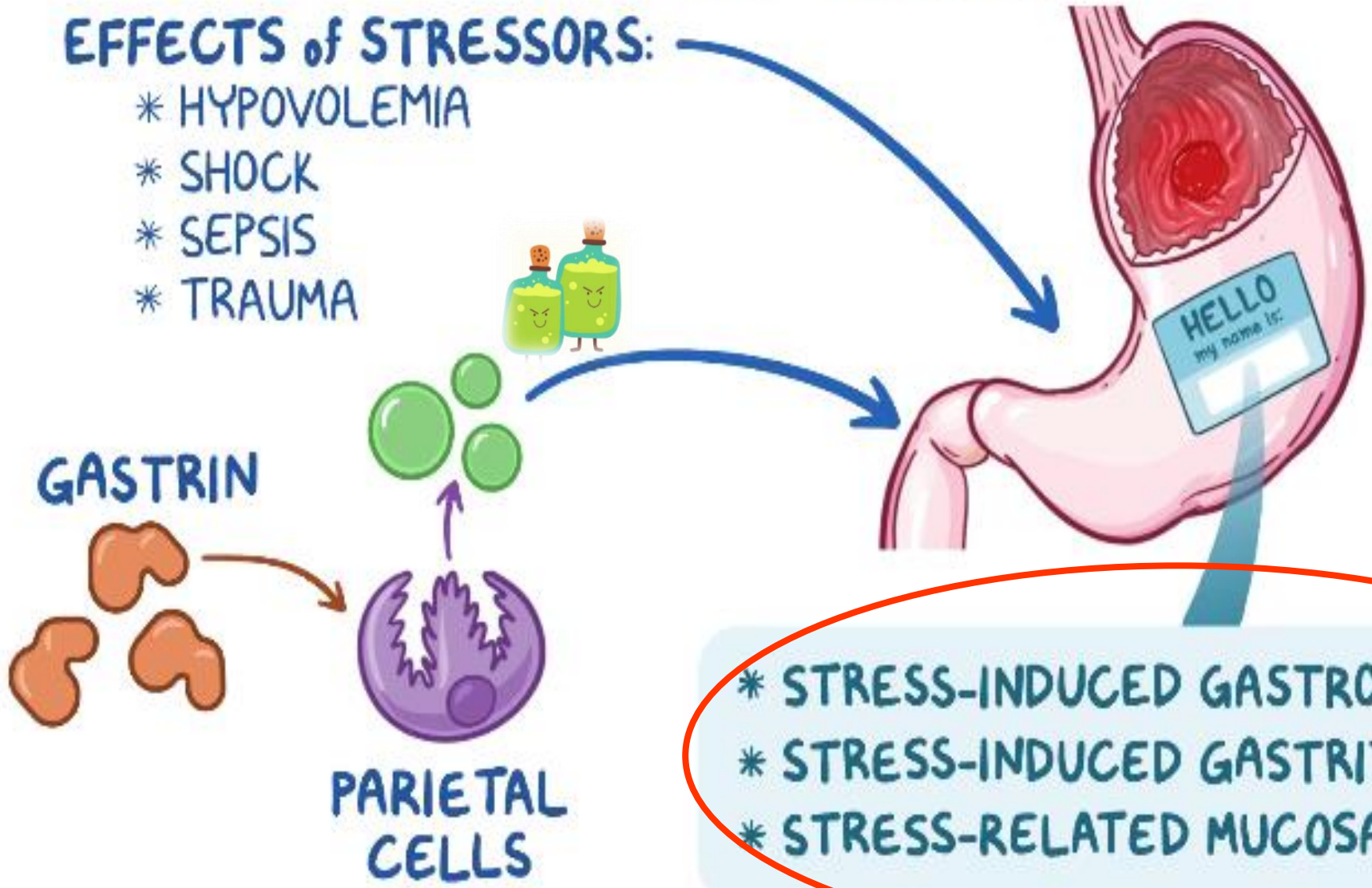
Pathophysiology and prophylaxis of stress ulcer in intensive care unit patients

Neil Stollman MD[a,*], David C. Metz MD[b]



Pathophysiology of stress ulcers. Adapted fromChest 2001;119:1222

STRESS ULCERS



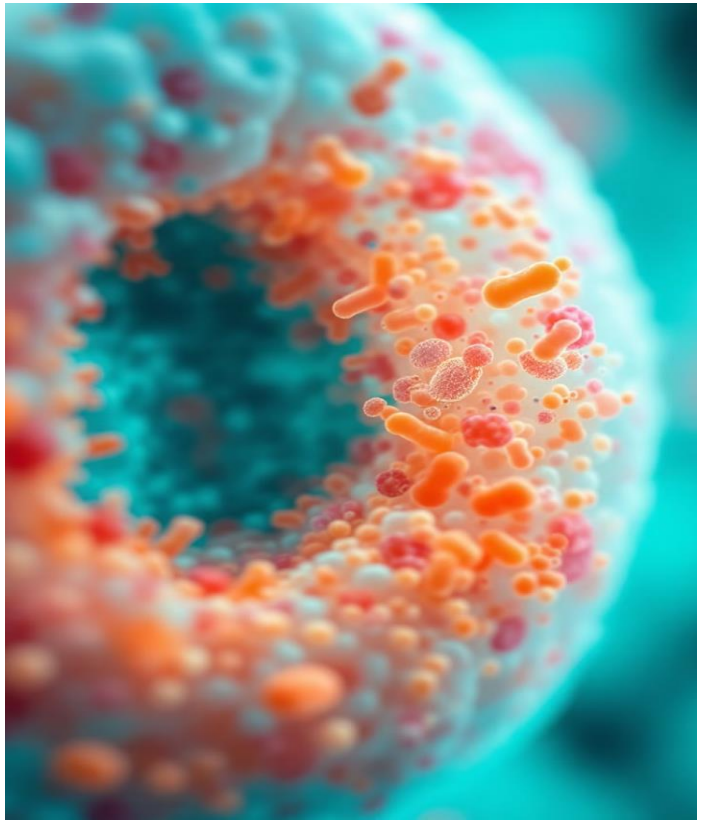
Définition

2024 *LITERATURE REVIEW*

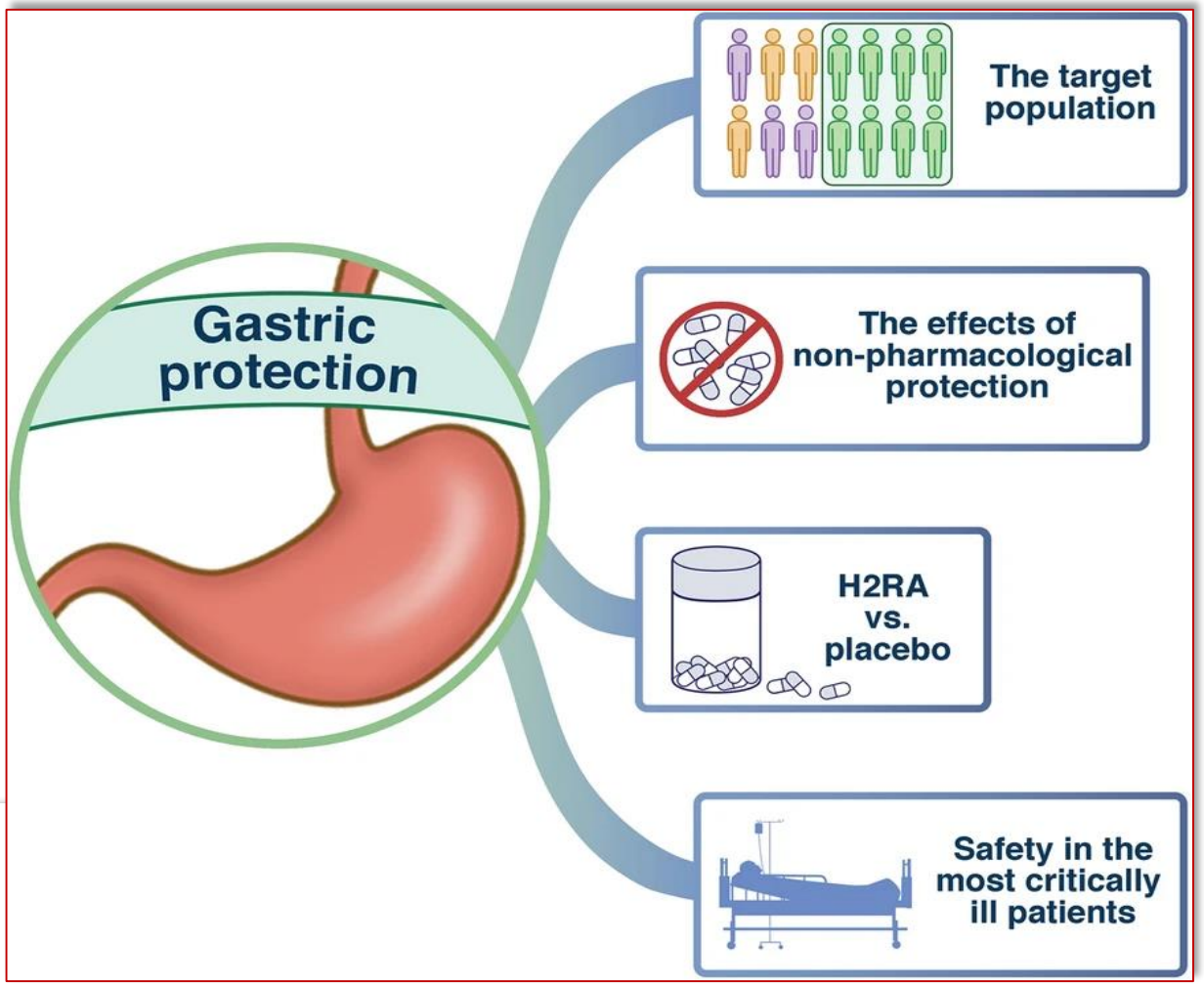
Prevention and Management of Stress Ulcers in Critically ill Patients

Zulfakhri✉, Akhmad Yun Jufan, Calcarina Fitriani Retno Wisudarti

Les ulcères de stress sont également appelés lésions muqueuses liées au stress (SMRD), un terme générique pour décrire l'ensemble des lésions associées à l'inflammation, à l'érosion et aux ulcérations du tractus gastro-intestinal supérieur chez les patients en état critique



➢« Knowledge gaps »?



Intensive Care Med (2023) 49:334–336
https://doi.org/10.1007/s00134-022-06959-9

2023

Fig. 1 Knowledge gaps in gastric protection in critical illness

LASTING LEGACY IN INTENSIVE CARE MEDICINE

Prevention of upper gastrointestinal bleeding in critical illness

Mette Krag[1,3], Waleed Alhazzani[4,5] and Morten Hylander Møller[2*]

Who needs SUP ?

➢ Facteurs de risques

Intensive Care Med (2019) 45:1347–1359
https://doi.org/10.1007/s00134-019-05751-6

SYSTEMATIC REVIEW

Predictors of gastrointestinal bleeding in adult ICU patients: a systematic review and meta-analysis

Anders Granholm[1], Linan Zeng[2,3], Joanna Colleen Dionne[3,4], Anders Perner[1,5], Søren Marker[1,5], Mette Krag[1,5], Robert MacLaren[6], Zhikang Ye[3], Morten Hylander Møller[1,5*], Waleed Alhazzani[3,4] and the GUIDE Group

➢ Facteurs de risques

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SYSTEMATIC REVIEW

Predictors of gastrointestinal bleeding in adult ICU patients: a systematic review and meta-analysis

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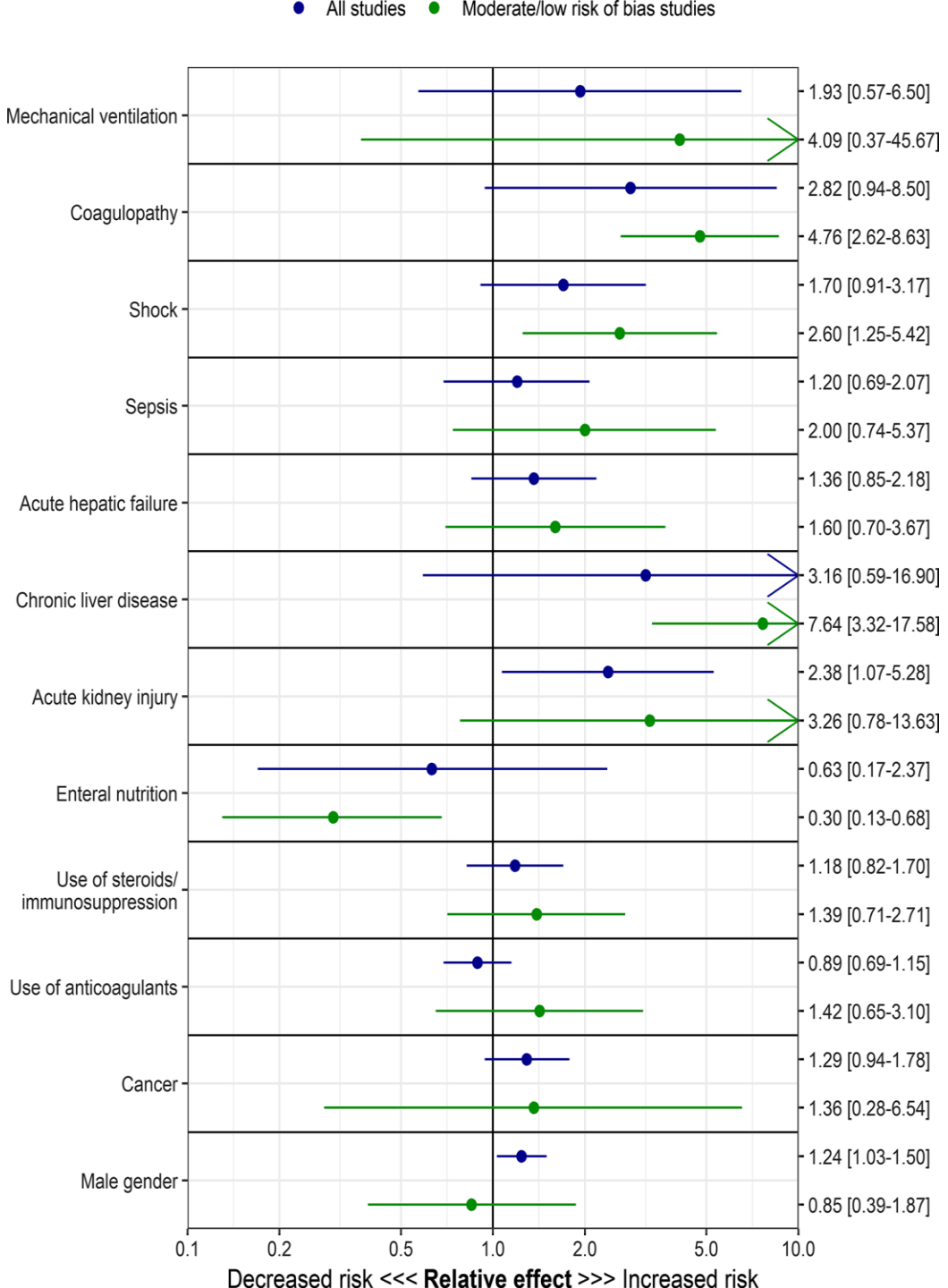
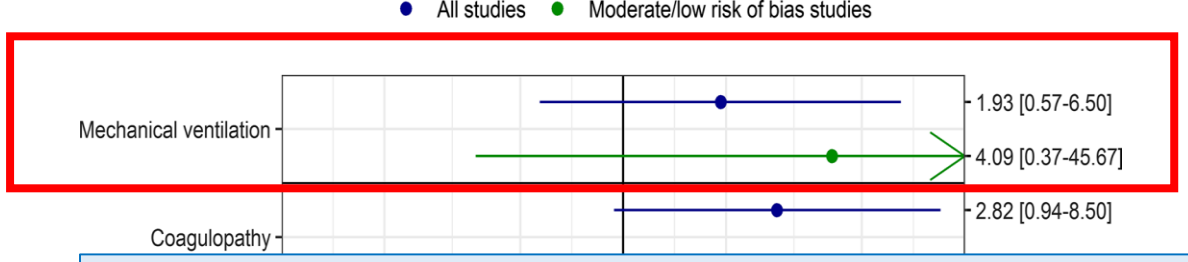
Identifier les facteurs prédictifs de saignement digestif (GIB) chez les patients adultes en soins intensifs .

8 études

116 497 patients.



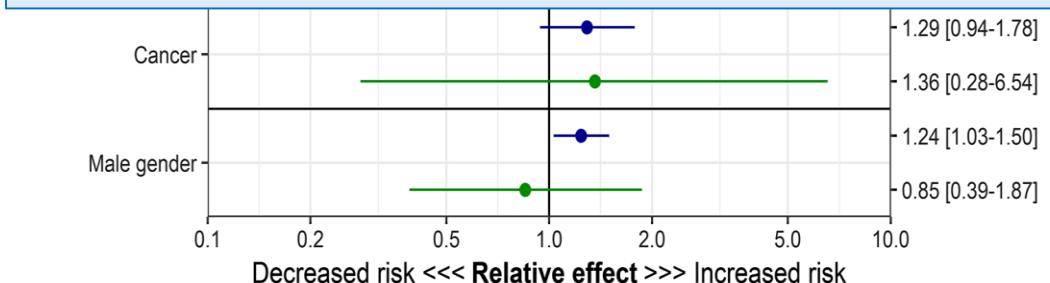
- **Coagulopathie** : RE 4,76 [2,62–8,63]
- **Choc** : RE 2,60 [1,25–5,42]
- **Maladie hépatique chronique** : RE 7,64 [3,32–17,58]
- **Insuffisance rénale aiguë** : RE 2,38 [1,07–5,28]
- **Sexe masculin** : RE 1,24 [1,03–1,50] (niveau de preuve faible)



L'effet de la ventilation mécanique demeure incertain

Effet relatif (RE) : 1,93; Intervalle de confiance à 95 % : 0,57 à 6,50

Niveau de certitude : très faible



REVISE

Re-Evaluating the Inhibition of Stress Erosions: Gastrointestinal Bleeding Prophylaxis In ICU

2024

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 4, 2024 VOL. 391 NO. 1

Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation

D. Cook, A. Deane, F. Lauzier, N. Zytaruk, G. Guyatt, L. Saunders, M. Hardie, D. Heels-Ansdell, W. Alhazzani, J. Marshall, J. Muscedere, J. Myburgh, S. English, Y.M. Arabi, M. Ostermann, S. Knowles, N. Hammond, K.M. Byrne, M. Chapman, B. Venkatesh, P. Young, D. Rajbhandari, A. Poole, A. Al-Fares, G. Reis, D. Johnson, M. Iqbal, R. Hall, M. Meade, L. Hand, E. Duan, F. Clarke, J.C. Dionne, J.L.Y. Tsang, B. Rochwerg, T. Karachi, F. Lamontagne, F. D'Aragon, C. St. Arnaud, B. Reeve, A. Geagea, D. Niven, G. Vazquez-Grande, R. Zarychanski, D. Ovakim, G. Wood, K.E.A. Burns, A. Goffi, M.E. Wilcox, W. Henderson, D. Forrest, R. Fowler, N.K.J. Adhikari, I. Ball, T. Mele, A. Binnie, S. Trop, S. Mehta, I. Morgan, O. Loubani, M. Vanstone, K. Fiest, E. Charbonney, Y.A. Cavayas, P. Archambault, O.G. Rewa, V. Lau, A.S. Kristof, K. Khwaja, D. Williamson, S. Kanji, E. Sy, B. Dennis, S. Reynolds, F. Marquis, F. Lellouche, A. Rahman, P. Hosek, J.F. Barletta, R. Cirrone, M. Tutschka, F. Xie, L. Billot, L. Thabane, and S. Finfer, for the REVISE Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

Ulcer Prophylaxis during Mechanical Ventilation

A PLAIN LANGUAGE SUMMARY

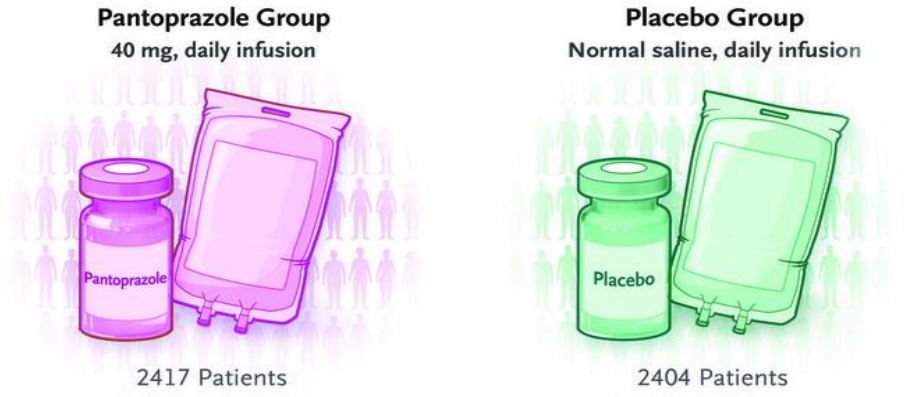
Based on the NEJM publication: Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation by D. Cook et al. (published June 14, 2024)

In this trial, researchers compared the effect of a proton-pump inhibitor on the risk of gastrointestinal bleeding with that of placebo in patients undergoing mechanical ventilation.

Critically ill patients in the intensive care unit have an increased risk of stress-induced gastrointestinal ulcers, which can cause gastrointestinal bleeding.

HOW WAS THE TRIAL CONDUCTED?

4821 critically ill adults undergoing invasive mechanical ventilation were assigned to receive infusions of either 40 mg of pantoprazole or placebo daily for up to 90 days. The primary efficacy outcome was clinically important upper gastrointestinal bleeding, and the primary safety outcome was death from any cause at 90 days.



PATIENTS

WHO

Mean age, 58 years

Men: 64%; Women: 36%

CLINICAL STATUS

23% were receiving pre-hospital acid suppression

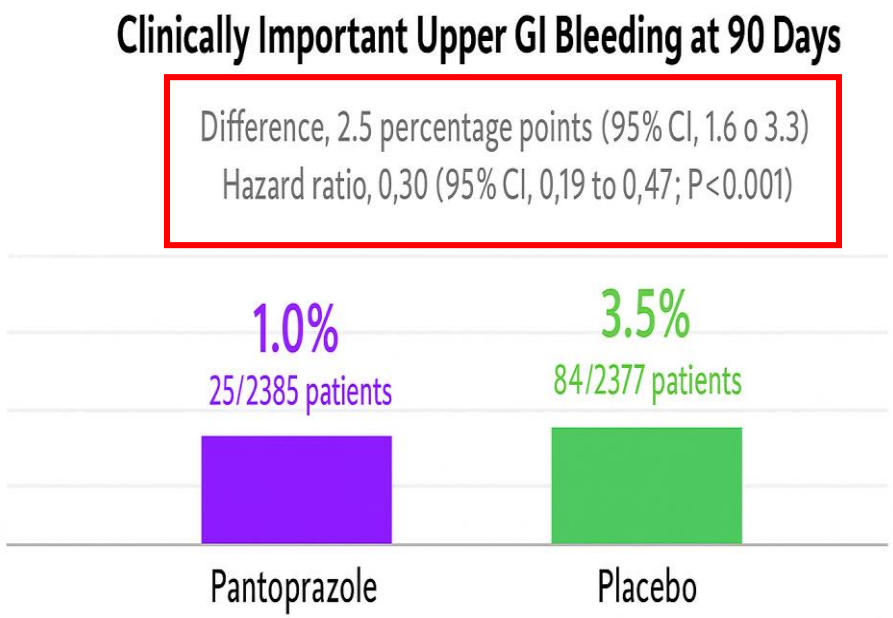
Median duration of infusion, 5 days

TRIAL DESIGN

- 68 CENTERS
- 8 COUNTRIES
- RANDOMIZED
- PLACEBO-CONTROLLED
- BLINDED TRIAL-GROUP ASSIGNMENTS AND ADJUDICATION OF BLEEDING EPISODES

RESULTS

The pantoprazole group had significantly fewer clinically important upper gastrointestintinal bleeding events than the placebo group.



Conclusion

Chez les patients en réanimation sous ventilation mécanique invasive, ceux ayant reçu du pantoprazole présentaient un risque significativement plus faible de saignement digestif haut cliniquement important comparé à ceux ayant reçu un placebo, sans impact significatif sur la mortalité..

NEJM Evidence

2024

Published June 14, 2024
NEJM Evid 2024;3(7)
DOI: 10.1056/EVIDoa2400134

ORIGINAL ARTICLE | CRITICAL CARE REVIEWS MEETING 2024

Proton-Pump Inhibitors to Prevent Gastrointestinal Bleeding — An Updated Meta-Analysis

Ying Wang, M.Sc.,[1] Sameer Parpia, Ph.D.,[2] Long Ge, Ph.D.,[3] Diane Heels-Ansdell, M.Sc.,[1] Honghao Lai, M.Sc.,[3] Meisam Abdar Esfahani, M.D., M.Sc.,[1] Bei Pan, Ph.D.,[4] Waleed Alhazzani, M.D., M.Sc.,[1,2] Stefan Schandelmaier, Ph.D.,[5,6,7] Francois Lauzier, M.D., M.Sc.,[8,9] Yaseen Arabi, M.D.,[10] Jeffrey Barletta, Pharm.D.,[11] Adam Deane, M.D.,[12] Simon Finfer, M.B.B.S.,[13,14,15] David Williamson, Pharm.D.,[16,17] Salmaan Kanji, Pharm.D.,[18,19] Morten H. Møller, M.D.,[20,21] Anders Perner, M.D.,[20,21] Mette Krag, M.D.,[21,22] Paul J. Young, Ph.D.,[23,24] Joanna C. Dionne, M.D., Ph.D.,[1,25,26] Naomi Hammond, Ph.D.,[27,28] Zhikang Ye, Ph.D.,[1] Quazi Ibrahim, M.Sc.,[1] and Deborah Cook, M.D., M.Sc.[1,29]

NEJM Evidence

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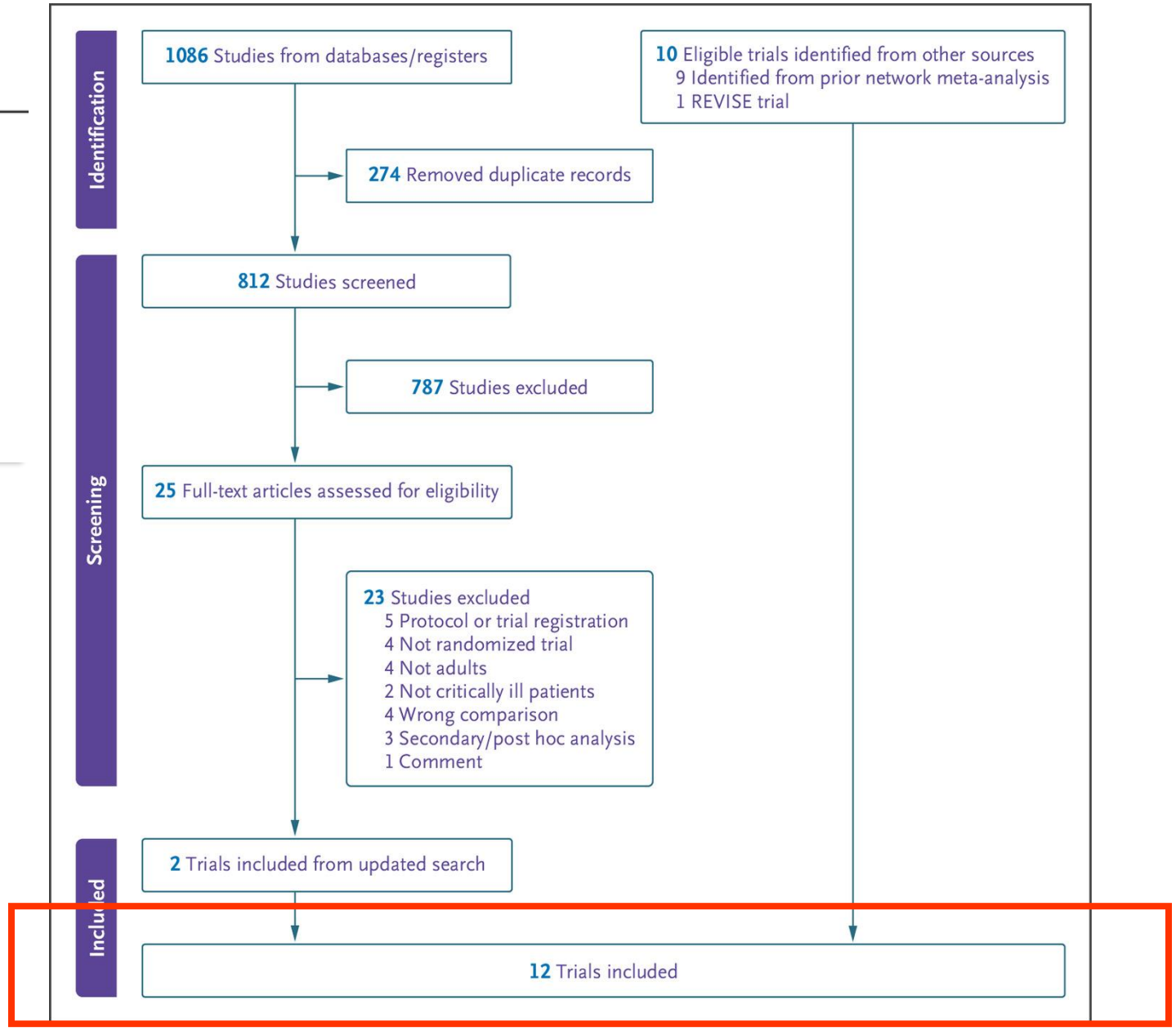
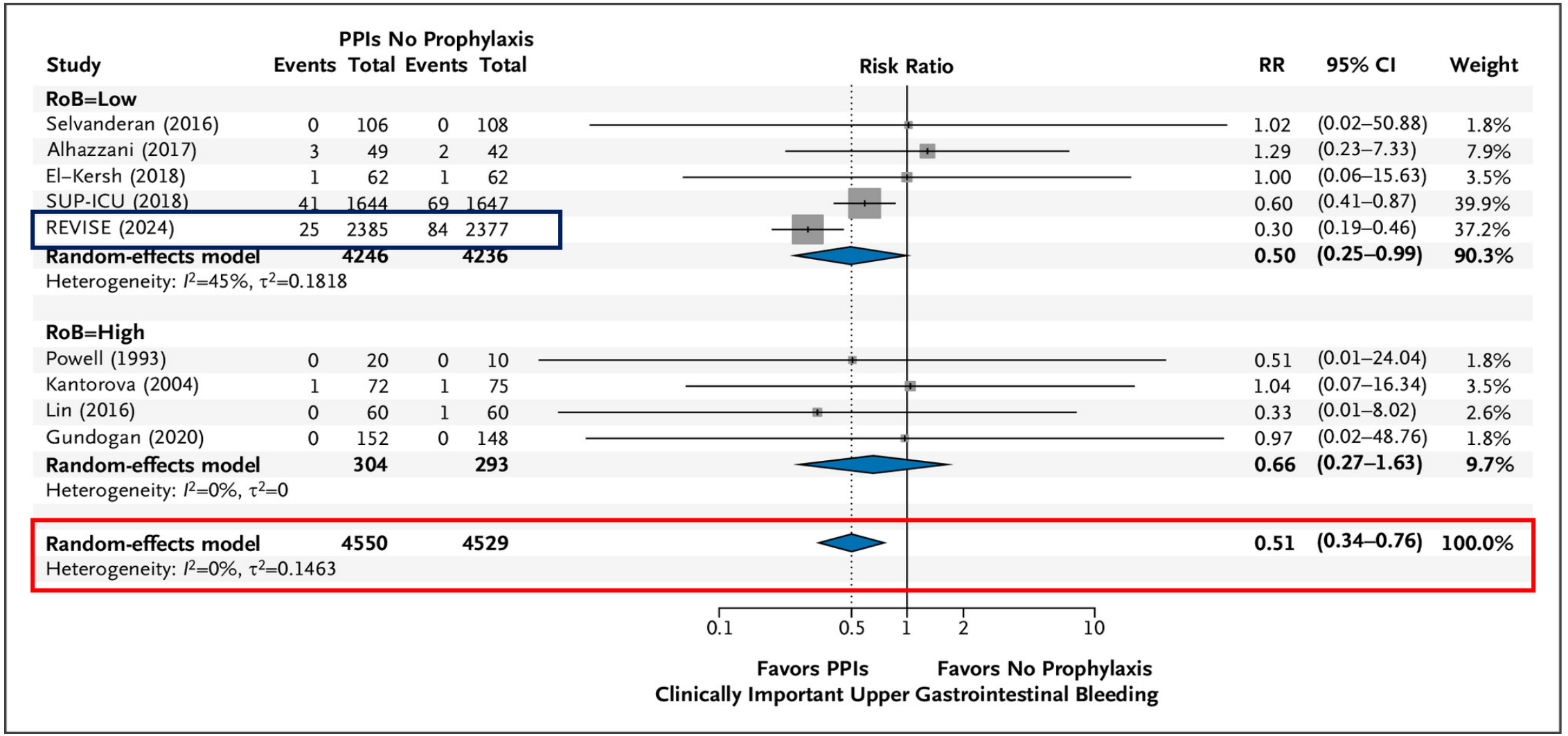
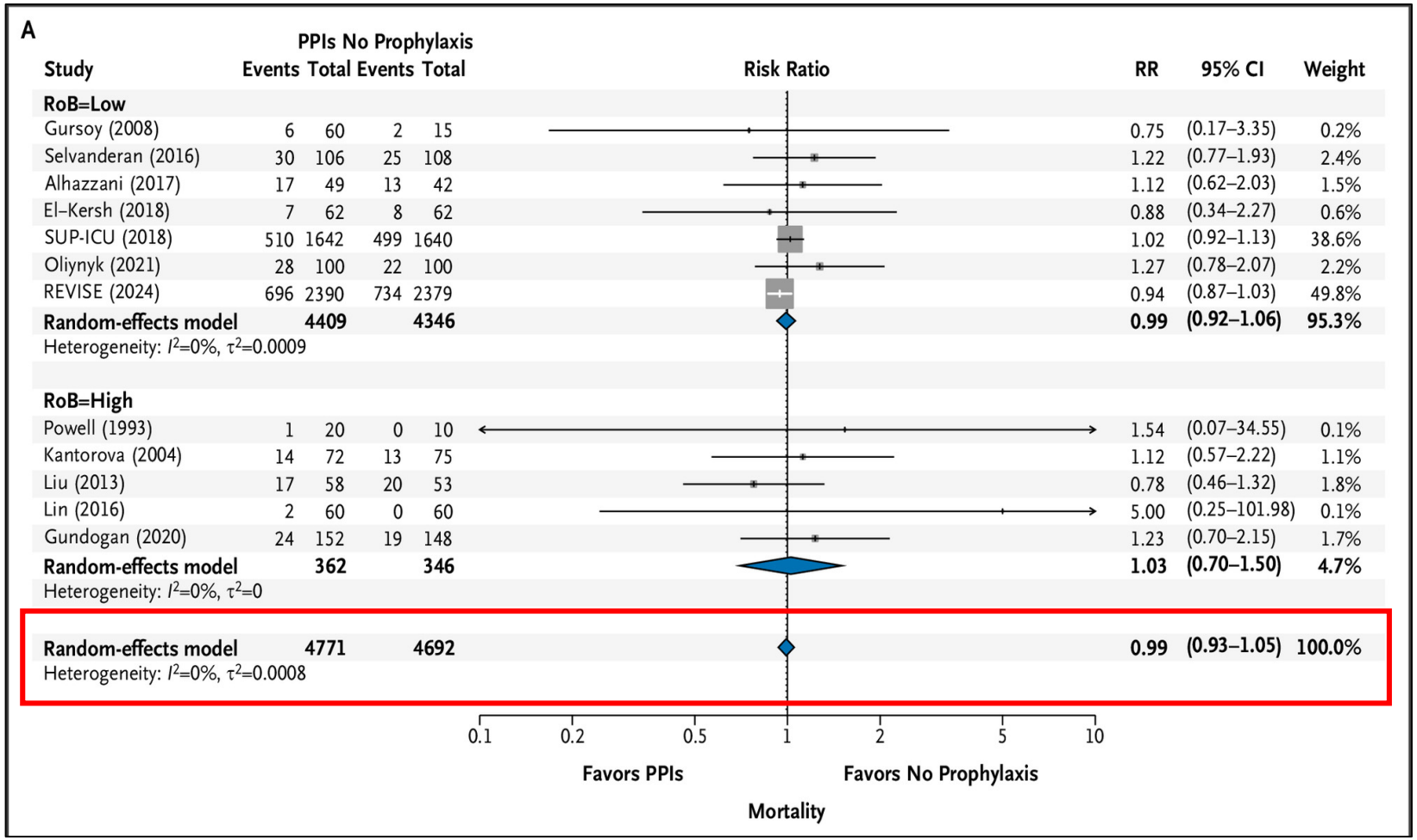


PRISMA Flow Diagram



Forest Plot for Clinically Important Gastrointestinal Bleeding.

Results for Mortality.



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VOL. 391 NO. 1

ical Ventilation

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. Fowler, N.K.J. Adhikari,
. Fiest, E. Charbonney,
, S. Kanji, E. Sy, B. Dennis,
Tutschka, F. Xie, L. Billot,

M.Sc.,[3]
elmaier, Ph.D.,[5,6,7]
[2]
. Møller, M.D.,[20,21]
[1,25,26]
,
c.[1,29]

Society of Critical Care Medicine
The Intensive Care Professionals

Guidelines
2024

American Society of Health-System Pharmacists

SCCM and ASHP Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Robert MacLaren, PharmD, MPH, MCCM; Joanna C. Dionne, MD, PhD, MSc; Waleed Alhazzani, MD, MSc

PUBLISHED: 07/15/2024

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Society of Critical Care Medicine
The Intensive Care Professionals

Guidelines
2024

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Robert MacLaren, PharmD, MPH, MCCM; Joanna C. Dionne, MD, PhD, MSc; Waleed Alhazzani, MD, MSc

PUBLISHED: 07/15/2024

Nous suggérons que les cliniciens administrent une prophylaxie anti-ulcéreuse (SUP) pour prévenir les hémorragies digestives hautes (UGIB) cliniquement significatives chez les adultes en soins intensifs **présentant des facteurs de risque,** comparativement à l'absence de SUP.
Niveau de certitude: Modéré

Pharmacologic SUP | Strong | SUP

Society of Critical Care Medicine
The Intensive Care Professionals

Guidelines
2024

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Robert MacLaren, PharmD, MPH, MCCM; Joanna C. Dionne, MD, PhD, MSc; Waleed Alhazzani, MD, MSc

PUBLISHED: 07/15/2024

Nous suggérons que les adultes en soins intensifs présentant une coagulopathie, un état de choc ou une maladie hépatique chronique soient considérés comme à risque de saignement digestif haut (UGIB) cliniquement significatif.
Niveau de certitude des données : faible à modéré

Risk factors for clinically important bleeding and overt UGIB	Conditional	Risk factors or clinically important UGIB

Society of Critical Care Medicine
The Intensive Care Professionals

Guidelines
2024

American Society of Health-System Pharmacists

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PUBLISHED: 07/15/2024

lww.com/CCM/H544). Mechanical ventilation may be inherent in the definition of critical illness as many patients in the individual studies required invasive mechanical ventilation, but mechanical ventilation alone probably is not a risk factor and does not necessitate SUP. No evidence is available for noninvasive ventila-

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REVISE

Re-Evaluating the Inhibition of Stress Erosions: Gastrointestinal Bleeding Prophylaxis in ICU

- Invasive mechanical ventilation, 100%
- Inotrope or vasopressor infusion, 70%
- Renal-replacement therapy, 6,4%

Society of Critical Care Medicine
The Intensive Care Professionals

Guidelines
2024

American Society of Health-System Pharmacists

SCCM and ASHP Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Robert MacLaren, PharmD, MPH, MCCM; Joanna C. Dionne, MD, PhD, MSc; Waleed Alhazzani, MD, MSc

PUBLISHED: 07/15/2024

Nous suggérons d'utiliser la prophylaxie de l'ulcère de stress (SUP) chez les adultes en neuro-réanimation pour réduire les hémorragies digestives hautes (UGIB) cliniquement significatives liées au stress, comparativement à l'absence de SUP.
Niveau de certitude des preuves : Très faible

SUP in neurocritical care | Conditional | SUP

Which Agent Would YOU Recommend?

➢ Chronologie des traitements pharmacologiques

PPI
H2RA
SAF

01

1980's

Antacids (gastric pH adjusted)

02

1990's

- ✓ **Anti-H2++**
- ✓ **Sucralfate +**

03

1999 (ASHP)

- ✓ **Anti-H2++**
- ✓ **Sucralfate+**
- ✓ **IPP** (émergents)

04

2000-2012

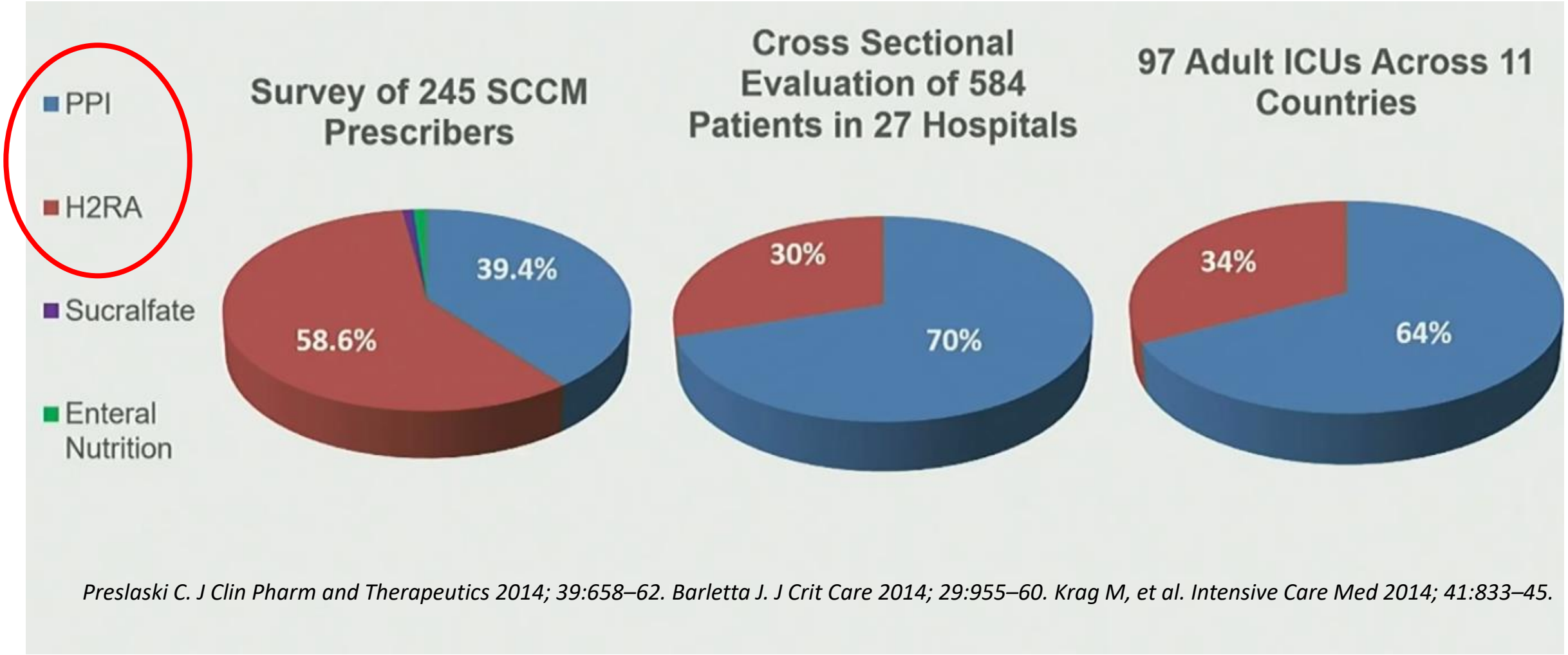
- ✓ **IPP ++**
- ✓ **Anti-H2+**
- ✓ **Sucralfate+/-**

05

2021 (SSC)

- ✓ **IPP/Anti-H2**
- **Sucralfate** ✗

➢ La prescription en réanimation?



Preslaski C. J Clin Pharm and Therapeutics 2014; 39:658–62. Barletta J. J Crit Care 2014; 29:955–60. Krag M, et al. Intensive Care Med 2014; 41:833–45.

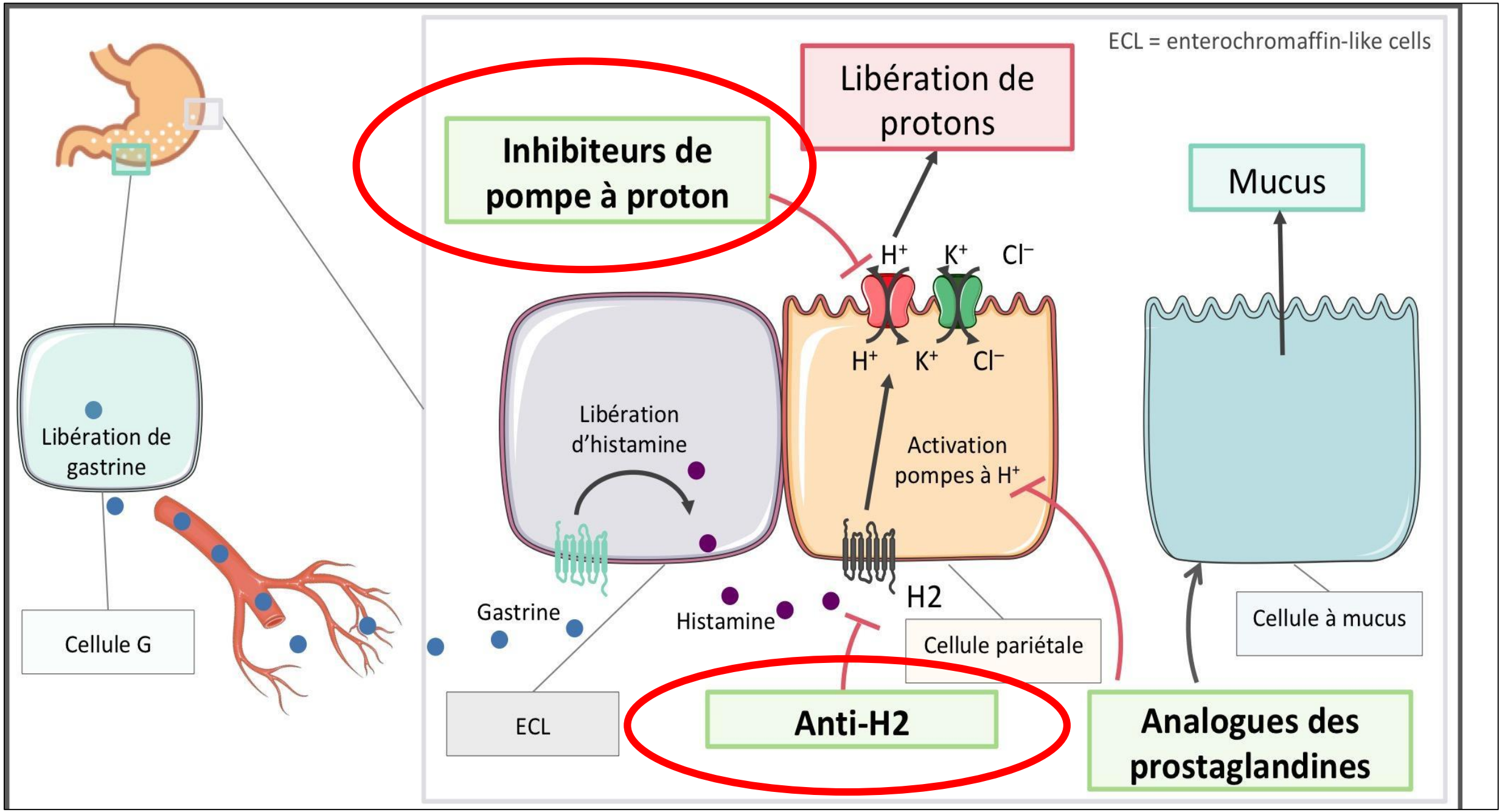
PPIs

Proton-pump inhibitors

IPP

H_2RAs

Histamine-2 receptor antagonists


ECL = enterochromaffin-like cells
Libération de protons
Inhibiteurs de pompe à proton
Mucus
H+ K+ Cl−
H+ K+ Cl−
Libération d'histamine
Activation pompes à H+
Libération de gastrine
Cellule G
Gastrine
Histamine
H2
Cellule pariétale
Cellule à mucus
ECL
Anti-H2
Analogues des prostaglandines

IPP versus anti-H2?

2020

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Stress Ulcer Prophylaxis With Proton Pump Inhibitors vs Histamine-2 Receptor Blockers on In-Hospital Mortality Among ICU Patients Receiving Invasive Mechanical Ventilation

The PEPTIC Randomized Clinical Trial

The PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, Alberta Health Services Critical Care Strategic Clinical Network, and the Irish Critical Care Trials Group

JAMA Network

QUESTION What is the comparative effect on in-hospital mortality of using proton pump inhibitors (PPIs) vs histamine-2 receptor blockers (H_2RBs) for stress ulcer prophylaxis in ICU patients requiring invasive mechanical ventilation?

CONCLUSION This clinical trial did not find a statistically significant difference between PPIs and H_2RBs for stress ulcer prophylaxis in ICU patients receiving mechanical ventilation, but study interpretation may be limited by crossover in medication use.

POPULATION

17 137 Men 9691 Women

Adults receiving mechanical ventilation within 24 hours of ICU admission

Mean age: 58 years

LOCATIONS

50
International ICUs

INTERVENTION

26 982 Patients randomized
26 771 Patients analyzed

13 415
PPI strategy

13 356
H_2RB strategy

PRIMARY OUTCOME

All-cause mortality during index hospitalization within 90 days

FINDINGS

All-cause mortality within 90 days

PPI strategy
2459 of 13 415 patients

H_2RB strategy
2333 of 13 356 patients

Absolute risk difference,
0.93 percentage points
(95% CI, −0.01 to 1.88); *P* =.054

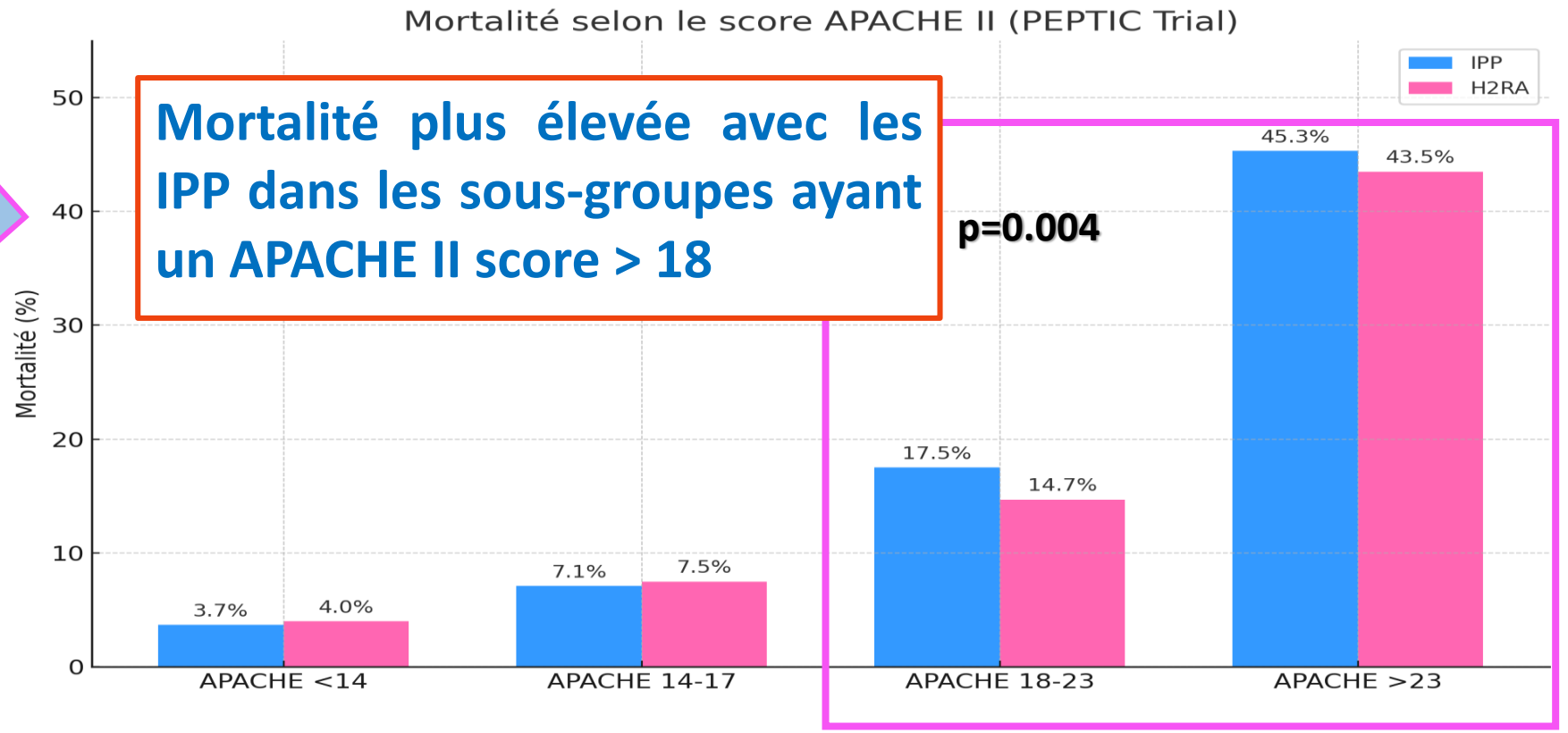
Table 2. Primary, Secondary, and Tertiary Outcomes

	Proton Pump Inhibitors	Histamine-2 Receptor Blockers	Estimate (95% CI)	Absolute Risk Difference (95% CI)	*P* Value
Primary Outcome					
Died at the hospital by 90 d, No./total No. (%)	2459/13 415 (18.3)	2333/13 356 (17.5)	RR, 1.05 (1.00 to 1.10)	0.93 (−0.01 to 1.88) percentage points	.054
Secondary Outcomes					
Types of complications, No./total No. (%)					
Clinically important upper gastrointestinal bleeding[a]	172/13 436 (1.3)	239/13 392 (1.8)	RR, 0.73 (0.57 to 0.92)	−0.51 (−0.90 to −0.12) percentage points	.009
Clostridioides difficile infection[b]	40/13 436 (0.30)	57/13 392 (0.43)	RR, 0.74 (0.51 to 1.09)	−0.11 (−0.25 to 0.03) percentage points	.13
Length of stay variables and duration of ventilation					
Days until discharged alive from the ICU					
No. of patients	13 425	13 384			
Median (interquartile range)[c]	3.6 (1.6 to 10.4)	3.3 (1.5 to 10.0)	ROM, 1.00 (0.97 to 1.03)[d]		.85
Days until discharged alive from the hospital					
No. of patients	13 418	13 370			
Median (interquartile range)[c]	12.2 (6.0 to 40.0)	12.0 (6.0 to 39.3)	ROM, 1.01 (0.98 to 1.03)[d]		.66

JAMA. 2020;323(7):616-626. doi:10.1001/jama.2019.22190

Table 3. Post Hoc Subgroup Analyses by Quartiles of Illness Severity Based on APACHE II Scores

APACHE II Score Quartile[a]	No. of Patients	Proton Pump Inhibitors	Histamine-2 Receptor Blockers	Estimate (95% CI)	*P* Value for Interaction
In-Hospital Mortality, No./Total No. (%)					
1 (Score range: 0-13)	7711	142/3872 (3.7)	155/3839 (4.0)	RR, 0.92 (0.77-1.11)	
2 (Score range: 14-17)	5860	211/2956 (7.1)	219/2904 (7.5)	RR, 0.96 (0.86-1.08)	
3 (Score range: 18-23)	6475	565/3229 (17.5)	477/3246 (14.7)	RR, 1.15 (1.05-1.25)	.004
4 (Score range: 24-61)	6610	1493/3296 (45.3)	1440/3314 (43.5)	RR, 1.05 (1.00-1.11)	



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 6, 2018 VOL. 379 NO. 23

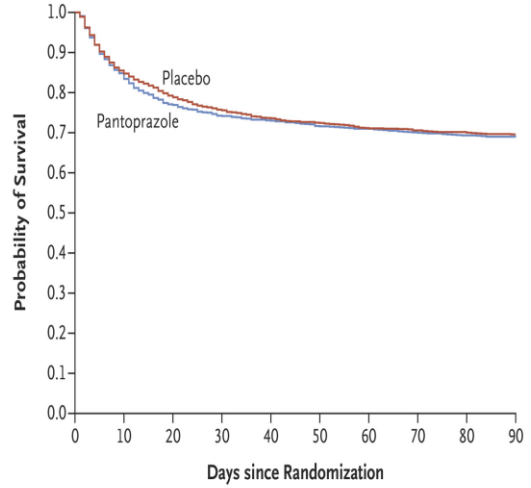
Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU

M. Krag, S. Marker, A. Perner, J. Wetterslev, M.P. Wise, J.C. Schefold, F. Keus, A.B. Guttormsen, S. Bendel, M. Borthwick, T. Lange, B.S. Rasmussen, M. Siegemund, H. Bundgaard, T. Elkmann, J.V. Jensen, R.D. Nielsen, L. Liboriussen, M.H. Bestle, J.M. Elkjær, D.F. Palmqvist, M. Bäcklund, J.H. Laake, P.M. Bådstøløkken, J. Grönlund, O. Breum, A. Walli, R. Winding, S. Iversen, I.-L. Jarnvig, J.O. White, B. Brand, M.B. Madsen, L. Quist, K.J. Thornberg, A. Møller, J. Wiis, A. Granholm, C.T. Anthon, T.S. Meyhoff, P.B. Hjortrup, S.R. Aagaard, J.B. Andreasen, C.A. Sørensen, P. Haure, J. Hauge, A. Hollinger, J. Scheuzger, D. Tuchscherer, T. Vuilliomenet, J. Takala, S.M. Jakob, M.L. Vang, K.B. Pælestik, K.L.D. Andersen, I.C.C. van der Horst, W. Dieperink, J. Fjølner, C.K.W. Kjer, C. Sølling, C.G. Sølling, J. Karttunen, M.P.G. Morgan, B. Siøbø, I. Engstrøm, B. Agerholm-Larsen, and M.H. Møller, for the SUP-ICU trial group*

Table 2. Primary and Secondary Outcome Measures.

Outcomes	Pantoprazole	Placebo	Relative Risk (95% CI)*	P Value†
Primary outcome: death by day 90 — no./total no. (%)	510/1642 (31.1)	499/1640 (30.4)	1.02 (0.91–1.13)	0.76
Secondary outcomes				
One or more clinically important events — no./total no. (%)‡	360/1644 (21.9)	372/1647 (22.6)	0.96 (0.83–1.11)	—
One or more episodes of clinically important gastrointestinal bleeding — no./total no. (%)	41/1644 (2.5)	69/1647 (4.2)	0.58 (0.40–0.86)	—
One or more infectious adverse events — no./total no. (%)§	276/1644 (16.8)	279/1647 (16.9)	0.99 (0.84–1.16)	—
Severe adverse reaction — no./total no. (%)¶	0/1644 (0)	0/1647 (0)	—	—
Median percentage of days alive without the use of life support (IQR)‖	92 (60–97)	92 (65–97)	—	—

A Time to Death

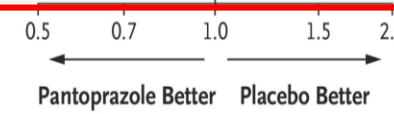


No. at Risk

Placebo	1647	1243	1167	1141
Pantoprazole	1643	1219	1163	1133

B Relative Risk of the Primary Outcome

Subgroup	Pantoprazole	Placebo	Relative Risk (95% CI)	P Value for Heterogeneity
	no. of events/no. of patients in subgroup			
Shock at randomization				0.92
Yes	413/1251	395/1210	1.01 (0.90–1.13)	
No	97/391	104/430	1.02 (0.80–1.31)	
Mechanical ventilation at randomization				0.74
Yes	399/1272	400/1310	1.03 (0.91–1.16)	
No	111/370	99/330	0.98 (0.77–1.25)	
Coagulopathy at randomization				0.54
Yes	135/352	118/299	0.95 (0.77–1.17)	
No	375/1290	381/1341	1.03 (0.91–1.16)	
History of liver disease				0.69
Yes	20/44	25/48	0.93 (0.60–1.44)	
No	490/1598	474/1592	1.02 (0.92–1.14)	
Type of ICU admission				0.38
Medical	361/1045	328/994	1.04 (0.92–1.18)	
Surgical	149/597	171/646	0.94 (0.78–1.14)	
SAPS II score >53				0.05
Yes	272/579	229/558	1.13 (0.99–1.30)	
No	205/929	231/967	0.92 (0.78–1.09)	
All patients	510/1642	499/1640	1.02 (0.91–1.13)	

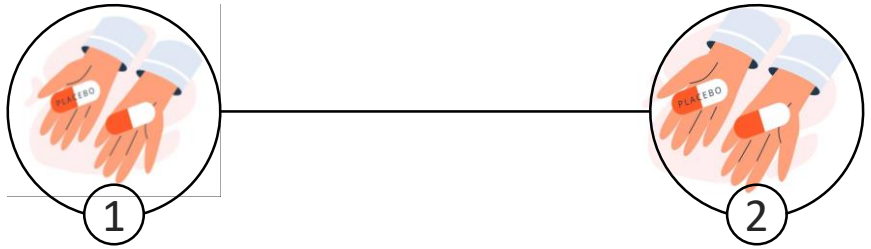


Intensive Care Med (2019) 45:609–618
https://doi.org/10.1007/s00134-019-05589-y

ORIGINAL

Pantoprazole prophylaxis in ICU patients with high severity of disease: a post hoc analysis of the placebo-controlled SUP-ICU trial

Søren Marker[1,2*], Anders Perner[1,2], Jørn Wetterslev[2,3], Mette Krag[1,2], Theis Lange[4,5], Matt P. Wise[6], Mark Borthwick[7], Stepani Bendel[8], Frederik Keus[9], Anne Berit Guttormsen[10,11], Joerg C. Schefold[12], Morten Hylander Møller[1,2] and The SUP-ICU investigators



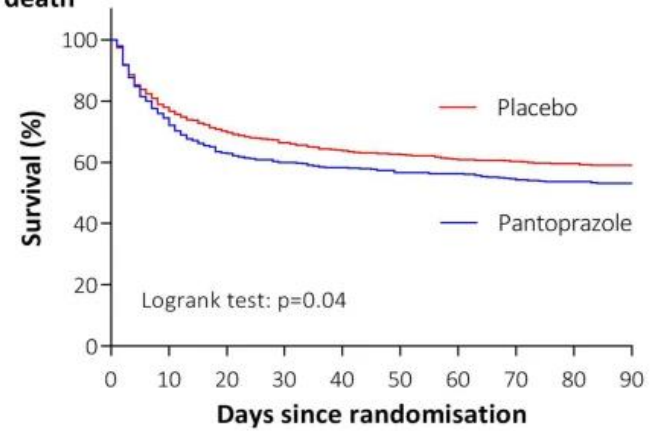
PTPZ group

580

Placebo group

560

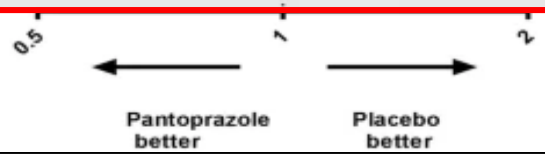
Part A - Time to death



Number at risk				
Pantoprazole	579	349	325	307
Placebo	558	375	341	329

Part B - Relative risk of the primary outcome

Subgroups	Pantoprazole	Placebo	Relative risk (95 % CI)	P value for heterogeneity
	No. of events / no. of patients in subgroup (%)			
Shock Yes (n=945)	237/487	198/458	1.12 (0.98 - 1.29)	0.92
No (n=192)	35/92	31/100	1.18 (0.81 - 1.72)	
Mechanical ventilation Yes (n=949)	229/484	186/465	1.16 (1.00 - 1.33)	0.47
No (n=188)	43/95	43/93	1.02 (0.75 - 1.39)	
Coagulopathy Yes (n=271)	83/160	54/111	1.07 (0.84 - 1.36)	0.72
No (n=866)	189/419	175/447	1.14 (0.98 - 1.33)	
History of liver disease Yes (n=40)	10/21	12/19	0.78 (0.45 - 1.36)	0.20
No (n=1097)	262/558	217/539	1.15 (1.01 - 1.31)	
Type of ICU admission Medical (n=771)	193/399	156/372	1.14 (0.96 - 1.32)	0.84
Surgical (n=366)	79/180	73/186	1.11 (0.88 - 1.40)	
ALL PATIENTS (n=1137)			1.13 (1.00 - 1.29)	0.05



Mortalité plus élevée avec les IPP dans le sous-groupe ayant un SAPS II > 53

Les IPP sont-ils plus efficaces que les antiH2 ?

2022

Research Report

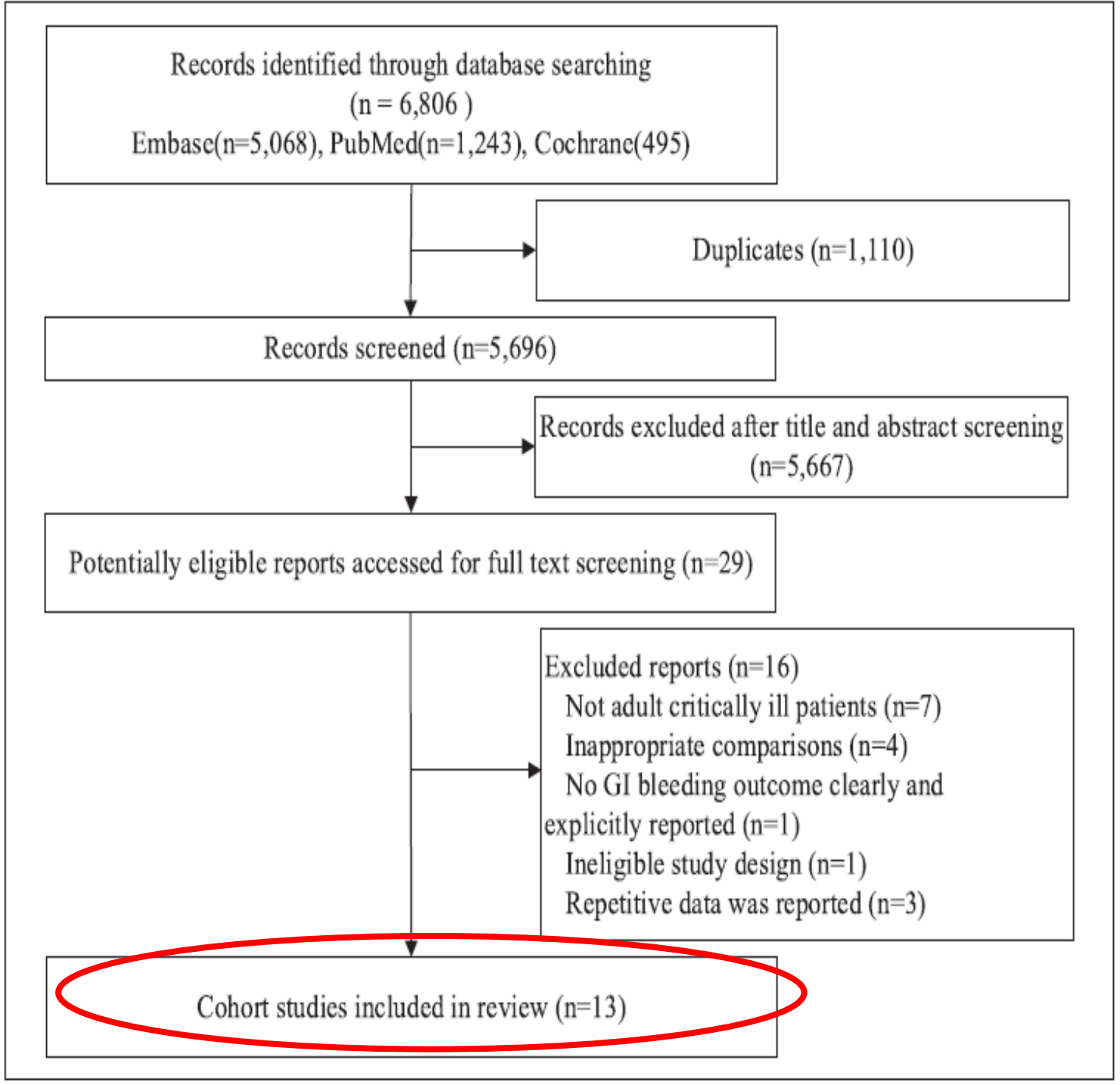
Are Proton Pump Inhibitors More Effective Than Histamine-2-Receptor Antagonists for Stress Ulcer Prophylaxis in Critically Ill Patients? A Systematic Review and Meta-Analysis of Cohort Studies

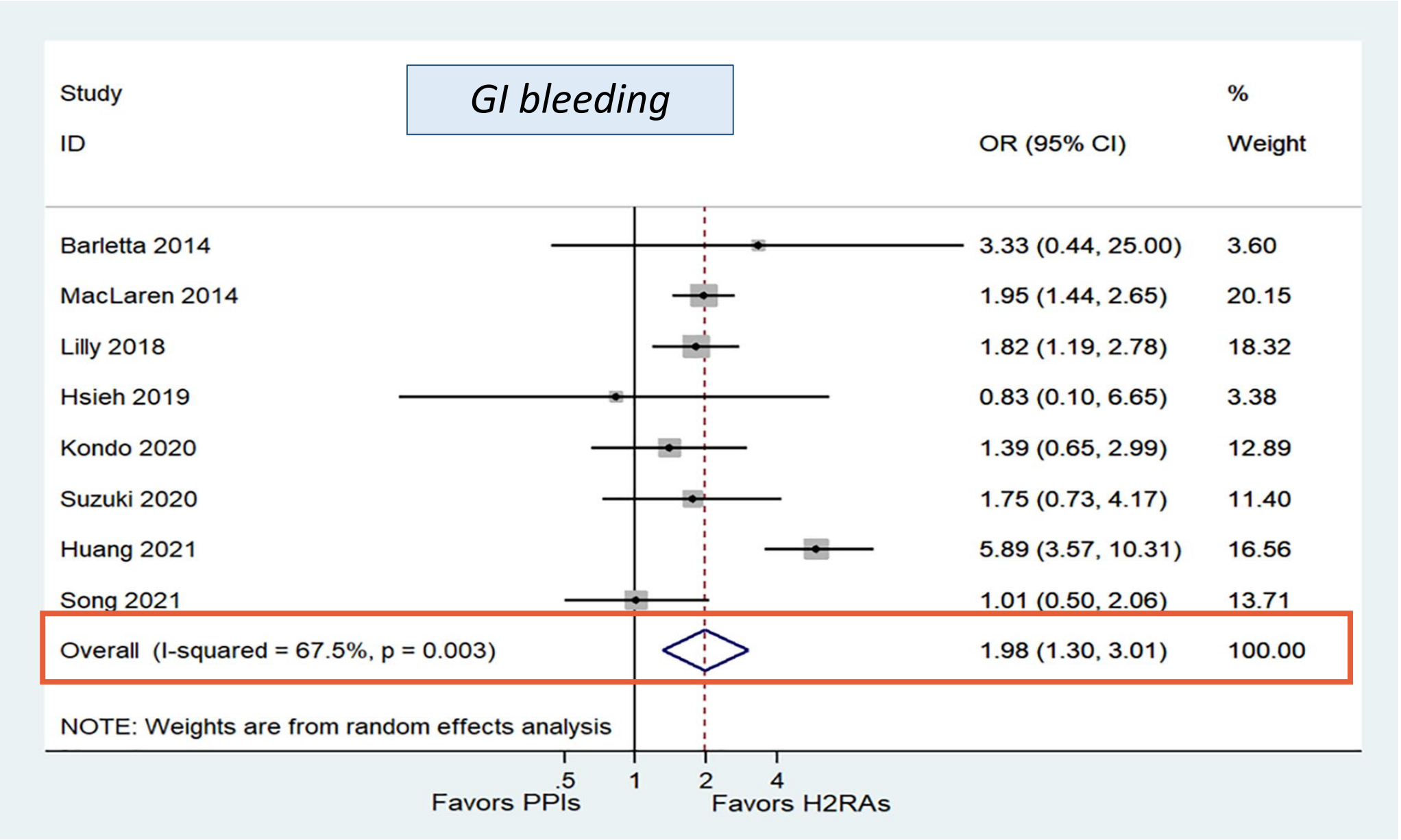
Annals of Pharmacotherapy
2022, Vol. 56(9) 988–997

DOI: 10.1177/10600280211059040
journals.sagepub.com/home/aop
SAGE

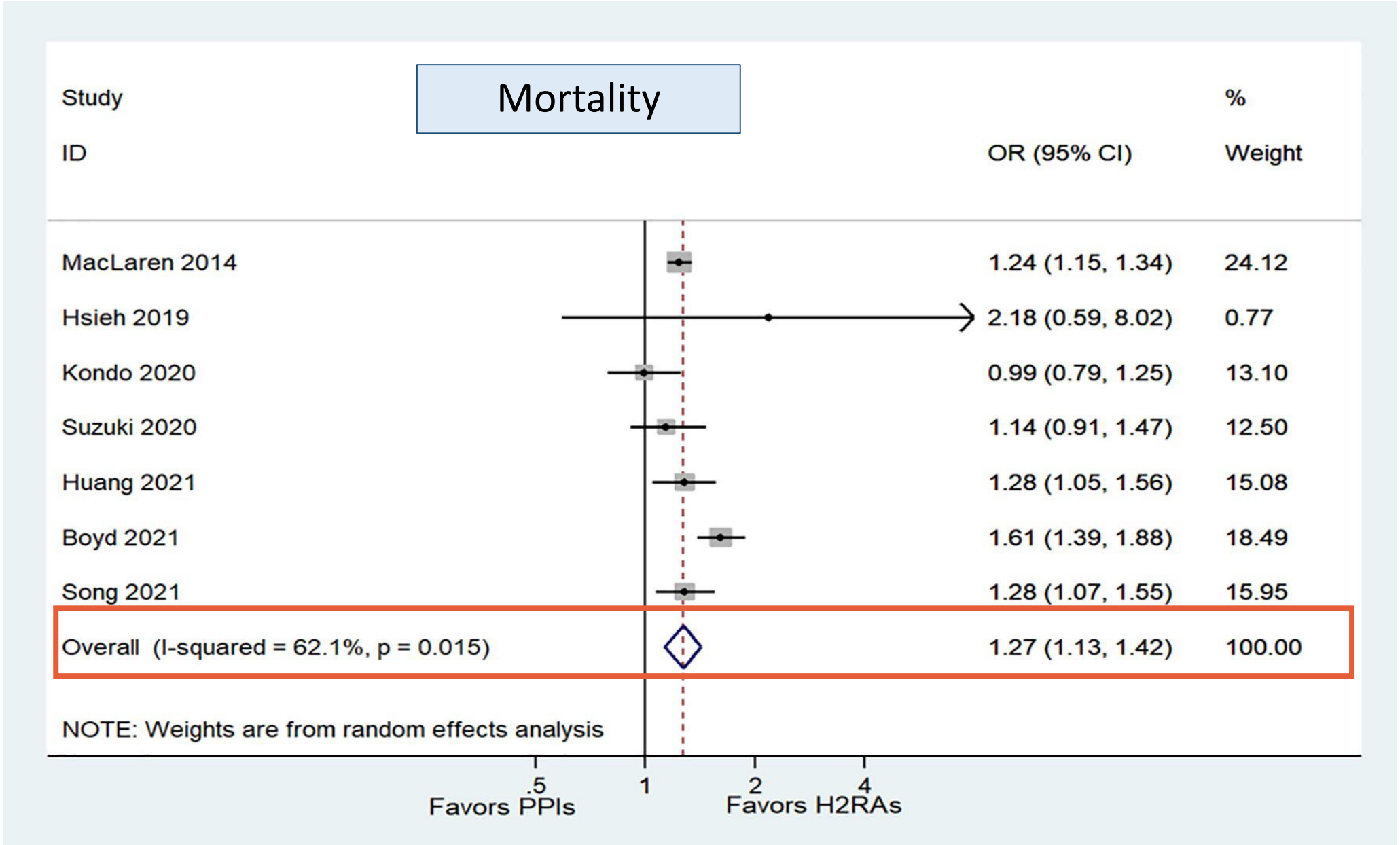
Na He, PhD[1,2*], Yingying Yan, PhD[1,3*], Shan Su, MSc[1,2], Qinggang Ge, MD[4], and Suodi Zhai, BS[1,3]

The flowchart of the study selection.





Pooled analysis of adjusted effect estimates for GI bleeding associated with PPIs versus H2RAs.



Pooled analysis of adjusted effect estimates for mortality risk associated with PPIs versus H2RAs.

Are Proton Pump Inhibitors More Effective Than Histamine-2-Receptor Antagonists for Stress Ulcer Prophylaxis in Critically Ill Patients? A Systematic Review and Meta-Analysis of Cohort Studies

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SAGE

Na He, PhD[1,2]*, Yingying Yan, PhD[1,3]*, Shan Su, MSc[1,2], Qinggang Ge, MD[4], and Suodi Zhai, BS[1,3]

Les IPP étaient associés à un risque accru de saignement digestif et de mortalité, bien que le niveau de preuve soit faible.

Globalement, **il est recommandé de ne pas exclure les H_2RA pour la prophylaxie des ulcères de stress.**

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Nous suggérons d'utiliser soit les inhibiteurs de la pompe à protons (IPP), soit les antagonistes des récepteurs H2 de l'histamine (anti-H2) comme agents de première ligne pour la prophylaxie de l'ulcère de stress (SUP) chez les patients adultes en réanimation présentant des facteurs de risque d'hémorragie digestive haute (UGIB) cliniquement significative, comparativement à l'absence d'IPP ou d'anti-H2.
Niveau de certitude des preuves : Modéré

Agents for SUP | Conditional | First-line agents

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

La prophylaxie de l'ulcère de stress (SUP) **à faible dose** doit être administrée chez les adultes en réanimation présentant des facteurs de risque d'hémorragie digestive haute liée au stress, plutôt qu'une SUP à forte dose.

Dosing Regimen in SUP | Best Practice Statement | Dosing Regimen

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Dose?

- IPP à faible dose : une dose quotidienne **≤ 40 mg d'ésoméprazole, d'oméprazole ou de pantoprazole, ou ≤ 30 mg de lansoprazole.**
- H2RA à faible dose : une dose quotidienne **≤ 40 mg de famotidine, ≤ 150 mg IV de ranitidine, ≤ 300 mg entérale de ranitidine, ou ≤ 1200 mg de cimétidine.**

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Chez les patients en état critique présentant des facteurs de risque d'hémorragie digestive haute liée au stress cliniquement significative, **la prophylaxie de l'ulcère de stress (SUP) doit être arrêtée lorsque ces facteurs de risque ne sont plus présents.** L'arrêt de la SUP avant la sortie de réanimation est nécessaire pour éviter une prescription inappropriée.

Cessation of SUP | Best Practice Statement | SUP Cessation

Nutrition Entérale Précoce : Une Stratégie Protectrice

Objectif: Explorer le rôle de la nutrition entérale dans la prévention des hémorragies digestives liées aux ulcères de stress (SUB) chez les patients en réanimation

G1

Groupe Nutrition

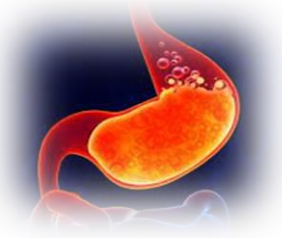
Entérale (NE) : 13 %

G2

Groupe Nutrition

Parentérale (PN) : 26 %

Incidence des saignements liés à un ulcère de stress.



HONG Jing-an et al; "The Function of Enteral Nutrition in Preventing the Stress Ulcer Bleeding among Critically Ill Patients"

Huang *et al. Critical Care* (2018) 22:20
DOI 10.1186/s13054-017-1937-1

Critical Care

RESEARCH Open Access

Stress ulcer prophylaxis in intensive care unit patients receiving enteral nutrition: a systematic review and meta-analysis

Hui-Bin Huang[1,2†], Wei Jiang[1†], Chun-Yao Wang[1], Han-Yu Qin[1] and Bin Du[1*]

comparaison de la prophylaxie pharmacologique des ulcères de stress (SUP) à un placebo ou à l'absence de prophylaxie chez des patients alimentés par voie entérale en réanimation.

Seven studies

n= 889 patients alimentés par voie entérale

Huang *et al. Critical Care* (2018) 22:20
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Critical Care

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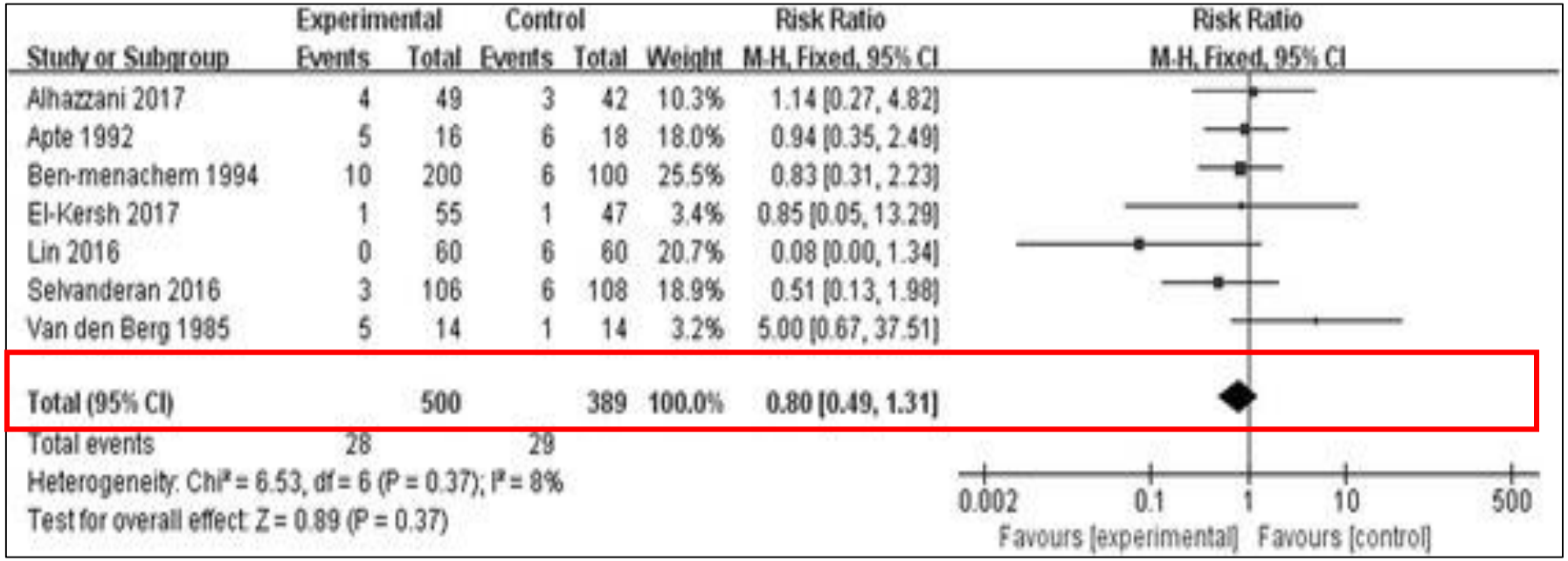
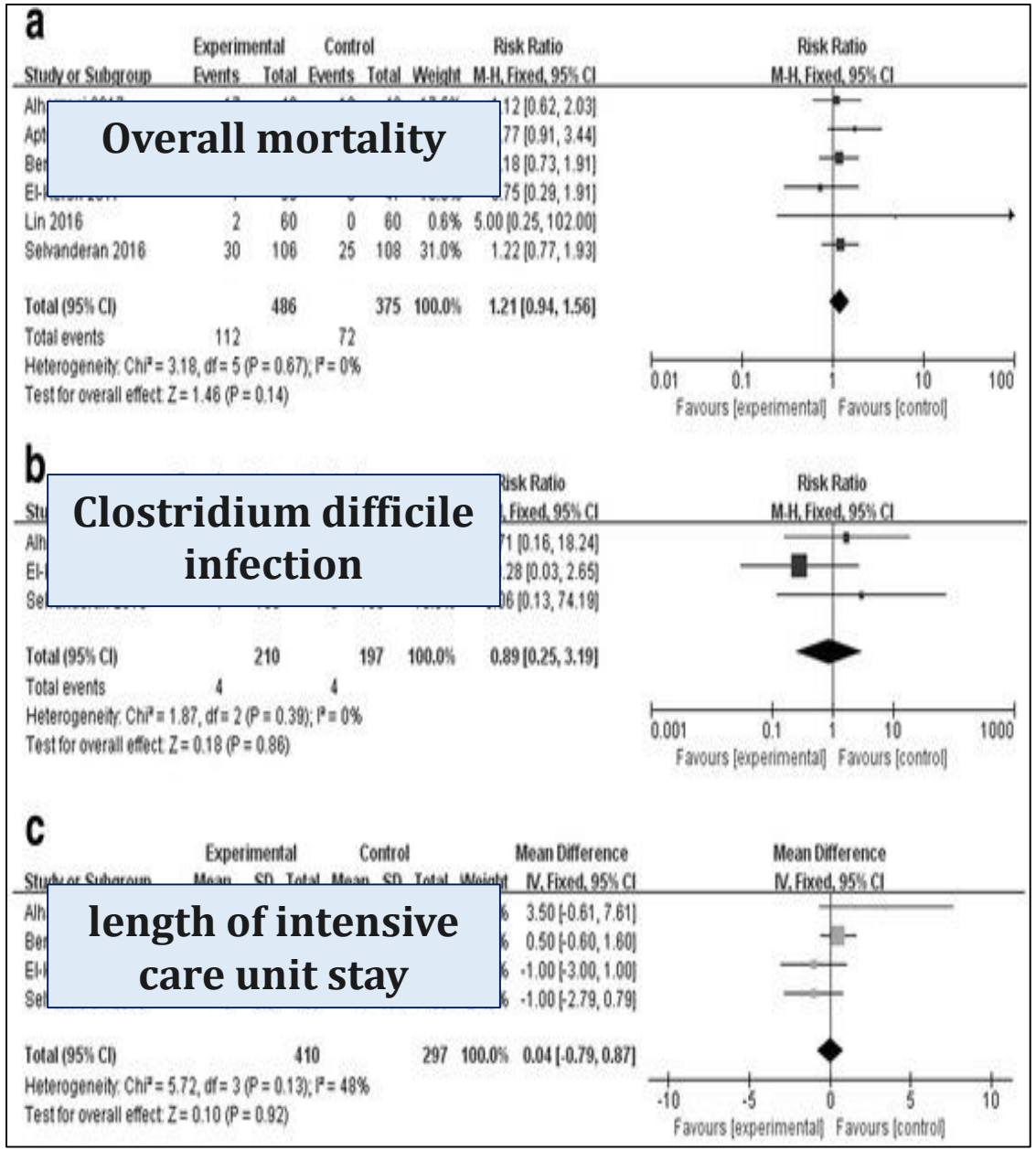
Gastrointestinal bleeding



Forest plot showing the effect of stress ulcer prophylaxis for gastrointestinal bleeding


a
Overall mortality
Experimental
Control
Risk Ratio
Risk Ratio
Study or Subgroup
Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
Lin 2016 2 60 0 60 0.6% 5.00 [0.25, 102.00]
Selvanderan 2016 30 106 25 108 31.0% 1.22 [0.77, 1.93]
Total (95% CI) 486 375 100.0% 1.21 [0.94, 1.56]
Total events 112 72
Heterogeneity: Chi² = 3.18, df = 5 (P = 0.67); I² = 0%
Test for overall effect: Z = 1.46 (P = 0.14)
0.01 0.1 1 10 100
Favours [experimental] Favours [control]
b
Clostridium difficile infection
Risk Ratio
Risk Ratio
M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
Total (95% CI) 210 197 100.0% 0.89 [0.25, 3.19]
Total events 4 4
Heterogeneity: Chi² = 1.87, df = 2 (P = 0.39); I² = 0%
Test for overall effect: Z = 0.18 (P = 0.86)
0.001 0.1 1 10 1000
Favours [experimental] Favours [control]
c
length of intensive care unit stay
Experimental
Control
Mean Difference
Mean Difference
IV, Fixed, 95% CI
IV, Fixed, 95% CI
3.50 [-0.61, 7.61]
0.50 [-0.60, 1.60]
-1.00 [-3.00, 1.00]
-1.00 [-2.79, 0.79]
Total (95% CI) 410 297 100.0% 0.04 [-0.79, 0.87]
Heterogeneity: Chi² = 5.72, df = 3 (P = 0.13); I² = 48%
Test for overall effect: Z = 0.10 (P = 0.92)
-10 -5 0 5 10
Favours [experimental] Favours [control]
d
Duration of mechanical ventilation
Mean Difference
IV, Fixed, 95% CI
Selvanderan 2016 7 18.5 106 7 15.7 108 5.7% 0.00 [-4.60, 4.60]
Total (95% CI) 410 297 100.0% -0.38 [-1.48, 0.72]
Heterogeneity: Chi² = 3.62, df = 3 (P = 0.31); I² = 17%
Test for overall effect: Z = 0.67 (P = 0.50)
-4 -2 0 2 4
Favours [experimental] Favours [control]
e
Hospital-acquired pneumonia
Experimental
Control
Risk Ratio
Risk Ratio
Study or Subgroup
Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
Lin 2016
Total (95% CI) 431 328 100.0% 1.53 [1.04, 2.27]
Total events 62 33
Heterogeneity: Chi² = 2.50, df = 4 (P = 0.65); I² = 0%
Test for overall effect: Z = 2.14 (P = 0.03)
0.002 0.1 1 10 500
Favours [experimental] Favours [control]
f
Ventilator-associated pneumonia
Risk Ratio
M-H, Fixed, 95% CI
Lin 2016
Total (95% CI) 215 210 100.0% 1.24 [0.72, 2.15]
Total events 26 20
Heterogeneity: Chi² = 1.32, df = 2 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.78 (P = 0.44)
0.005 0.1 1 10 200
Favours [experimental] Favours [control]

Huang et al. Critical Care (2018) 22:20
DOI 10.1186/s13054-017-1937-1

Critical Care

RESEARCH Open Access

Stress ulcer prophylaxis in intensive care unit patients receiving enteral nutrition: a systematic review and meta-analysis

Hui-Bin Huang[1,2†], Wei Jiang[1†], Chun-Yao Wang[1], Han-Yu Qin[1] and Bin Du[1*]

Chez les patients de réanimation recevant une nutrition entérale, **la prophylaxie pharmacologique des ulcères de stress n'avait aucun impact sur le risque de saignement digestif, la mortalité globale, l'infection à C. difficile, la durée de ventilation mécanique ni la durée de séjour en réanimation, mais elle était associée à une augmentation du risque de pneumopathie acquise sous ventilation .**

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Nous suggérons d'utiliser une prophylaxie anti-ulcéreuse (SUP) chez les adultes en soins intensifs alimentés par voie entérale et présentant un ou plusieurs facteurs de risque d'hémorragie digestive haute liée au stress cliniquement significative, comparé à l'absence de SUP.

Certitude des preuves : Très faible.

SUP and enteral nutrition	Strong	SUP

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Nous suggérons de ne pas utiliser de SUP chez les adultes en soins intensifs alimentés par voie entérale et **présentant un faible risque** d'hémorragie digestive haute liée au stress cliniquement significative.

Certitude des preuves : Très faible

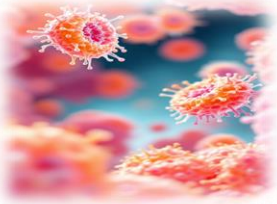
SUP and enteral nutrition	Strong	SUP

ONLINE SPECIAL ARTICLE

Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults

Nous suggérons que les cliniciens administrent une nutrition entérale afin de réduire les hémorragies digestives hautes liées au stress cliniquement significatives chez les adultes en soins intensifs, comparé à l'absence de nutrition entérale.
Certitude des preuves : Modérée

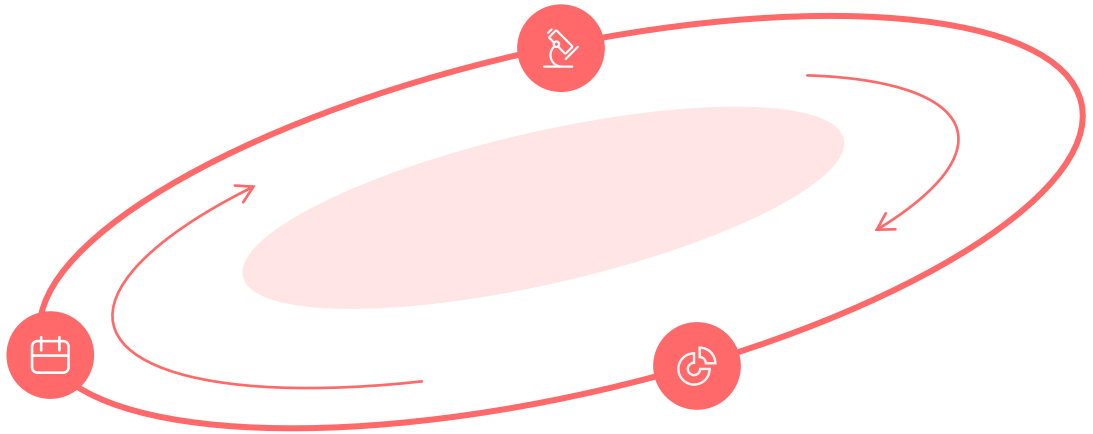
Risk factors for clinically important bleeding and overt UGIB	Conditional	Enteral Nutrition



➢ Perspectives:

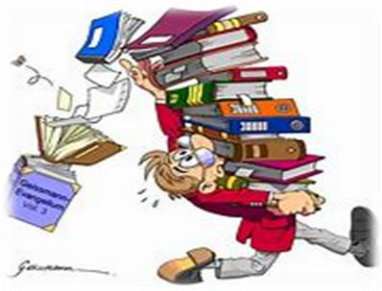
Vers une prévention personnalisée..

Profilage génétique pour un SUP personnalisé



Études sur la sécurité des IPP selon les phénotypes

Outils de scores décisionnels intégrant IA



Conclusion

- Les facteurs de risque avérés: la coagulopathie, le choc et l'insuffisance hépatique chronique
- Les IPP sont les plus utilisés, mais les anti-H2 ne doivent pas être exclus
- L'alimentation entérale doit être instaurée précocement dès que possible.
- La stratégie de prophylaxie doit être adaptée au profil de chaque patient