Désescalade de l'antibiothérapie en réanimation

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Journée soins critiques du RésO Infectio PACA-Est. 29 avril 2022

Conflits d'intérêt

- Aucun

Journée soins critiques du RésO Infectio PACA-Est. 29 avril 2022

Epidémiologie des infections en réanimation

- Peu de données récentes
- 20 à 25 % des motifs d'hospitalisation en réa
- 25 à 30 % des patients de réa développeront un sepsis durant leur hospit.
- P YLIPALOSAARI, 2006 ; S. Karger AG, Basel, 2008 ; C Alberti, 2002

La désescalade : c'est quoi ?

- Assurer l'adéquation de l'antibiothérapie initiale probabiliste
- Diminuer l'émergence de germes réssistants

O. Leroy et al. Indications, intérêts et limites de la descalade antibiotique en réanimation. Réanimation 15 (2006) 159–167

1. Remplacer les antimicrobiens à large spectre par des agents à spectre plus étroit ou à impact écologique moindre. ou alors

2. Arrêter les composants d'une combinaison antimicrobienne. Deux situations différentes peuvent être incluses dans ce cas

    2.a. Arrêt d'un agent antimicrobien administré en polythérapie pour assurer une double couverture à certains pathogènes

    2.b. Arrêt d'un agent antimicrobien administré dans le régime empirique pour couvrir les pathogènes qui ne sont finalement pas isolés dans les cultures cliniques

    3. L'arrêt précoce de tout traitement antimicrobien si l'infection est exclue n'est pas considéré comme une désescalade.

Antimicrobial de-escalation in critically ill patients: a position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patients Study Group (ESGCIP). Tabah A. et al. ICM 2019

Assurer un traitement adapté aux preuves microbiologiques avec le spectre le plus restreint possible

Antimicrobial-associated harm in critical care: a narrative review

Nishkantha Arulkumaran[1], Matthew Routledge[2,3], Sanmarié Schlebusch[4,5], Jeffrey Lipman[4,6,7] and Andrew Conway Morris[8,9*]

Intensive Care Med (2020) 46:225–235

Abstract

The belief that, for the individual patient, the benefit of prompt and continued use of antimicrobials outweighs any potential harm is a significant barrier to improved stewardship of these vital agents. Antimicrobial stewardship may be perceived as utilitarian rationing, seeking to preserve the availability of effective antimicrobials by limiting the development of resistance in a manner which could conflict with the immediate treatment of the patient in need. This view does not account for the growing evidence of antimicrobial-associated harm to individual patients. This review sets out the evidence for antimicrobial-associated harm and how this should be balanced with the need for prompt and appropriate therapy in infection. It describes the mechanisms by which antimicrobials may harm patients including: mitochondrial toxicity; immune cell toxicity; adverse drug reactions; selection of resistant organisms within a given patient; and disruption of the microbiome. Finally, the article indicates how the harms of antimicrobials may be mitigated and identifies areas for research and development in this field.

Keywords: Antibiotics, Antifungals, Drug-related side effects and adverse reactions, Critical care

ICU MANAGEMENT & PRACTICE

Doing More Can Be Worse: Ten Common Errors in the ICU

Some of the most common interventions in the ICU can be associated with poor results. We present ten situations in which doing less is better for the critically ill patient.

J. López-Fermín, D. Escarramán-Martínez, R. Flores-Ramírez et al, ICU Management & Practice 1 - 2022

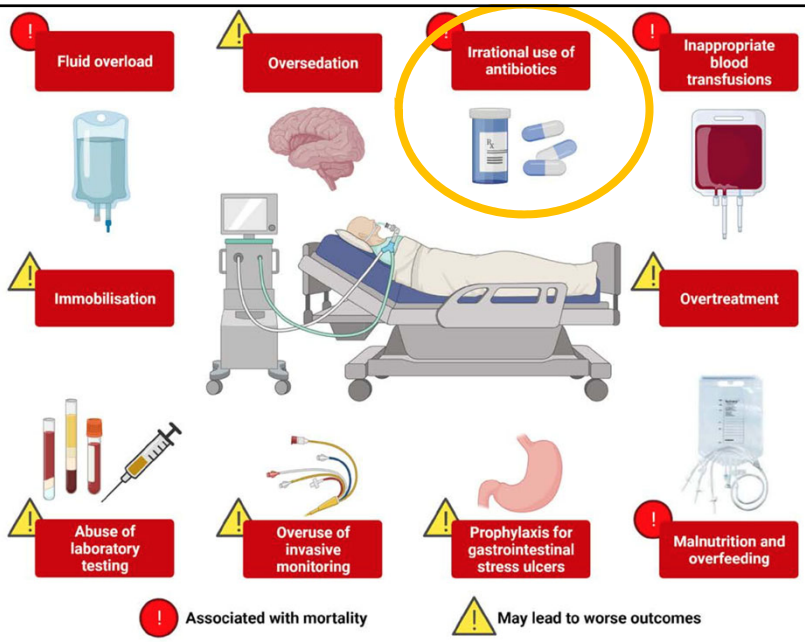


Figure 1. 10 common pitfalls in the management of critically ill patients

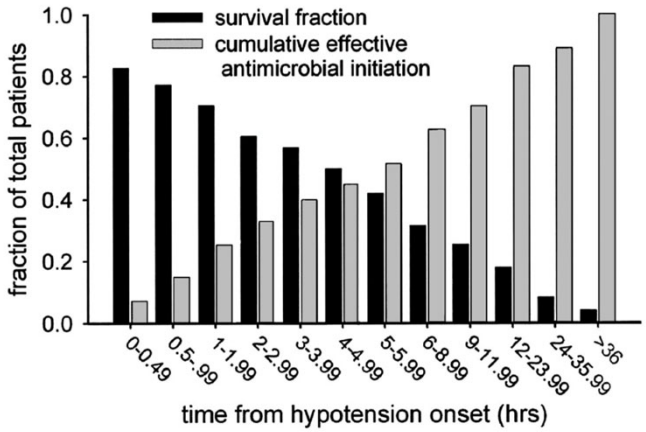
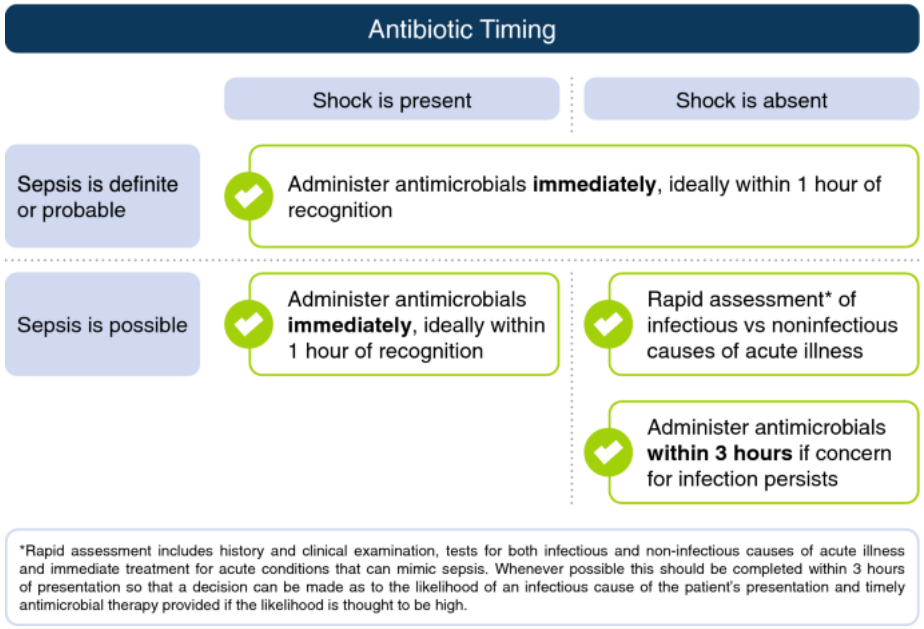


Figure 1. Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival. The x-axis represents time (hrs) following first documentation of septic shock-associated hypotension. *Black bars* represent the fraction of patients surviving to hospital discharge for effective therapy initiated within the given time interval. The *gray bars* represent the cumulative fraction of patients having received effective antimicrobials at any given time point.

Kumar A et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006



From: [Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021]

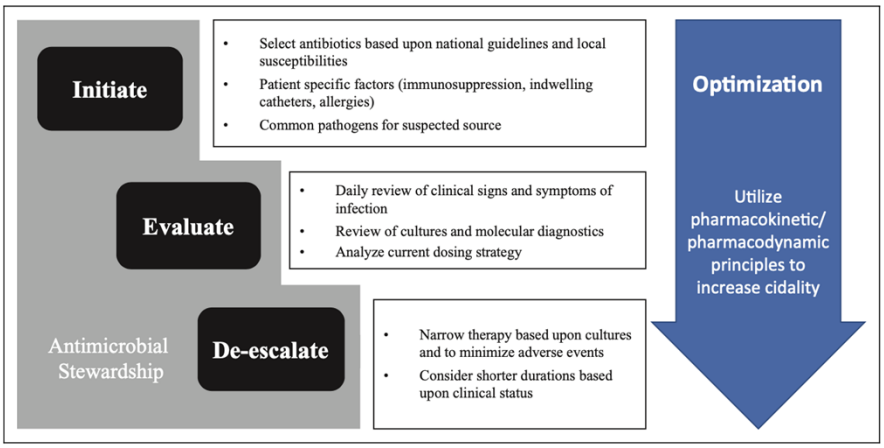


Figure 1. Approach to antibiotic use in the intensive care unit (ICU).

Campion M, Scully G. Antibiotic Use in the Intensive Care Unit: Optimization and De-Escalation. J Intensive Care Med. 2018 Dec;33(12):647-655. doi: 10.1177/0885066618762747. Epub 2018 Mar 13. PMID: 29534630.

Pourquoi réduire spectre alors que le patient s'améliore ?

Diminuer les résistances

Risk factors for carbapenem-resistant Gram-negative bacterial infections: a systematic review

Zaira R. Palacios-Baena [1,*], Maddalena Giannella [2], Davide Manissero [3], Jesus Rodríguez-Baño [4], Pierluigi Viale [2], Sara Lopes [5], Katy Wilson [6], Rachael McCool [6], Christopher Longshaw [7]

Clin Microbiol Infect. 2021 Feb;27(2):228-235. doi: 10.1016/j.cmi.2020.10.016. Epub 2020 Oct 23. PMID: 33130270.

- Revue de littérature de 2007 à 2018
- Objectif : identifier les facteurs de risque de survenue de résistances aux carbapénems
- Inclusion : études de cohorte, cas témoin prospectives ou rétrospectives
- Rapportant données quantitatives sur les facteurs de risque associés aux infections à BGN carbapeneme R
- 92 études

Table 2
Proportion of studies demonstrating an association between chosen risk factors and carbapenem resistance infections

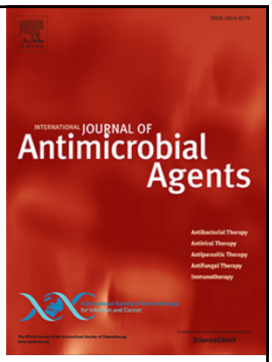
Risk factor group/ individual factor	Studies examining risk factor grouping, *n* (%)	Significant association with CR infection, *n* (%)								
		Overall	Range of odds ratios for CR-significant studies	Endemicity			Study size			
				High	Medium	Low	*N* > 500	200 < *N* < 500	50 < *N* < 200	*N* < 50
Antibiotic use	79 (85.9)	72/79 (91.1)	1.18–78.17	35/37 (94.6)	25/27 (92.6)	11/14 (78.6)	3/4 (75.0)	14/14 (100)	48/50 (96.0)	4/7 (57.1)
~~Unspecified agent~~	~~33 (37.9)~~	~~30/33 (97.3)~~	1.4–78.17	19/30 (63.3)	13/16 (81.3)	3/6 (50.0)	3/3 (100)	6/6 (100)	19/38 (50.0)	3/4 (75.0)
Unspecified broad-spectrum agent	3 (3.3)	2/3 (66.7)	1.4–53.21	1/1 (100)	1/1 (100)	0/1 (0.0)	—	1/2 (50.0)	—	—
Specific antibiotic classes										
Aminoglycoside	41 (44.6)	9/41 (22.0)	1.18–25.92	5/17 (29.4)	3/14 (21.4)	1/10 (10.0)	0/1 (0.0)	5/9 (55.6)	4/26 (15.4)	0/3 (0.0)
β-lactam/β-lactamase inhibitor	35 (38.0)	13/35 (37.1)	2.22–5.69	2/13 (15.4)	8/17 (47.1)	3/5 (60.0)	0/2 (0.0)	7/10 (70.0)	6/22 (27.3)	0/1 (0.0)
β-lactam/penicillin	26 (28.3)	10/26 (38.5)	2.17–8.57	6/13 (46.2)	0/3 (0.0)	4/10 (40.0)	1/1 (100)	5/5 (100)	4/19 (21.1)	1/2 (50.0)
Carbapenem	69 (75.0)	57/69 (82.6)	1.2–75.05	26/31 (83.9)	22/25 (88.0)	8/12 (66.7)	1/2 (50.0)	13/14 (92.9)	39/44 (88.6)	2/6 (33.3)
Cephalosporin	55 (59.8)	20/55 (36.4)	2.23–32.67	8/20 (40.0)	5/22 (22.7)	6/12 (50.0)	1/2 (50.0)	8/13 (61.5)	9/28 (32.1)	1/6 (16.7)
Colistin	7 (7.6)	4/7 (57.1)	4.17–12.1	3/5 (60.0)	1/2 (50.0)	—	—	1/1 (100)	3/6 (50.0)	—
Fluoroquinolone	54 (58.7)	21/54 (38.9)	1.87–20.62	9/21 (42.9)	8/22 (36.4)	4/11 (36.4)	1/2 (50.0)	8/13 (61.5)	11/35 (31.4)	1/4 (25.0)
~~Other~~	~~38 (41.3)~~	~~21/38 (55.2)~~	1.977–19.86	7/16 (43.8)	11/15 (73.3)	3/7 (42.9)	1/1 (100)	6/9 (66.7)	14/25 (56.0)	0/3 (0.0)
Clinical severity assessment scores	45 (48.9)	26/45 (59.1)	1.04–14.00	7/19 (36.8)	11/16 (68.8)	8/10 (80.0)	2/4 (50.0)	9/11 (81.8)	13/25 (52.0)	2/5 (40.0)
APACHE II Score	29 (31.5)	15/29 (51.7)	1.04–8.33	4/12 (33.3)	8/13 (61.5)	3/4 (75.0)	0/1 (0.0)	8/9 (88.9)	5/14 (35.7)	2/5 (40.0)
Charlson Comorbidity Index	13 (14.1)	4/13 (30.8)	1.44	2/7 (28.6)	1/3 (33.3)	1/3 (33.3)	1/3 (33.3)	0/3 (0.0)	3/7 (42.9)	—
McCabe Score	5 (5.4)	1/5 (20.0)	2.31	1/3 (100)	0/4 (0.0)	—	—	0/1 (0.0)	1/4 (25.0)	—
Pitt Score	8 (8.7)	8/8 (100)	2.96–14.00	1/1 (100)	3/3 (100)	4/4 (100)	1/1 (100)	2/2 (100)	5/5 (100)	—
SOFA Score	6 (6.5)	2/6 (33.3)	4.08	1/3 (33.3)	0/2 (0.0)	1/1 (100)	1/1 (100)	1/5 (20.0)	—	—
SAPS II Score	2 (2.2)	0/2 (0.0)	—	0/1 (0.0)	0/1 (0.0)	—	—	—	0/2 (0.0)	—
~~Other~~	~~5 (5.4)~~	~~2/5 (40.0)~~	4.39–14.00	0/2 (0.0)	2/3 (66.7)	—	—	1/2 (50.0)	1/3 (33.3)	—
Demographics	76 (82.6)	15/76 (19.7)	1.03–7.83	8/35 (22.9)	5/25 (20.0)	1/15 (6.7)	1/3 (33.3)	2/14 (14.3)	11/50 (22.0)	1/7 (14.3)
Age	72 (78.3)	9/72 (12.5)	1.03	3/32 (9.4)	5/24 (20.8)	1/15 (6.7)	0/3 (0.0)	2/14 (14.3)	7/46 (15.2)	0/7 (0.0)
Ethnicity	5 (5.4)	2/5 (40.0)	1.25–7.83	2/5 (40.0)	—	—	1/1 (100)	—	1/3 (33.3)	—
Sex	73 (79.3)	6/73 (8.2)	1.94–5.63	5/33 (15.2)	0/25 (0.0)	0/14 (0.0)	1/4 (25.0)	1/14 (7.1)	3/47 (6.4)	1/7 (14.3)
Hospital-related factors	86 (93.5)	60/86 (69.8)	1.01–50.4	35/43 (81.4)	14/28 (50.0)	11/15 (73.3)	3/4 (75.0)	11/14 (78.6)	42/59 (71.2)	2/6 (33.3)
~~Hospital-acquired infection~~	~~10 (10.9)~~	~~4/10 (40.0)~~	4.49–4.65	0/2 (0.0)	2/6 (33.3)	2/2 (100)	1/2 (50.0)	2/4 (50.0)	1/4 (25.0)	—
ICU stay	59 (64.1)	38/59 (64.4)	1.58–33.01	19/30 (63.3)	13/18 (72.2)	6/11 (54.5)	1/1 (100)	9/11 (81.8)	25/42 (59.5)	1/3 (33.3)
Length of stay	55 (59.8)	30/55 (54.5)	1.01–17.6	18/29 (62.1)	6/16 (37.5)	6/10 (60.0)	3/3 (100)	6/11 (54.5)	20/37 (54.1)	1/1 (100)
Prior hospitalization	41 (44.6)	15/41 (36.6)	2.5–13.15	8/20 (40.0)	5/15 (33.3)	2/6 (33.3)	0/3 (0.0)	4/9 (44.4)	11/27 (40.7)	0/3 (0.0)
Specific admission reason/location (excl. ICU)	8 (8.7)	2/8 (25.0)	2.01–2.72	0/2 (0.0)	1/4 (25.0)	1/2 (50.0)	0/1 (0.0)	1/2 (50.0)	1/4 (25.0)	0/1 (0.0)
~~Other~~	~~11 (12.0)~~	~~5/11 (45.5)~~	1.1–50.4	4/8 (50.0)	1/2 (50.0)	0/1 (0.0)	—	2/2 (100)	3/9 (33.3)	—
Invasive procedures/devices (excl. surgery)	78 (84.8)	59/78 (75.6)	1.03–129.15	28/36 (77.8)	19/27 (70.4)	11/15 (73.3)	3/4 (75.0)	11/12 (91.7)	37/53 (69.8)	5/6 (83.3)
Catheter placement	69 (75.0)	40/69 (58.0)	1.74–70.81	17/30 (56.7)	14/24 (58.3)	8/14 (57.1)	2/3 (66.7)	9/11 (81.8)	22/46 (47.8)	4/6 (66.7)
Diagnostic procedures	6 (6.5)	2/6 (33.3)	1.73–3.09	—	2/5 (40.0)	0/1 (0.0)	0/1 (0.0)	1/1 (100)	1/4 (25.0)	—
Dialysis	18 (19.6)	11/18 (61.1)	2.64–9.00	4/8 (50.0)	6/8 (75.0)	1/1 (100)	1/1 (100)	4/6 (66.7)	4/8 (50.0)	0/1 (0.0)
Drainage	12 (13.0)	3/12 (25.0)	2.14–2.93	0/4 (0.0)	2/6 (33.3)	1/2 (50.0)	—	3/3 (100)	0/6 (0.0)	0/2 (0.0)
Intubation (gastric/nasogastric/tracheal)	35 (38.0)	18/35 (51.4)	1.49–19.8	7/13 (53.8)	8/12 (66.7)	2/9 (22.2)	1/1 (100)	5/6 (83.3)	9/21 (42.9)	1/4 (25.0)
Mechanical ventilation	54 (58.7)	36/54 (66.7)	1.03–25.88	12/22 (54.5)	14/19 (73.7)	9/12 (75.0)	1/2 (50.0)	11/12 (91.7)	20/34 (58.8)	2/4 (50.0)
Non-specific devices	8 (8.7)	6/8 (75.0)	2.5–14.11	4/5 (80.0)	1/1 (100)	1/2 (50.0)	—	1/1 (100)	4/6 (66.7)	1/1 (100)
Nutrition support therapy	22 (23.9)	10/22 (45.5)	2.17–5.7	5/11 (45.5)	1/6 (16.7)	4/5 (80.0)	1/2 (50.0)	3/4 (75.0)	6/15 (40.0)	0/1 (0.0)
Other	7 (7.6)	5/7 (71.4)	2.76–129.15	3/3 (100)	1/2 (50.0)	1/2 (50.0)	—	2/2 (100)	3/5 (60.0)	—
~~Transfusion~~	~~5 (5.4)~~	~~2/5 (40.0)~~	2.43–9.11	1/4 (25.0)	1/1 (100)	—	—	—	2/4 (50.0)	0/1 (0.0)
Surgery	47 (51.1)	11/47 (23.4)	1.94–20.0	5/19 (26.3)	5/20 (25.0)	1/7 (14.3)	0/1 (0.0)	2/8 (25.0)	9/33 (27.3)	0/5 (0.0)
Prior admission	~~20 (21.7)~~	~~5/20 (25.0)~~	1.94–20.0	1/8 (12.5)	4/11 (36.4)	0/1 (0.0)	0/1 (0.0)	2/4 (50.0)	3/13 (23.1)	0/2 (0.0)
Current admission	31 (33.7)	6/31 (19.4)	2.53–5.9	4/14 (28.6)	1/10 (10.0)	1/6 (16.7)	—	0/4 (0.0)	6/24 (25.0)	0/3 (0.0)
Other risk factors	82 (89.1)	59/82 (72.0)	1.05–50.4	32/40 (80.0)	18/28 (64.3)	9/14 (64.3)	3/4 (75.0)	12/14 (85.7)	41/54 (75.9)	0/6 (0.0)
Previous colonization	11 (12.0)	8/11 (72.7)	4.44–47.65	6/7 (85.7)	0/2 (0.0)	2/2 (100)	2/2 (100)	1/1 (100)	5/8 (62.5)	—
~~Comorbidity~~	~~74 (80.4)~~	~~39/74 (52.7)~~	1.22–33.75	17/35 (48.6)	15/27 (55.6)	7/12 (58.3)	3/4 (75.0)	11/13 (84.6)	24/49 (49.0)	0/5 (0.0)

Many studies examined multiple individual risk factors; therefore, counts and proportions are based on studies finding a significant association with CR infection on any individual risk factor tested; study size columns total less than 100% as several studies reported numbers of isolates or infections instead of patient numbers.
CR, carbapenem resistant; ICU, intensive care unit.

Table 3
Summary of studies reporting significant association with CR infections on multivariate analysis, by risk factor: studies examining antibiotic use; also includes an analysis by infecting pathogen

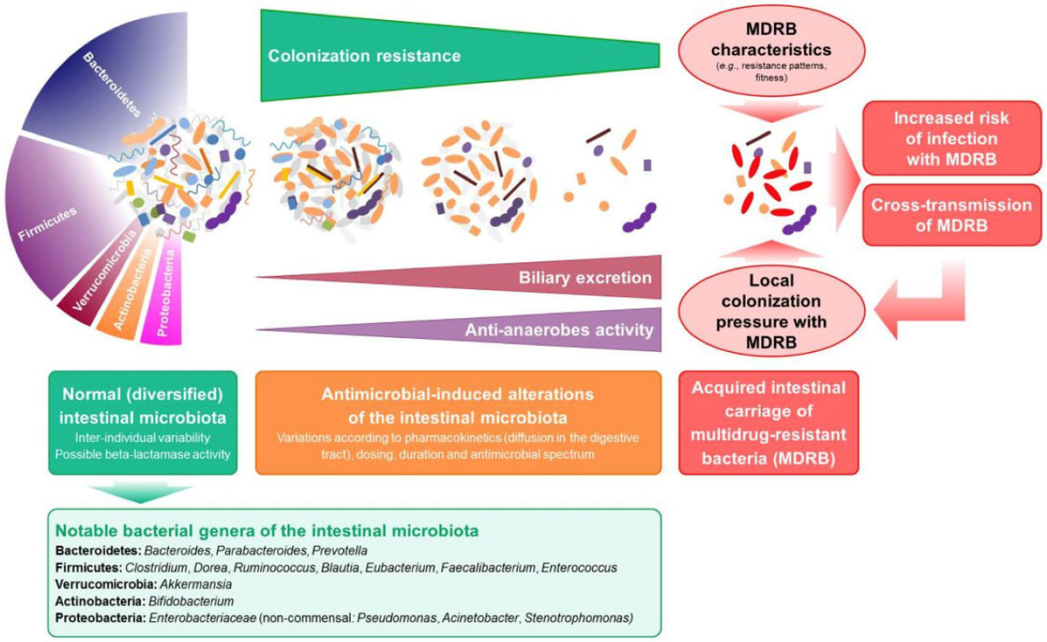
Risk factor	Studies showing significant association with CR on multivariate analysis, *n (%)* (range of odds ratios for significant studies)						
	Overall	*Acinetobacter baumannii*	*Acinetobacter nosocomialis*	*Pseudomonas aeruginosa*	*Escherichia coli*	*Klebsiella pneumoniae*	Mixed pathogens
Antibiotic use	41/79 (51.9) (1.01–360.72)	8/18 (44.4) (2.57–80.65)	1/1 (100) (6.36–N/A)	8/15 (53.3) (1.99–360.72)	1/1 (100) (29.17)	18/29 (62.1) (1.01–40.32)	4/14 (28.6) (1.07–11.37)
Unspecified agent	10/53 (18.9) (1.08–38.4)	2/11 (18.2) (5.05–20.06)	—	1/8 (12.5) (5.0)	—	6/22 (27.3) (1.08–38.4)	0/11 (0)
Unspecified broad-spectrum agent	2/3 (66.7) (11.25–N/A)	1/2 (50.0) (N/A)	—	—	—	—	—
Specific antibiotic classes							
Aminoglycoside	2/41 (4.9) (11.8–34.8)	1/10 (10.0) (11.8–N/A)	0/1 (0.0)	0/8 (0.0)	0/1 (0.0)	1/15 (6.7) (34.8–N/A)	0/6 (0.0)
β-Lactam/β-lactamase inhibitor	3/35 (8.6) (4.77–5.6)	1/8 (12.5) (5.6–N/A)	0/1 (0.0)	1/8 (12.5) (5.0–N/A)	—	1/15 (6.7) (4.77–N/A)	0/3 (0.0)
β-lactam/penicillin	1/26 (3.8) (3.58–N/A)	0/7 (0.0)	0/1 (0.0)	0/3 (0.0)	0/1 (0.0)	0/7 (0.0)	1/7 (14.3) (3.58–N/A)
Carbapenem	30/71 (42.2) (1.01–360.72)	6/14 (42.9) (2.57–54.8)	1/1 (100) (6.36)	7/15 (46.7) (1.99–360.72)	1/1 (100) (29.17)	11/26 (42.3) (1.01–25.12)	3/12 (25.0) (3.6–11.37)
Cephalosporin	11/55 (20.0) (1.22–28.1)	3/14 (21.4) (2.6–8.14)	0/1 (0.0)	1/9 (11.1) (3.33–N/A)	0/1 (0)	6/23 (26.1) (1.22–28.05)	1/7 (14.3) (3.49–N/A)
Colistin	1/7 (14.3) (1.07–N/A)	0/1 (0.0)	—	0/2 (0.0)	—	0/3 (0)	1/1 (100) (1.07–N/A)
Fluoroquinolone	7/54 (13.0) (1.76–80.65)	1/12 (8.3) (80.65–N/A)	0/1 (0.0)	1/12 (8.3) (5.41)	0/1 (0.0)	5/21 (23.8) (1.76–28.9)	0/7 (0.0)
Other	6/38 (15.8) (3.3–40.32)	1/8 (12.5) (32.9–N/A)	—	0/6 (0.0)	0/1 (0.0)	4/17 (23.5) (3.3–40.32)	1/6 (16.7) (7.75–N/A)

Carbapenems and alternative beta-lactams for the treatment of infections due to ESBL-producing Enterobacteriaceae: what impact on intestinal colonization resistance?



WOETHER PL et al.

- Objectif : évaluer l'impact des carbapénèmes et leurs principales alternatives sur les EBLSE sur l'écosystème intestinal et le risque d'EPC intestinale qui en découle
- Revue de littérature jusqu'à 2017



Diminuer les résistances

- Bien souvent résistance entérobactéries
- Anti anaérobies, céphalosporines, pénem
- Mécanisme d'excrétion probablement important
  - Excrétion biliaire

Quel antibiotique choisir ?

D'après E. RUPPE, Impact of antibiotics on the intestinal microbiota needs to be re-defined to optimize antibiotic usage. Clinical Microbiology and Infection 24 (2018)

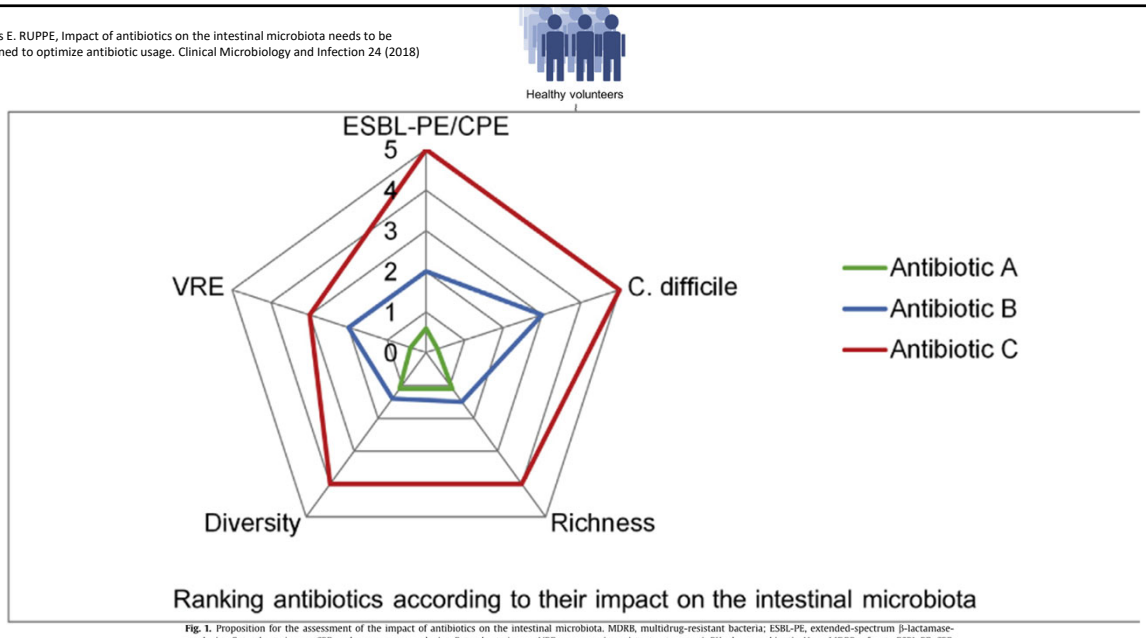


Fig. 1. Proposition for the assessment of the impact of antibiotics on the intestinal microbiota. MDRB, multidrug-resistant bacteria; ESBL-PE, extended-spectrum β-lactamase-producing *Enterobacteriaceae*; CPE, carbapenemase-producing *Enterobacteriaceae*; VRE, vancomycin-resistant enterococci; PK, pharmacokinetic. Here, MDRB refers to ESBL-PE, CPE, VRE and *Clostridium difficile*. The score reflecting the impact on the intestinal concentrations of ESBL-PE, CPE, VRE and *C. difficile* is calculated as the $\log_{10}$ of the ratio between their intestinal concentrations after and before antibiotic exposure. A positive ratio therefore means that the antibiotic promoted the growth of ESBL-PE, CPE, VRE or *C. difficile*. Conversely, antibiotics are expected to decrease the intestinal richness and diversity. To be consistent with the direction of the previous MDRB scores, that reflecting the impact on diversity and richness of gut microbiota was defined the other way round, i.e. by the ratio between the respective diversity indices (Shannon or Simpson) and richness before and after antibiotic exposure. Hence, the higher the score, the greater the impact of the antibiotic on the microbiota in terms of diversity and richness. The values of the scores for the antibiotics A, B and C were arbitrarily chosen for illustrative purposes.

Améliorer la survie ?

Invasive and Noninvasive Strategies for Management of Suspected Ventilator-Associated Pneumonia

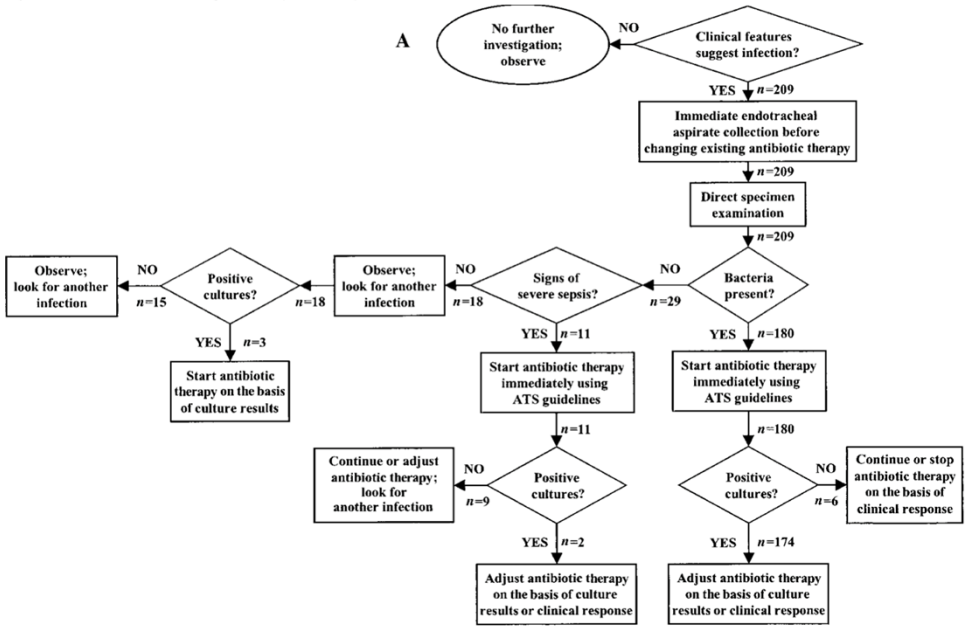
A Randomized Trial

Jean-Yves Fagon, MD; Jean Chastre, MD; Michel Wolff, MD; Claude Gervais, MD; Sylvie Parer-Aubas, MD; François Stéphan, MD; Thomas Similowski, MD; Alain Mercat, MD; Jean-Luc Diehl, MD; Jean-Pierre Sollet, MD; and Alain Tenaillon, MD, for the VAP Trial Group*

Ann Intern Med. 2000;132:621-630

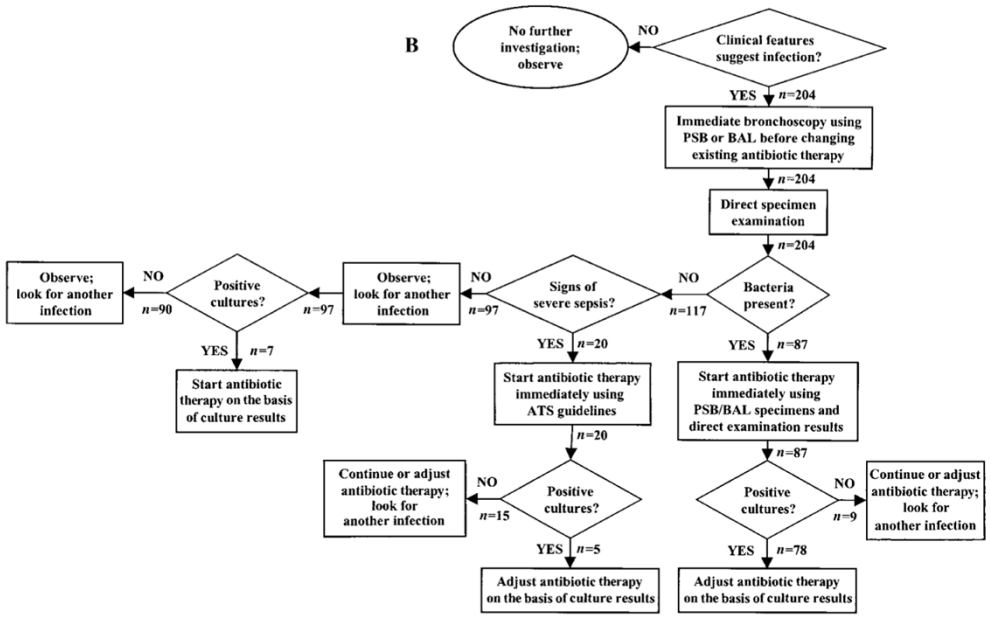
- Essai contrôlé randomisé
- PAVM
- Evaluer l'effet de l'exposition réduite aux anti-microbiens :
  - Décès toutes causes confondues
  - Défaillance d'organe
  - Utilisation d'antibiotiques à J14 et J28

Figure 1. Diagnostic and therapeutic strategy applied to patients managed with the clinical strategy (A) or invasive strategy (B). ATS = American Thoracic Society; BAL = bronchoalveolar lavage; PSB = protected specimen brush.



Journée soins critiques du RésO Infectio PACA-Est. 29 avril 2022

Figure 1. Diagnostic and therapeutic strategy applied to patients managed with the clinical strategy (A) or invasive strategy (B). ATS = American Thoracic Society; BAL = bronchoalveolar lavage; PSB = protected specimen brush.



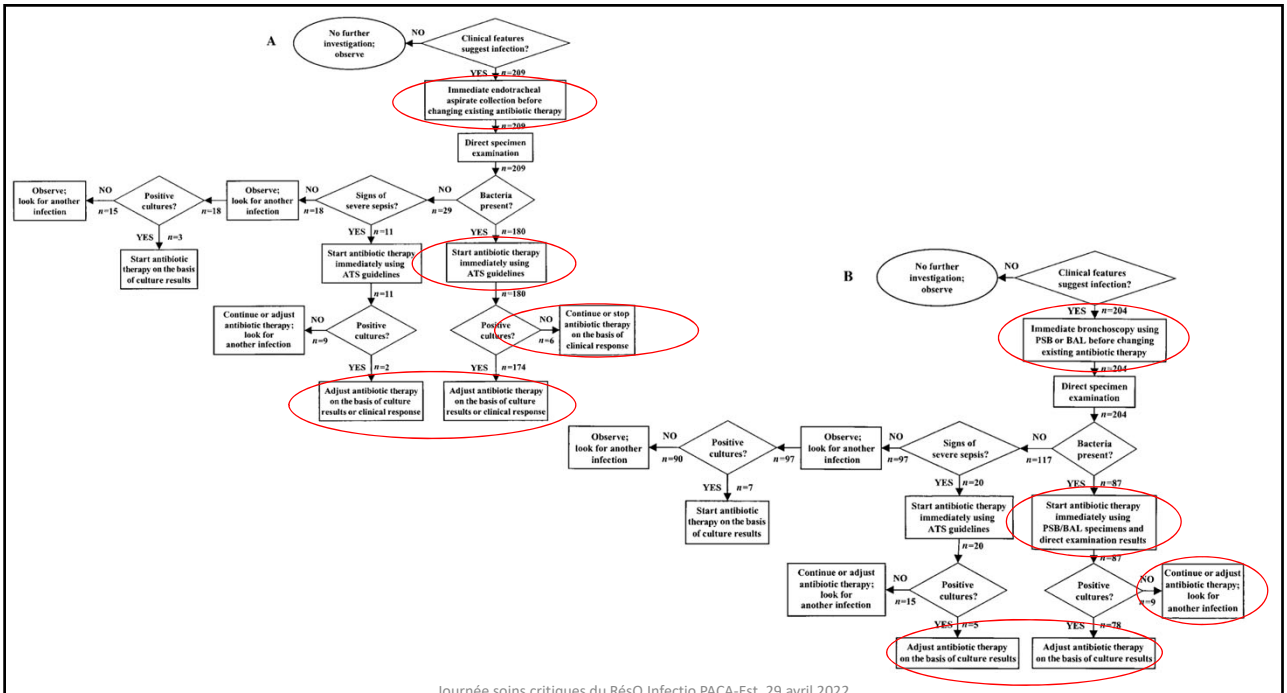


Table 3. Study Outcomes according to the Intention-to-Treat Analysis*

End Point	Patients Who Received Invasive Management (n = 204)	Patients Who Received Clinical Management (n = 209)	Difference (95% CI)	P Value
Primary				
Mortality at 14 days, *n (%)*	33 (16.2)	54 (25.8)	−9.6 (−17.4 to −1.8)†	0.022
Multiple organ dysfunction‡§				
At 3 days				
SOFA score	6.1 ± 4.0	7.0 ± 4.3	−0.9 (−1.7 to −0.1)	0.033
ODIN score	1.7 ± 0.9	1.9 ± 1.1	−0.2 (−0.4 to −0.05)	0.014
At 7 days				
SOFA score	4.9 ± 4.0	5.8 ± 4.4	−0.9 (−1.8 to −0.03)	0.043
ODIN score	1.4 ± 1.0	1.6 ± 1.1	−0.2 (−0.4 to 0.02)	0.082
At 14 days				
SOFA score	3.9 ± 4.1	4.3 ± 4.3	−0.4 (−1.3 to 0.6)	>0.2
ODIN score	1.2 ± 1.2	1.2 ± 1.2	−0.03 (−0.3 to 0.2)	>0.2
Antibiotic-free days at 14 days, *d*‡	5.0 ± 5.1	2.2 ± 3.5	2.8 (1.9 to 3.6)	<0.001
Antibiotics per day at 14 days, *n*	1.2 ± 0.8	1.5 ± 0.7	−0.3 (−0.5 to −0.2)	<0.001
Antibiotic-treatment days at 14 days, *d*	8.7 ± 5.4	10.9 ± 4.5	−2.2 (−3.2 to −1.2)	<0.001
Secondary				
Mortality at 28 days, *n (%)*	63 (30.9)	81 (38.8)	−7.9 (−17.0 to 1.2)	0.099
Multiple organ dysfunction at 28 days‡§				
SOFA score	3.1 ± 3.4	3.1 ± 3.8	−0.02 (−1.2 to 1.1)	>0.2
ODIN score	1.0 ± 1.0	1.0 ± 1.0	−0.06 (−0.4 to 0.3)	>0.2
Antibiotic-free days at 28 days, *d*‡	11.5 ± 9.0	7.5 ± 7.6	−3.9 (−5.5 to −2.3)	<0.001
Antibiotics per day at 28 days, *n*	1.0 ± 1.8	1.3 ± 0.7	−0.3 (−0.45 to −0.16)	<0.001
Antibiotic-treatment days at 28 days, *d*	12.8 ± 8.5	14.9 ± 7.9	−2.1 (−3.7 to −0.5)	0.009
Duration of intensive care unit stay, *d*	19.3 ± 9.0	17.6 ± 9.4	1.5 (−0.3 to 3.2)	0.11
Duration of hospital stay, *d*	26.7 ± 23.9	25.1 ± 28.5	1.6 (−0.3 to 3.4)	>0.2
Mechanical ventilation–free days, *d*‡	7.8 ± 9.8	7.0 ± 9.4	0.8 (−1.0 to 2.9)	>0.2
Emergence of resistant bacteria, *n (%)*	125 (61.3)	125 (59.8)	1.5 (−7.9 to 10.9)	>0.2
Emergence of *Candida* species, *n (%)*	23 (11.3)	47 (22.5)	−11.2 (−18.3 to −4.1)	0.0025

* Unless otherwise indicated, data are presented as the mean ± SD. ODIN = Organ Dysfunction and Infection; SOFA = Sepsis-related Organ Failure Assessment.
† Expressed as percentage points.
‡ Described more fully in the Methods section.
§ Higher values indicate greater severity.

Améliorer la survie ?

A Systematic Review of the Definitions, Determinants, and Clinical Outcomes of Antimicrobial De-escalation in the Intensive Care Unit

Alexis Tabah,[1,2,a] Menino Osbert Cotta,[1,2,3,a] Jose Garnacho-Montero,[6] Jeroen Schouten,[7] Jason A. Roberts,[1,2,3] Jeffrey Lipman,[1,2,4] Mark Tacey,[5] Jean-François Timsit,[8,9] Marc Leone,[10] Jean Ralph Zahar,[11] and Jan J. De Waele[12]; for the Working Group for Antimicrobial Use in the ICU

Clin Infect Dis. 2016 Apr 15;62(8):1009-1017

- Revue de littérature
- Tous articles de 1966 à 2015
- 3 bases de données
- Critères inclusion :
  - Desecalade antibiothérapie
  - ICU
  - Données interventionnelles ou épidémio permettant de juger l'effet ADE

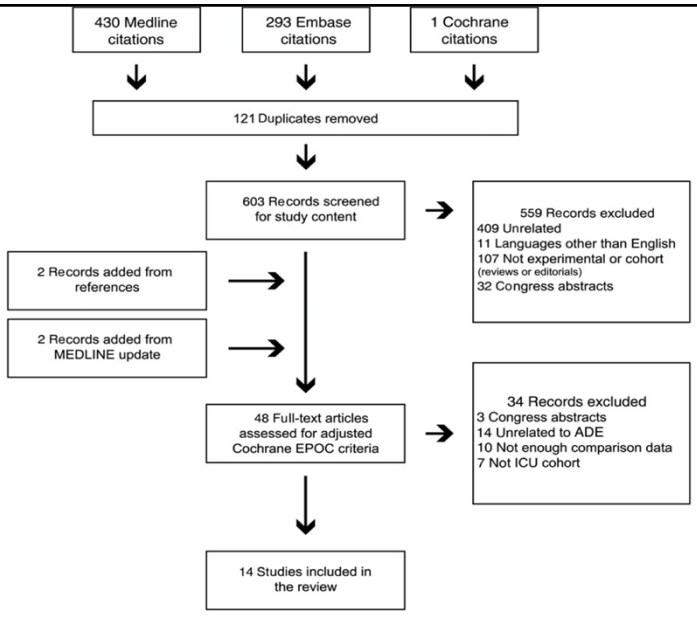


Figure 1. Flow chart detailing study extraction and selection. Abbreviations: ADE, antimicrobial de-escalation; EPOC, Effective Practice and Organization of Care; ICU, intensive care unit.

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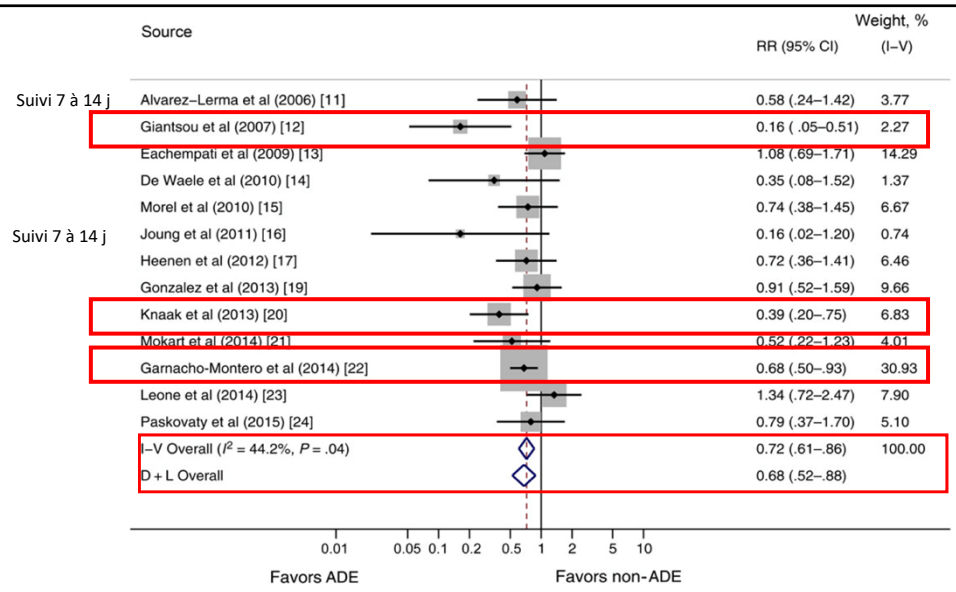

Figure 2. Difference in patient mortality rates between antimicrobial de-escalation (ADE) and non-ADE. Heterogeneity $\chi^2 = 21.52$ ($df = 12$); $P = .04$; $I^2 = 44.2\%$ (variation in RR attributable to heterogeneity). Test of RR = 1: $z = 3.72$; $P < .001$. Abbreviations: CI, confidence interval; D + L, random-effects model proposed by DerSimonian and Laird [10]; I-V, inverse variance; RR, relative risk.

Conditions à la désescalade

- Etat clinique du patient
- Identification microbiologique => importance des prélèvements

Moyens

- Moyens « d'identification » :
  - « vieux moyens » :
    - Examen direct
    - Culture (hémoc, LBA, ascite, …)
  - « moyens récents » :
    - Spectrométrie
    - PCR multiplexe
- Moyens « d'évaluation de l'efficacité »

Cultures

- Gold standard
- ⚠ Importance de la qualité de prélèvement :
  - 2 paires d'hémoc
  - 10-20 mL / flacon
  - Désinfection cutanée
- LBA
- …

Table 5 Rapid diagnostic tools for early optimization of antimicrobial therapy in patients with bloodstream infections: methods, turn-around time and diagnostic performances

Name	Manufacturer	Method	Input	TAT	Sensitivity	Specificity	References
Magicplex™ Sepsis Test	Seegene	RT-PCR	Blood sample	5 h	0.65	0.92	Carrara et al. [135]
					0.29	0.95	Zboromyrska et al. [136]
					0.47	0.66	Ziegler et al. [137]
T2Bacteria® Panel	T2Biosystems	Magnetic resonance	Blood sample	3.5	0.9% (95% CI, 0.76–0.96)	0.9 (95% CI, 0.88–0.91)	Nguyen et al. [28]
FilmArray® Blood Culture	bioFire	PCR	Positive BC	1 h	0.92-1[a]	0.76-1[a]	Altun et al. [138]
					0.95	ND	Bhatti et al. [139]
Verigene® Blood culture tests	Luminex	PCR	Positive BC	2.5 h	0.99	ND	Bhatti et al. [139]
					0.95	ND	Kim et al. [140]
Accelerate Pheno™	Accelerate Diagnostics	FISH and microscopy	Positive BC	1.5 h (identification) 7 h (AST)	0.95	0.99	Lutgring et al. [141]
					0.96	0.99	Charnot-Katsikas et al. [142]
VitekMS Biotyper	bioMérieux Bruker	MALDI-TOF	Positive BC	<1 h (identification), < 1 h-4 h (AST)	Concordance for Gram-negative[b]: 0.83–1 Concordance for Gram-positive[b]: 0.32–0.89		Faron [31]

RT-PCR real-time polymerase chain reaction, *ESI–MS* electrospray ionization mass spectrometry, *BC* blood culture, *FISH* fluorescence in situ hybridization, *AST* antibiotic susceptibility testing, *MALDI-TOF* matrix-assisted laser desorption ionization–time of flight mass spectrometry

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection

D.T. Huang, D.M. Yealy, M.R. Filbin, A.M. Brown, C.-C.H. Chang, Y. Doi, M.W. Donnino, J. Fine, M.J. Fine, M.A. Fischer, J.M. Holst, P.C. Hou, J.A. Kellum, F. Khan, M.C. Kurz, S. Lotfipour, F. LoVecchio, O.M. Peck-Palmer, F. Pike, H. Prunty, R.L. Sherwin, L. Southerland, T. Terndrup, L.A. Weissfeld, J. Yabes, and D.C. Angus, for the ProACT Investigators*

- Etude randomisée en 1:1, muticentrique, USA
- Patients suspects de pneumonie communautaire
- Objectif : montrer qu'utiliser la PCT pour la prescription d'anibiotiques dans les suspicions de pneumonies réduirait l'exposition aux antibiotiques

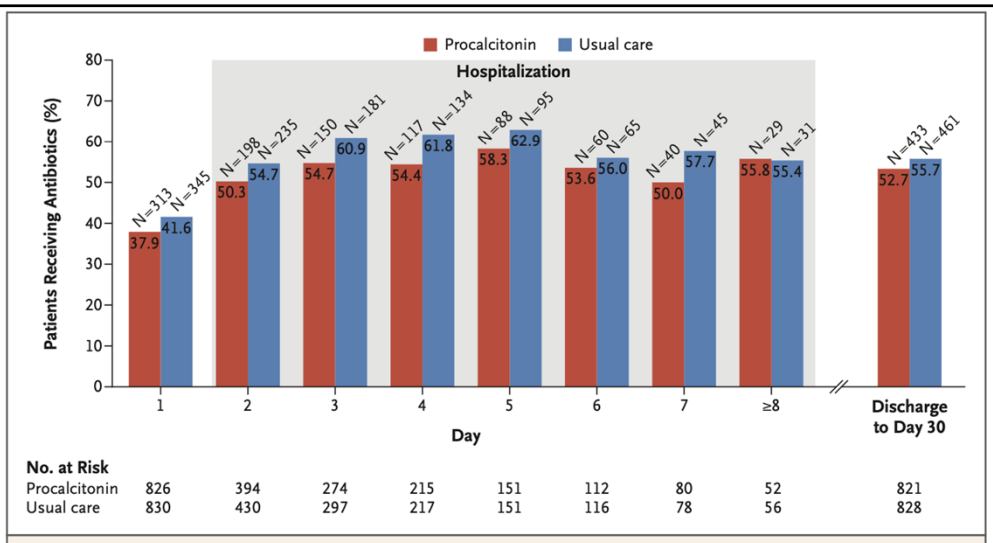

Figure 3. Antibiotic Exposure over Time.

Day 1 is from the time of enrollment to midnight. Day 2 and beyond are from midnight to midnight. Serial procalcitonin levels were obtained from hospitalized patients through day 7. Data on post-discharge antibiotic exposure were derived from the intention-to-treat analysis of the primary outcome.

Efficacy and Safety of Procalcitonin Guidance in Patients With Suspected or Confirmed Sepsis: A Systematic Review and Meta-Analysis

Irena Iankova, PhD[1]; Philippe Thompson-Leduc, MSc[2]; Noam Y. Kirson, PhD[2]; Bernie Rice, BS[3]; Juliane Hey, PharmD[1]; Alexander Krause, PhD[1]; Sophie A. Schonfeld, BA[2]; Christopher R. DeBrase, BS[2]; Samuel Bozzette, MD[4]; Philipp Schuetz, MD[5]

- Meta analyse
- 2 bases de données
- 2004 à 2016
- Critères étudiés : durée d'antibiothérapie, mortalité toutes causes, durée de séjour en réa
- Résultat : 10 études randomisées – contrôlées incluses, 3489 patients

TABLE 1. Randomized Controlled Trials Included in Meta-Analysis

First Author	Time to Endpoint	PCT Cohort	Control Cohort	PCT Algorithm for AB Cessation (ng/mL)	Adherence (%)	Mean AB Duration (d)	Mean ICU Length of Stay (d)	Mortality
Annane et al (24)	Time until ICU discharge	31	31	< 0.5	63	4.7 (PCT), 4.0 (control)	24.0 (PCT), 31.0 (control)	23% (PCT), 32% (control)
Bouadma et al (25)	28 d	307	314	< 0.5; > 80% change from peak	47	10.3 (PCT), 13.3 (control)	15.9 (PCT), 14.4 (control)	21% (PCT), 20% (control)
de Jong et al (26)	28 d	761	785	≤ 0.5; ≥ 80% change from peak	93	5.7 (PCT), 7.3 (control)	10.2 (PCT), 10.0 (control)	20% (PCT), 25% (control)
Deliberato et al (27)	Time until ICU discharge	42	39	< 0.5; > 90% change from peak	NR	15.5 (PCT), 17.3 (control)	16.3 (PCT), 8.8 (control)	2% (PCT), 10% (control)
Hochreiter et al (28)	Time until ICU discharge	57	53	< 1.0; ≥ 65–75% change from initial level and current level > 1.0	NR	5.9 (PCT), 7.9 (control)	15.5 (PCT), 17.7 (control)	26% (PCT), 26% (control)
Layios et al (29)	Time until ICU discharge	258	251	< 0.5	NR	NA	9.0 (PCT), 9.7 (control)	22% (PCT), 21% (control)
Najafi et al (30)	Length of hospital stay	30	30	≤ 0.5	NR	NA	7.5 (PCT), 10.5 (control)	17% (PCT), 13% (control)
Nobre et al (31)	28 d	39	40	< 0.25 if initial level ≥ 1.0; < 0.1 if initial level < 1.0; > 90% change if initial PCT ≥ 1.0	81	12.3 (PCT), 13.5 (control)	7.5 (PCT), 26.5 (control)	21% (PCT), 20% (control)
Schroeder et al (32)	Length of hospital stay	14	13	≤ 1.0; ≥ 65–75% change from initial level	NR	6.6 (PCT), 8.3 (control)	16.4 (PCT), 16.7 (control)	21% (PCT), 23% (control)
Shehabi et al (33)	28 d	196	198	< 0.1; < 0.1–0.25 if infection unlikely; > 90% change from baseline level	NR	11.7 (PCT), 13.0 (control)	6.2 (PCT), 6.7 (control)	11% (PCT), 8% (control)

AB = antibiotic, NA = not applicable, NR = not reported, PCT = procalcitonin.

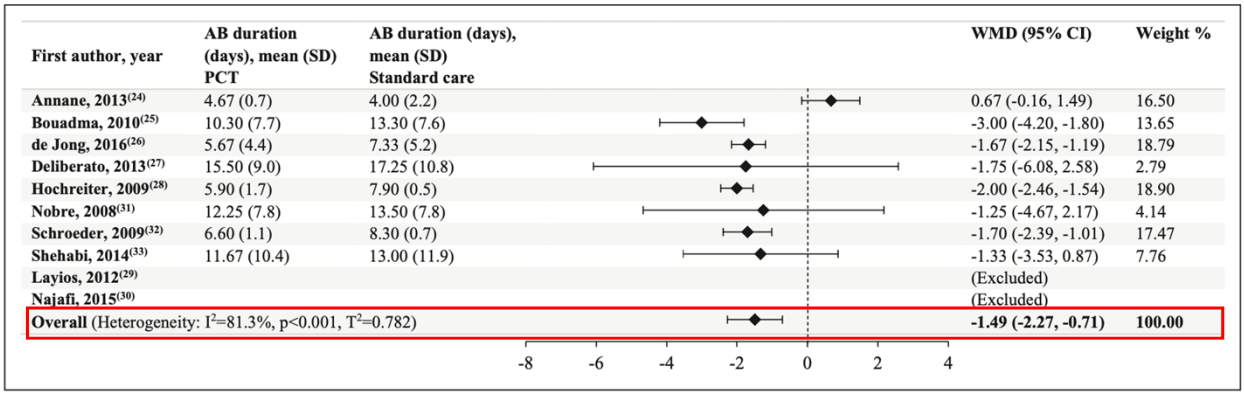

Figure 2. Antibiotic (AB) duration. Layios et al (29) was excluded because it reported the proportion of days with ABs during patients' stay in the ICU. Najafi et al (30) was excluded because it reported the sum of AB exposure days for each study arm, with no information on variance. *Diamonds* are point estimates. PCT = procalcitonin, WMD = weighted mean difference.

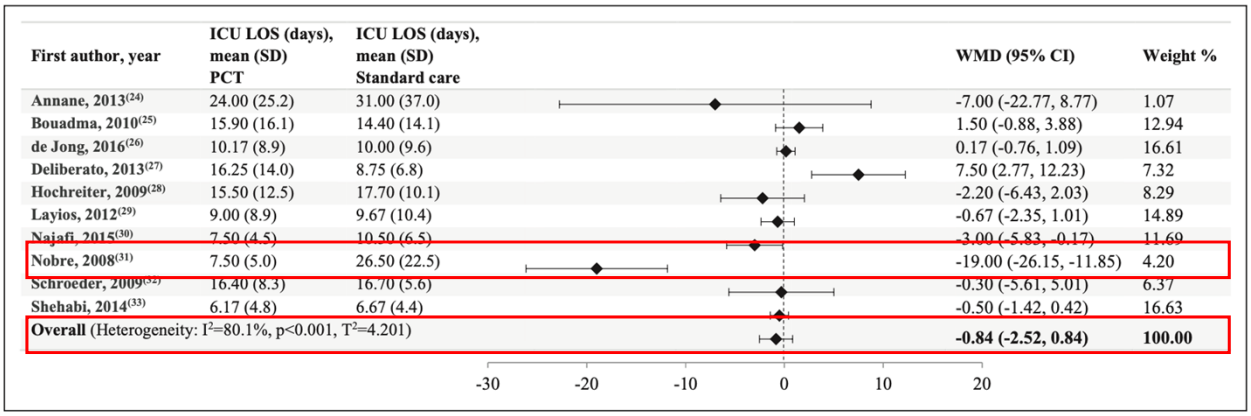

Figure 3. ICU length of stay (LOS). *Diamonds* are point estimates. PCT = procalcitonin, WMD = weighted mean difference.

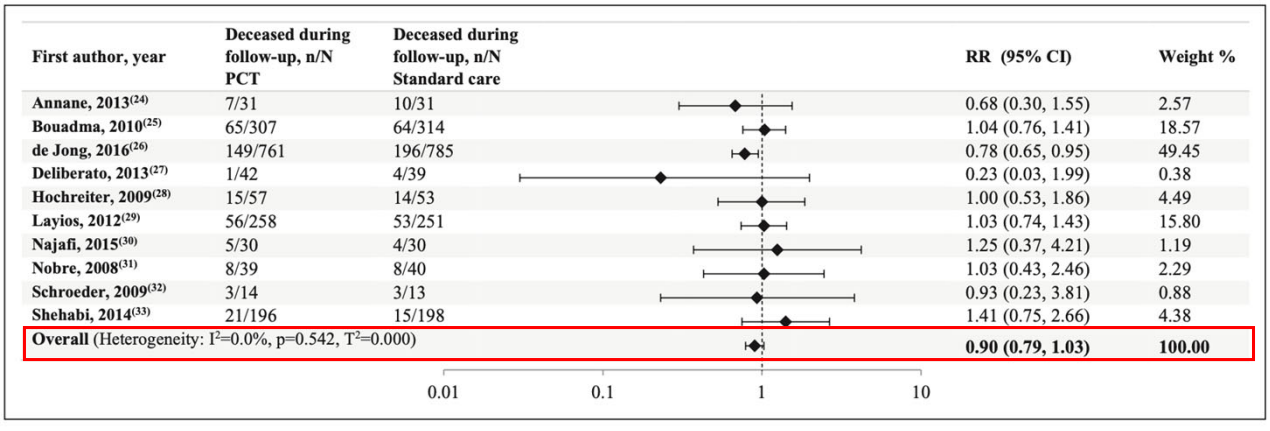

Figure 4. Mortality. *Diamonds* are point estimates. PCT = procalcitonin, RR = risk ratio.

Q6: In critically ill patients receiving antimicrobials for an infection, when is it recommended to perform de-escalation of the empirical antimicrobial regimen?

We recommend ADE is performed within 24 h of definitive culture results and antibiograms availability. (Strong recommendation; low quality of evidence.)

Q7: In critically ill patients receiving antimicrobials for an infection, are recommendations for or against antimicrobial de-escalation different for certain bacterial pathogens? For which?

Recommendations for or against ADE are similar for all bacterial pathogens except for difficult-to-treat pathogens in patients with a high risk of death. (Moderate recommendation, low quality of evidence.)

Q8: In critically ill patients receiving antifungal agents for invasive candidiasis, does the panel recommend antifungal de-escalation compared to no de-escalation?

We recommend ADE of antifungal agents after clinical and microbiological resolution of invasive candidiasis when the pathogens are susceptible to azole antifungal agents. (Strong recommendation; low-quality evidence.)

Q9: In critically ill patients receiving antimicrobials for a culture-negative infection, does the panel recommend antimicrobial de-escalation compared to no de-escalation?

We recommend that consideration is given to alternate non-infectious diagnosis and stopping all or part of the antibiotic regimen in critically ill patients with culture-negative infections. (Moderate recommendation; low-quality evidence.)

Antimicrobial de-escalation in critically ill patients: a position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patients Study Group (ESGCIP). ICM 2019

Take Home message

- La désescalade est une question quotidienne
- Sans risque pour le patient voire diminue probablement la mortalité
- Spectre étroit diminue probablement l'apparition de BMR
- Voie d'élimination importante