Collège des Universitaires de Maladies Infectieuses et Tropicales

30 janvier 2019

L'antibiothérapie probabiliste dans le contexte d'un choc septique

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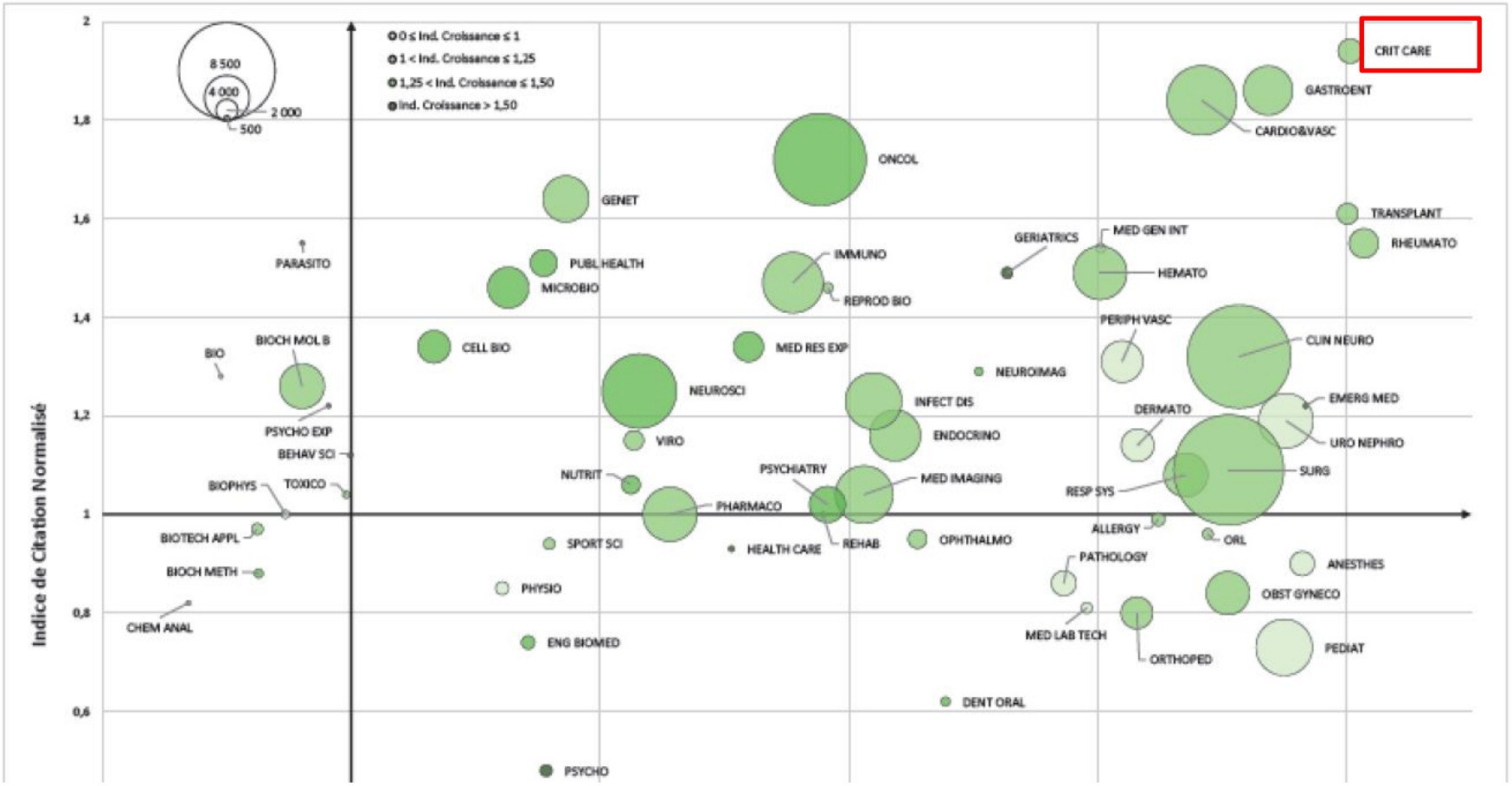
DESMIR

Un peu de pub !

Figure 9. Indice de spécialisation par discipline WoS (abscisse) et Indice de citation normalisé (ordonnée) des publications des CHU, 2006-2015. La taille des cercles est proportionnelle au nombre d'articles. Les couleurs indiquent l'augmentation du volume de publication dans la discipline entre deux périodes : 2006-2010 et 2011-2015.



Un fond de jalousie !

Le nombre de décès dus au sepsis sévère en France par an ?

22 000

→ A titre de comparaison, les accidents de la route font chaque année environ 4 000 morts

Traiter tôt…

… et bien

Traiter tôt…

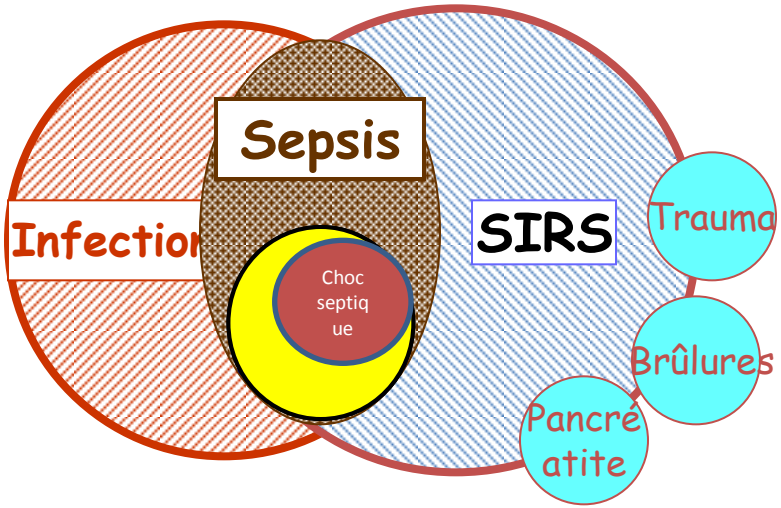
…donc repérer et faire le diagnostic tôt

Changement de définition
de 1991 à 2016

Sepsis sévère/choc septique

1991 Conférence Consensus ACCP-SCCM

Infection SIRS Sepsis **Choc septique**



Sepsis Sévère + Hypo TA :

Résistante à une expansion volémique

Nécessité de Catécholamines

Bone et al. *Chest*. 1992;101:1644.

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) *JAMA*. 2016

Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.
  - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
  - A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.
- In lay terms, sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.
- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, ie, alteration in mental status, systolic blood pressure ≤100 mm Hg, or respiratory rate ≥22/min.

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

JAMA. 2016

Quick SOFA

Respiratory rate ≥22/min

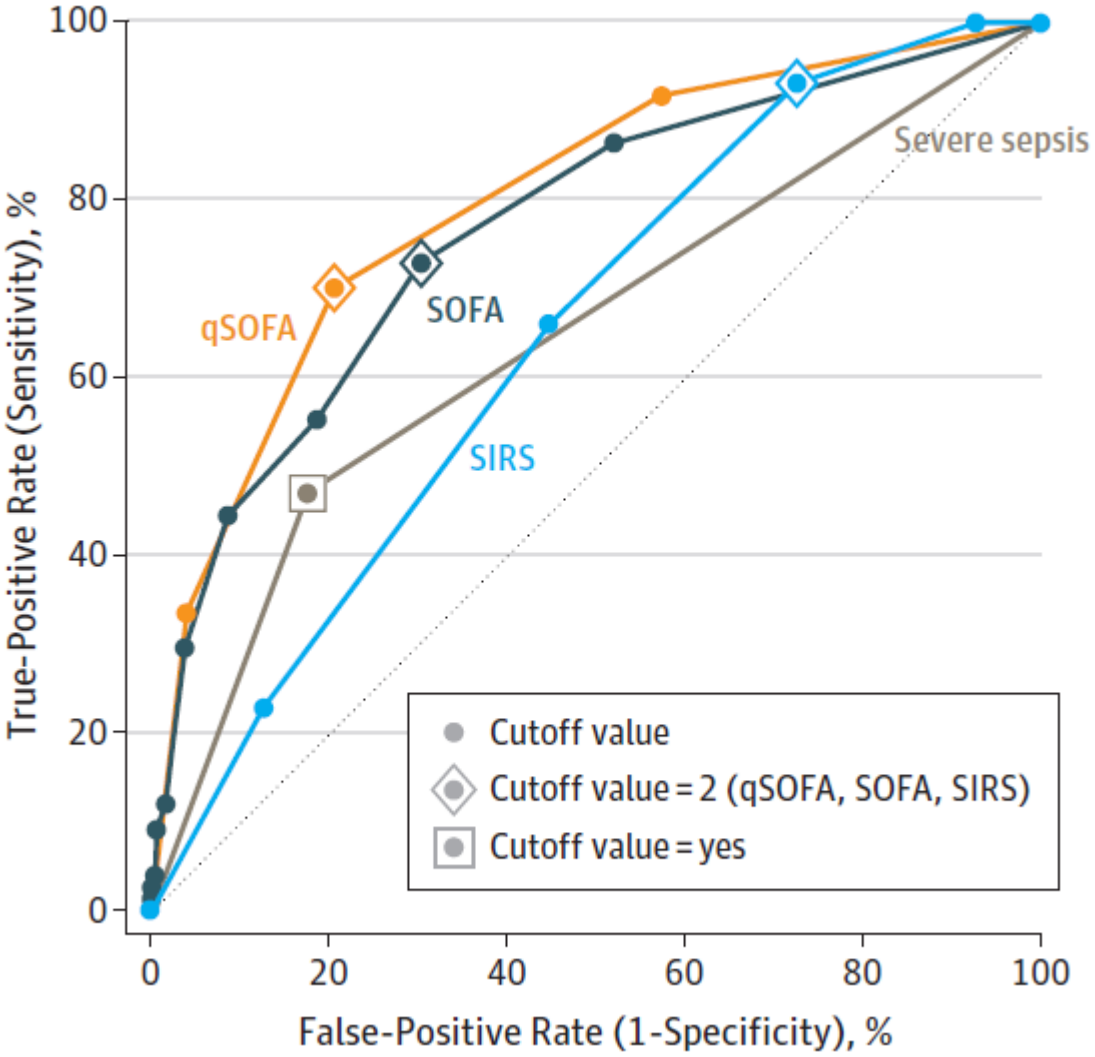
Altered mentation

Systolic blood pressure ≤100 mm Hg

Progno Mortali Present lospital tion

JAMA. 2016

Yonathan Freund,
Yann-Erick Claesse
Jennifer Truchot, M
Fabrice Dami, MD;
for the French Soc



Mortalité avec qSOFA <2/≥2 : 3% vs 24%

VPN du qSOFA <2: 97%

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) *JAMA*. 2016

- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
- Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.

Traiter tôt…

…donc repérer et faire le diagnostic tôt

Quick sofa OK

mais ne pas passer à côté de l’infection

The Absence of Fever Is Associated With Higher Mortality and Decreased Antibiotic and IV Fluid Administration in Emergency Department Patients With Suspected Septic Shock

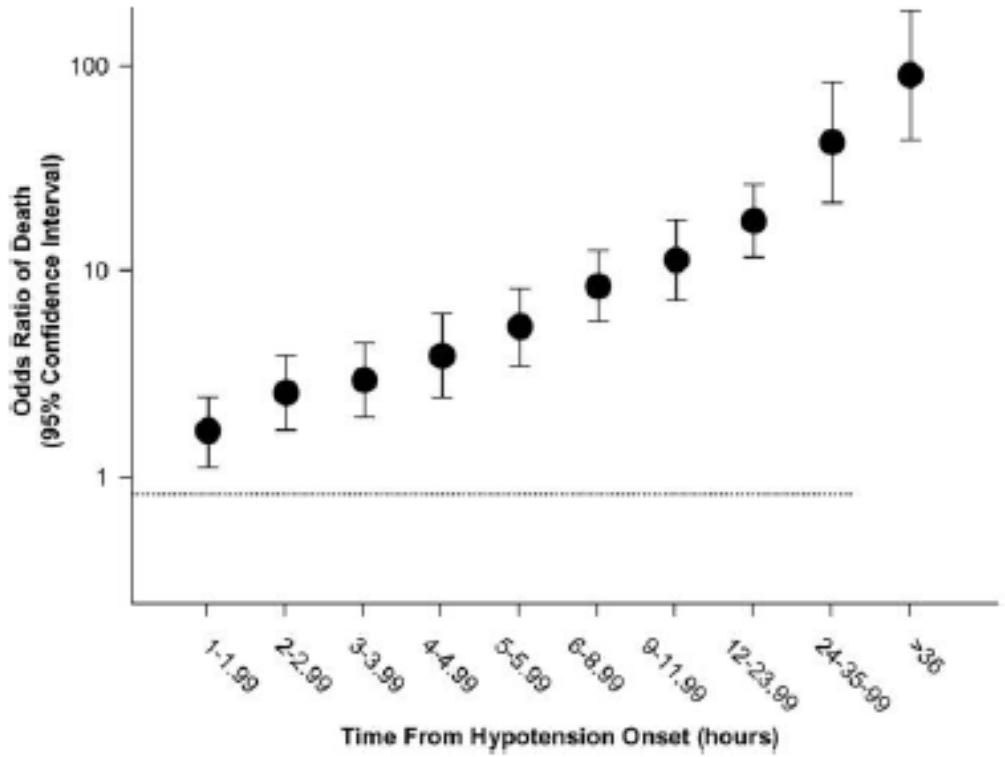
Daniel J. Henning, MD, MPH[1,2]; Jeremy R. Carey, MD[1]; Kimie Oedorf, BSc[1]; Danielle E. Day, BSc[1]; Colby S. Redfield, MD[1]; Colin J. Huguenel, MD[1]; Jonathan C. Roberts, MD[1]; Leon D. Sanchez, MD, MPH[1]; Richard E. Wolfe, MD[1]; Nathan I. Shapiro, MD, MPH[1,3]

2017

TABLE 4. Results From the Multivariable Logistic Regression Model Predicting Mortality

Covariate	OR	95% CI	*p*
Afebrile	4.29	2.24–8.23	< 0.001
Tachypnea > 24 breaths/min	2.14	1.12–4.07	0.02
Bicarbonate < 20 mEq/L	2.31	1.21–4.41	0.01
Lactate (mmol/L)	1.42	1.23–1.64	< 0.001
No emergency department antibiotics	0.26	0.09–0.80	0.02
Total IV fluids (L)	0.69	0.57–0.85	< 0.001

Traiter tôt



Kumar 2006

Temps entre début de hypotension et ATB approprié

The timing of early antibiotics and hospital mortality in sepsis

2017

AJRCCM

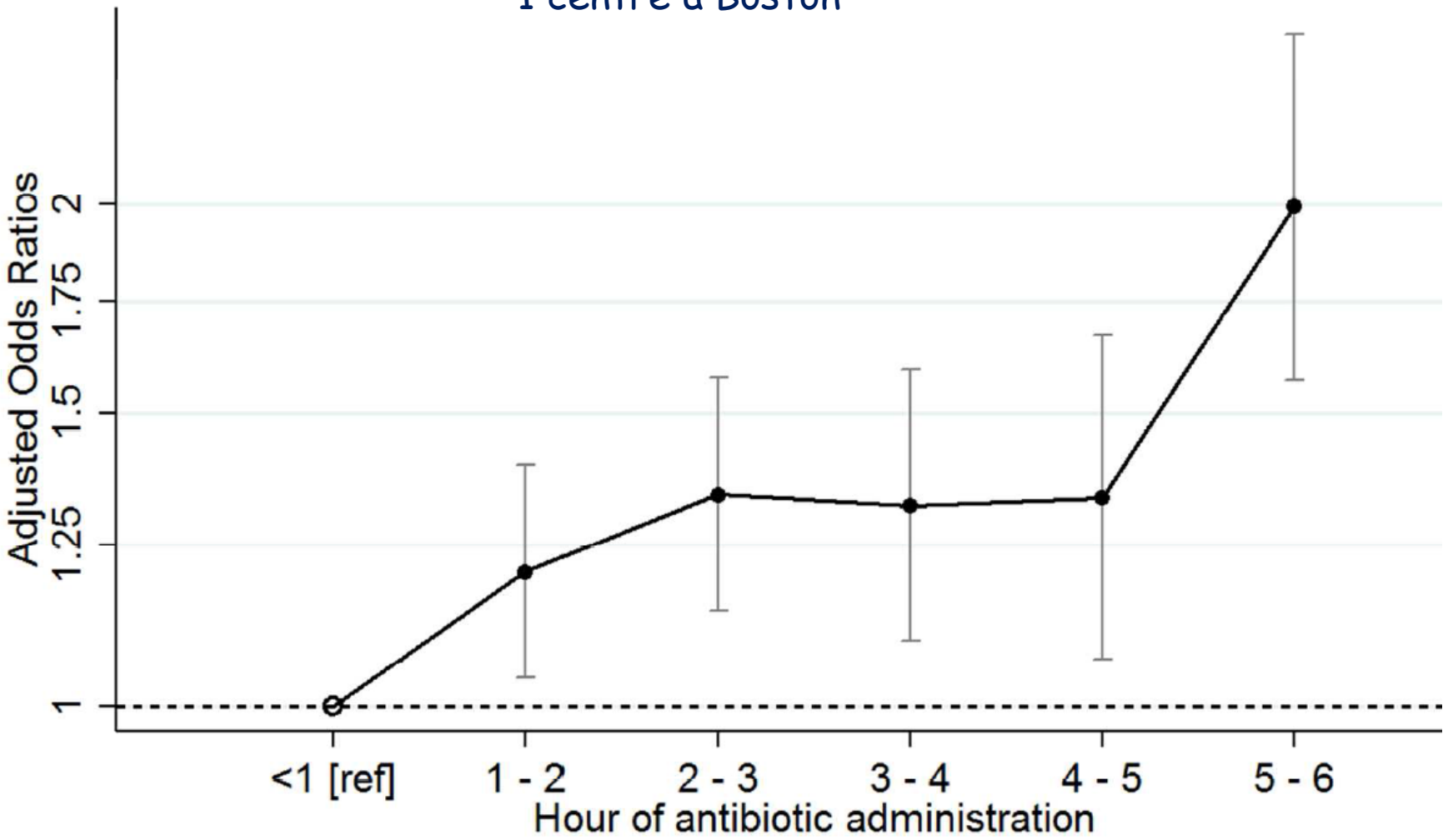
Vincent X Liu

Ère moderne, ATB plus rapide

Encore pertinent ?

Ne risque-t-on pas de surtraiter des patients par ATB ?

1 centre à Boston

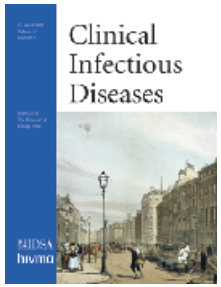


Donc il faut

- ❑ Faire le diagnostic d'infection rapidement
- ❑ Évaluer la gravité avec le quickSOFA
- ❑ Administrer des ATB aussi vite que possible

Traiter tôt…

… et bien

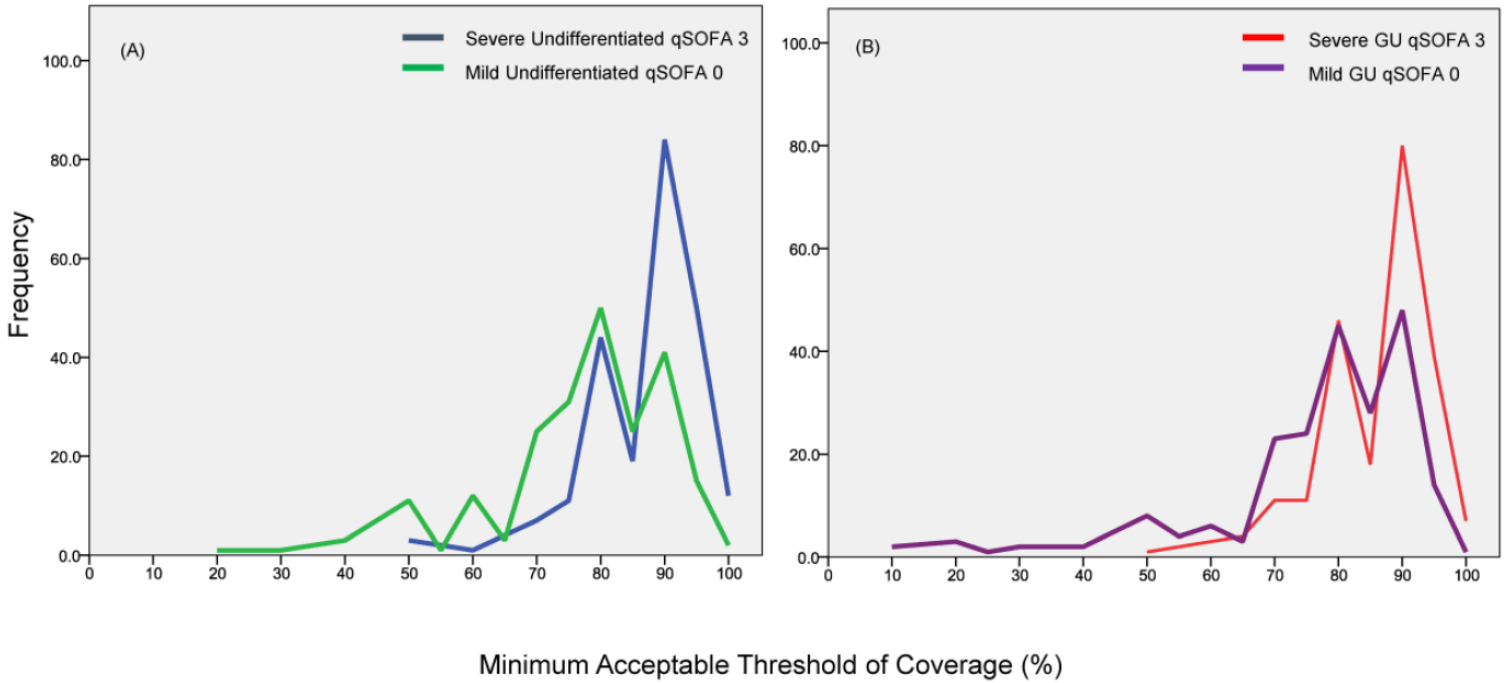


Empiric Antibiotic Treatment Thresholds for Serious Bacterial Infections: A Scenario-Based Survey Study

Alex M Cressman MD MSc[1,2], Derek R MacFadden MD[1,3], Amol A Verma MD MPhil[1,4,5],

Fahad Razak MD MSc[1,4,5] and Nick Daneman MD MSc[1-3]

2018



4 scénarios présentés à différents médecins (spécialistes ID ou non, expérimentés ou non)
Plutôt 90% si sévère, plutôt 80% sinon
Ids plus exigeants que les autres spécialités, expérience rend plus exigeant aussi

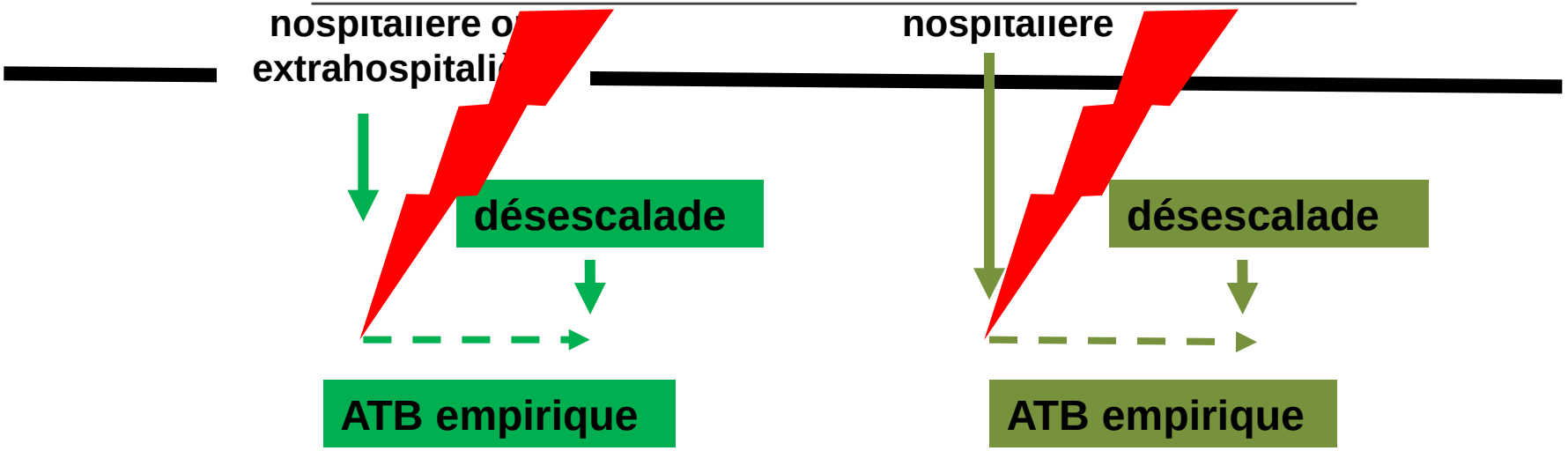
Traiter bien

Principe n°1 ATB approprié

Admission

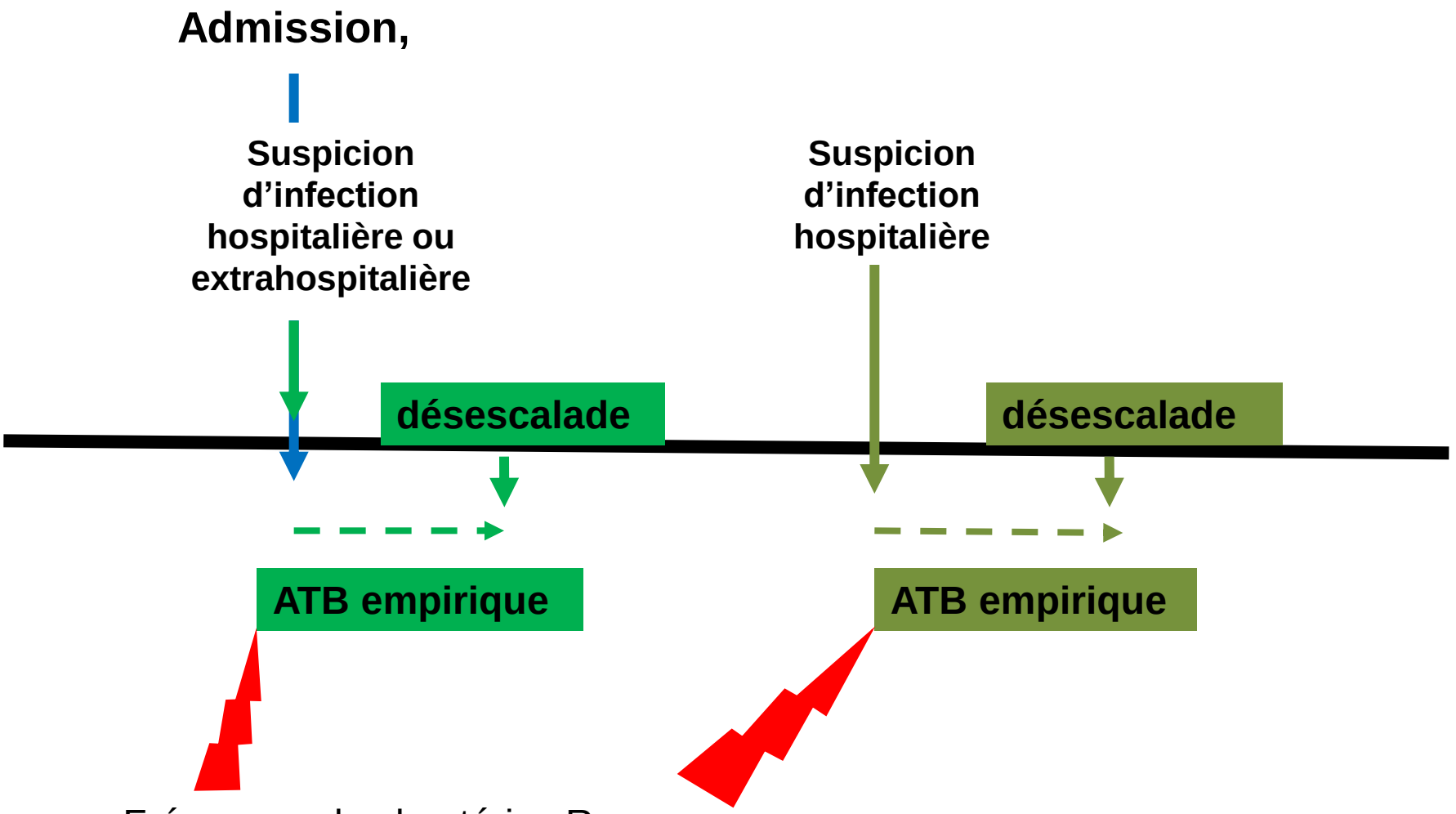
TABLE 3. MORTALITY RATES ACCORDING TO INITIAL EMPIRIC ANTIBIOTIC THERAPY

First Author	Ref.	Crude Mortality Rates of Patients Receiving: Inadequate Antibiotic Therapy	Crude Mortality Rates of Patients Receiving: Adequate Antibiotic Therapy	p Value
Luna	58	92.2% (n = 34)	37.5% (n = 15)	< 0.001
Alvarez-Lerma	74	34.9% (n = 146)	32.5% (n = 284)	NS
Rello	21	63.0% (n = 27)	41.5% (n = 58)	0.06
Kollef	60	60.8% (n = 51)	26.6% (n = 79)	0.001
Sanchez-Nieto	61	42.9% (n = 14)	25.0% (n = 24)	NS
Ruiz	62	50.0% (n = 18)	39.3% (n = 28)	NS
Dupont	76	60.7% (n = 56)	47.3% (n = 55)	NS



Traiter bien

Principe n°2 pour être approprié
connaitre le spectre



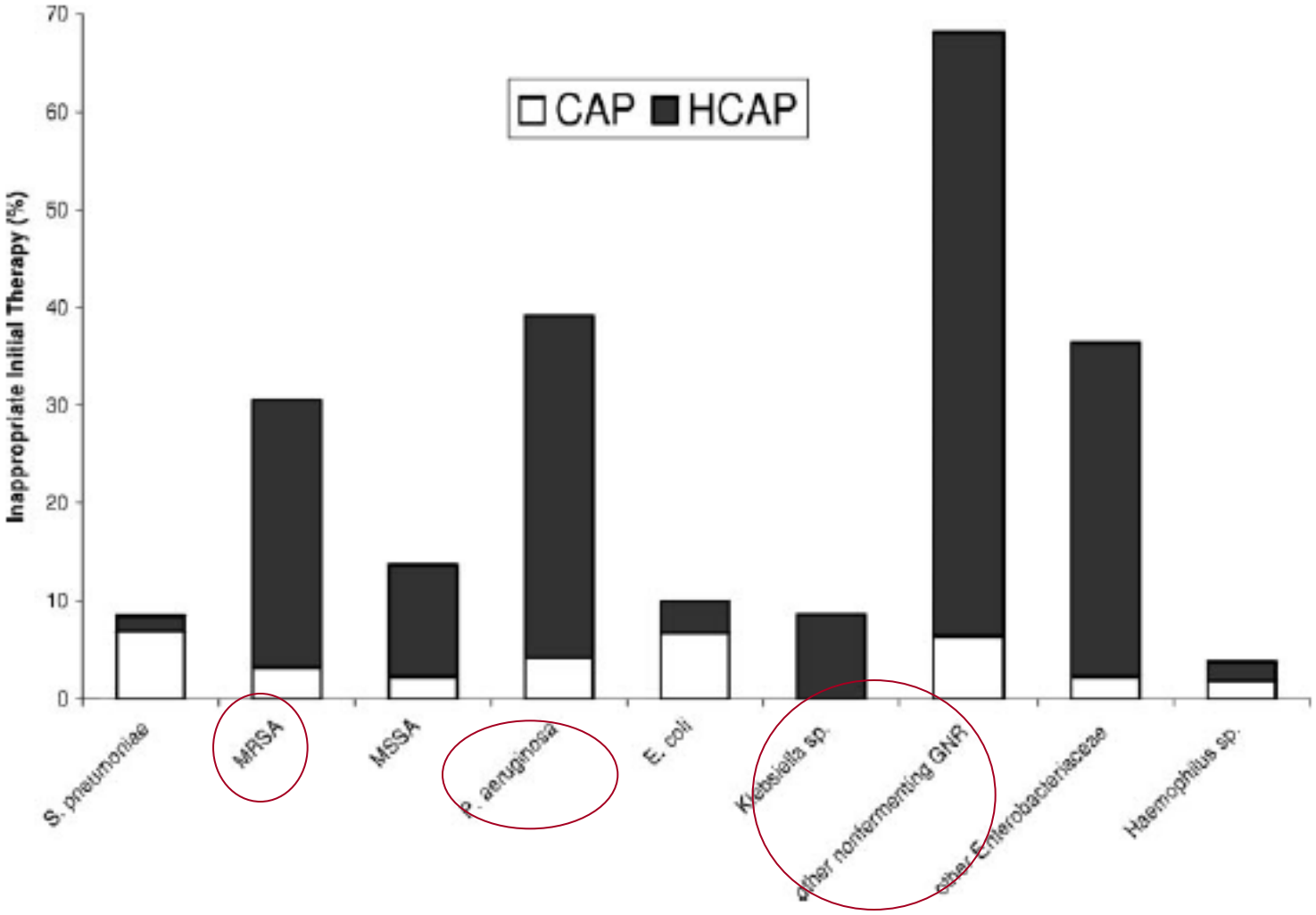
Fréquence des bactéries R
Dépend de origine comm vs health-care

ex: 50% si HCAP (Shorr et al. Chest 2010)

Health Care-Associated Pneumonia and Community-Acquired Pneumonia: a Single-Center Experience[▽]

Scott T. Micek,[1] Katherine E. Kollef,[2] Richard M. Reichley,[3] Nareg Roubinian,[2] and Marin H. Kollef[2]

2007



Une vision purement épidémiologique ?

RESEARCH ARTICLE Open Access

Severe community-acquired *Enterobacter* pneumonia: a plea for greater awareness of the concept of health-care-associated pneumonia

Alexandre Boyer[1,2,3*], Brice Amadeo[2,3], Frédéric Vargas[1], Ma Yu[1], Sylvie Maurice-Tison[4], Véronique Dubois[5], Cécile Bébéar[5], Anne Marie Rogues[2,3] and Didier Gruson[1]

BMC Infectious Diseases

2011

30 pneumopathies communautaires vraies documentées

10 pneumopathies "communautaires"

Surprise : *Enterobacter sp. !*

inadéquate

Retard dans l'amélioration ?

ATB empirique

Retour des
examens bactério

	Enterobacter (n=10)	Comm. (n=30)	p value
Empirical antimicrobial treatment appropriateness[$], %	20	97	<0.01
Time between hospital admission[£] and definite appropriate antimicrobial treatment (days)	3.3±1.6	1.2±0.6	<0.01
Time between onset of empirical antimicrobial therapy and apyrexia (days)[¤]	5.6±2.1	3.8±2.4	0.06
Length of antimicrobial treatment (days)	11.8±5.2	9.6±3.8	0.16
Vasoactive or inotropic drug length of use (days)**	8±3.9	4.8±3.2	0.13
Dialysis, n (%)	3 (30)	3 (10)	0.14
Ventilation[¤¤], n (%)	10 (100)	18 (60)	0.96
Length of ventilation (days)	8.4±5.2	4±4.3	0.01
Length of ICU stay (days)	21±15	11.9±9.2	0.04
Hospital mortality, n (%)	3 (30)	5 (17)	0.37

	Univariate analysis		Multivariate analysis
	Odds ratio[£] (95% confidence interval)	p	Odds ratio[£] (95% confidence interval)
Male Sex	0.33 (0.06-1.81)	0.20	…
SAPS II	1.04 (0.98-1.1)	0.21	…
Time between onset of symptoms and admission	1 (0.74-1.34)	0.97	…
Highest temperature	2.07 (0.84-5.14)	0.12	…
Sepsis classification		0.4	…
Leukocytosis (G/L)	0.87 (0.76-1)	0.05	0.75 (0.59-0.96)
Blood urea (mmol/L)	1.06 (1-1.13)	0.07	…
Radiographic findings		0.41	…
Predominant alveolar	1		
Predominant interstitiel	1.85 (0.43-7.96		
ARDS	0.22 (0.04-1.21)	0.08	…
Criteria for HCAP		<0.0	
No criterion	1	1	1
At least one criterion	45 (4.61-439.16)		244.6 (7.48-999.99)

Traiter bien

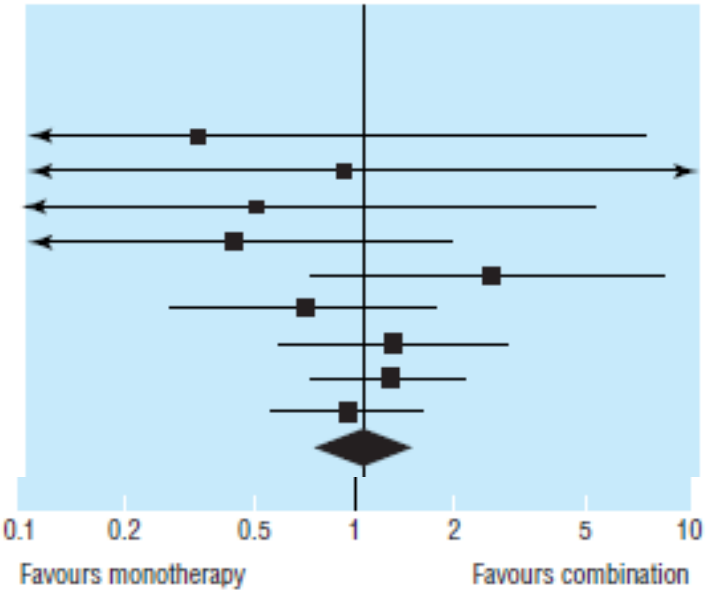
Principe n°3 pour être approprié
Associer plusieurs familles

β lactam monotherapy versus β lactam-aminoglycoside combination therapy for sepsis in immunocompetent patients: systematic review and meta-analysis of randomised trials

Mical Paul, Ishay Benuri-Silbiger, Karla Soares-Weiser, Leonard Leibovici

2004

Study or subcategory	Monotherapy No/Total	Combination therapy No/Total	Weight (%)	Relative risk (95% CI)
01 Same β lactam				
Abrams 1979	0/12	0/12		Not estimable
Cardozo 2001	0/56	0/48		Not estimable
Sandberg 1997	0/37	0/36		Not estimable
Sculier 1982	0/10	1/10	0.28	0.33 (0.02 to 7.32)
Carbon 1987	1/25	1/22	0.37	0.88 (0.06 to 13.25)
Ribera 1996	1/45	2/45	0.48	0.50 (0.05 to 5.32)
Korzeniowski 1982	2/33	6/41	1.13	0.41 (0.09 to 1.92)
Klastersky 1973	7/22	3/23	1.76	2.44 (0.72 to 8.26)
D'Antonio 1992	7/144	10/142	2.89	0.69 (0.27 to 1.76)
Kljucar 1990	11/49	9/50	3.98	1.25 (0.57 to 2.74)
Cometta 1994	24/148	19/144	7.31	1.23 (0.70 to 2.14)
Dupont 2000	21/111	24/116	8.06	0.91 (0.54 to 1.55)
Subtotal (95% CI)	692	689	26.27	1.02 (0.76 to 1.38)

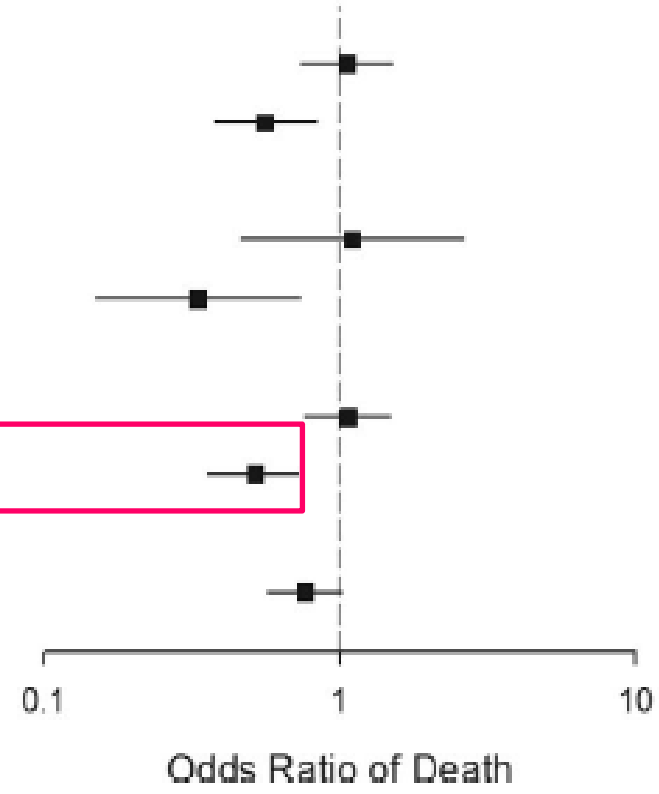


A survival benefit of combination antibiotic therapy for serious infections associated with sepsis and septic shock is contingent only on the risk of death: A meta-analytic/meta-regression study

Anand Kumar, MD; Nasia Safdar, MD; Shravan Kethireddy, MD; Dan Chateau, PhD

2010

Group	Monotherapy Mortality (%)	Combination Therapy Mortality (%)	Odds Ratio	I^2 (%)	P-value
non-shock	86/680 (12.6)	96/686 (14.4)	1.06 (0.73-1.52)	13.7	.7721
shock	96/188 (51.1)	177/422 (41.9)	0.56 (0.39-0.83)	0.8	.0043
non-critically ill	23/313 (7.3)	35/339 (10.3)	1.10 (0.46-2.60)	45.3	.8321
critically ill	32/64 (50.0)	34/128 (26.6)	0.33 (0.15-0.74)	0	.0067
non-shock/non-critically ill	109/993 (11.0)	131/1005 (13.0)	1.06 (0.76-1.47)	19.1	.7178
shock/critically ill	128/252 (50.1)	211/550 (38.4)	0.51 (0.36-0.72)	0	.0002
overall	237/1245 (19.0)	342/1555 (22.0)	0.76 (0.57-1.02)	33.8	.0622



Traiter bien

Principe n°4 pour être approprié
Faire attention à la première dose

George L Drusano University of Florida , Gainesville

Infectious Diseases, Applied Mathematics

M.D.

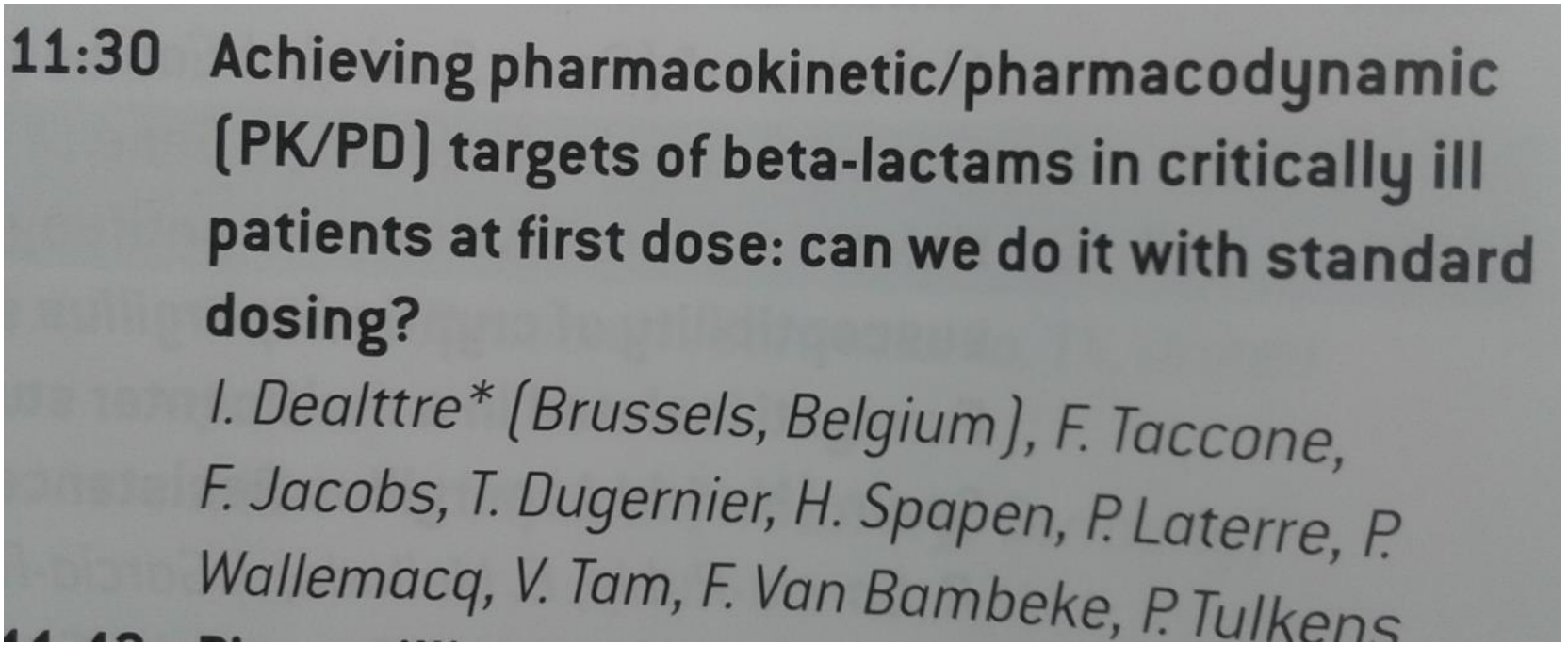
48.02

First dose supremacy

Roberts 2009

grande variabilité chez les patients en choc septique
explique la nécessité du monitorage PK/PD

La première dose: back to the future !



11:30 Achieving pharmacokinetic/pharmacodynamic (PK/PD) targets of beta-lactams in critically ill patients at first dose: can we do it with standard dosing?

I. Dealttre (Brussels, Belgium), F. Taccone, F. Jacobs, T. Dugernier, H. Spapen, P. Laterre, P. Wallemacq, V. Tam, F. Van Bambeke, P. Tulkens*

Étude non encore publiée mais selon un modèle de Monte Carlo première dose de tazocilline jusqu'à 14g…

Therapeutic Drug Monitoring of Amikacin In Septic Patients

2013

Wieslawa Duszynska[1], Fabio Silvio Taccone[2], Magdalena Hurkacz,[3] Beata Kowalska-Krochmal[4], Anna Wiela-Hojeńska[3], Andrzej Kübler[1]

Critical Care

La corrélation Cpeak/CMI en fonction de première dose vs doses suivantes et évolution clinique dans les sepsis sévères

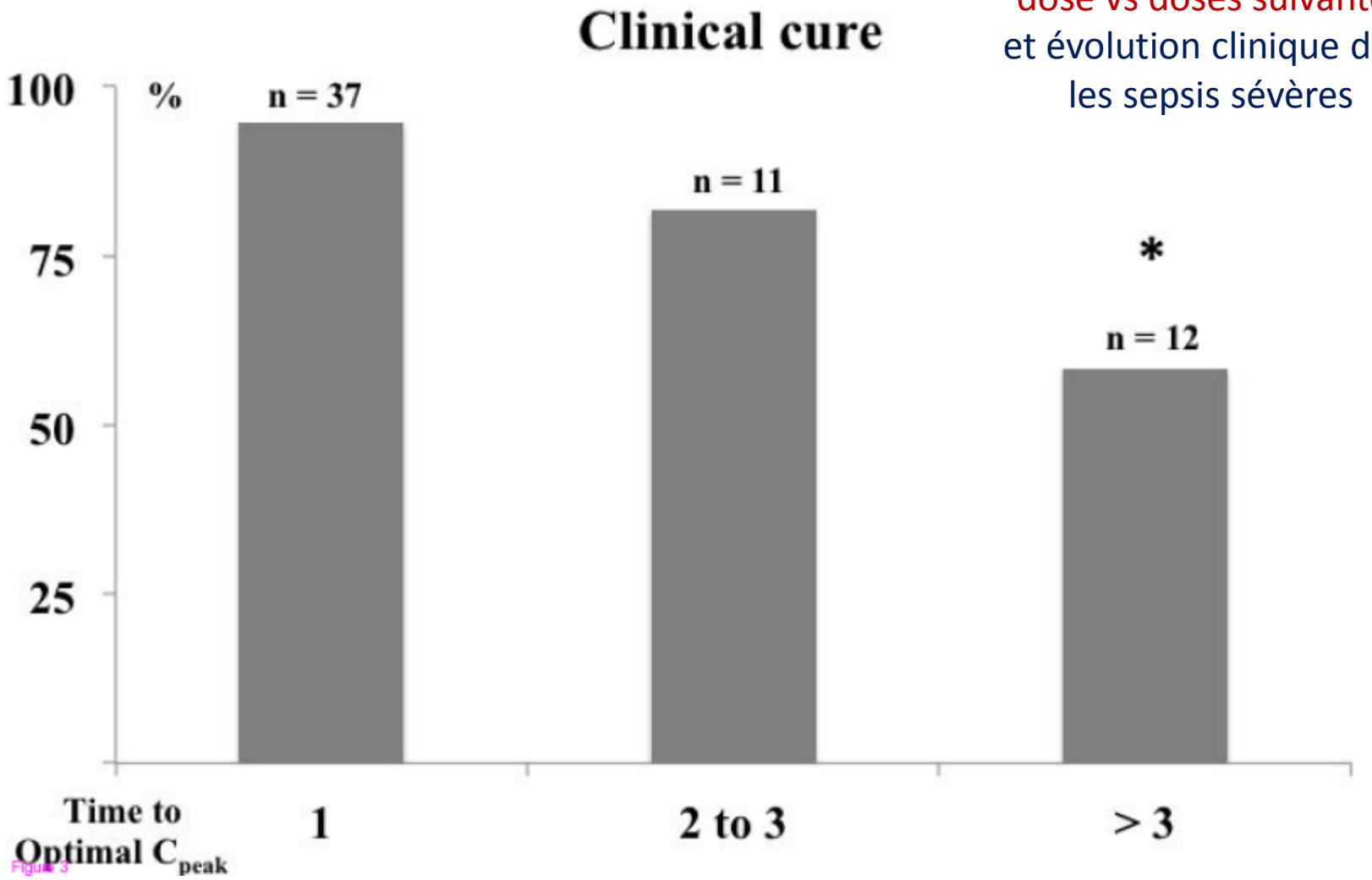


Figure 3

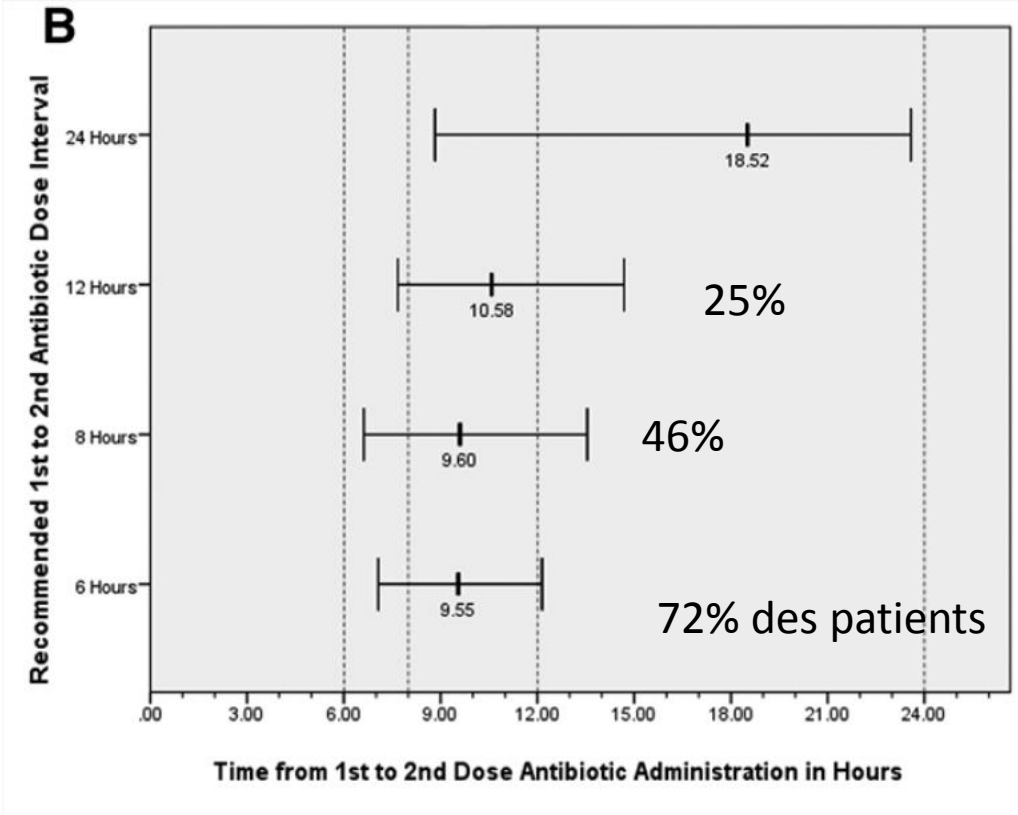
Traiter bien

Principe n°5 pour être approprié
Faire attention à la seconde dose etc…

Delayed Second Dose Antibiotics for Patients Admitted From the Emergency Department With Sepsis: Prevalence, Risk Factors, and Outcomes

Daniel Leisman, BS[1,2]; Victor Huang, MD[1]; Qiuping Zhou, DO[1]; Jeanie Gribben, BS[1]; Andrea Bianculli, BS[1]; Michelle Bernshteyn, BS[3]; Mary Frances Ward, RN, MS, ANP[4,5]; Sandra M. Schneider, MD[1,6]

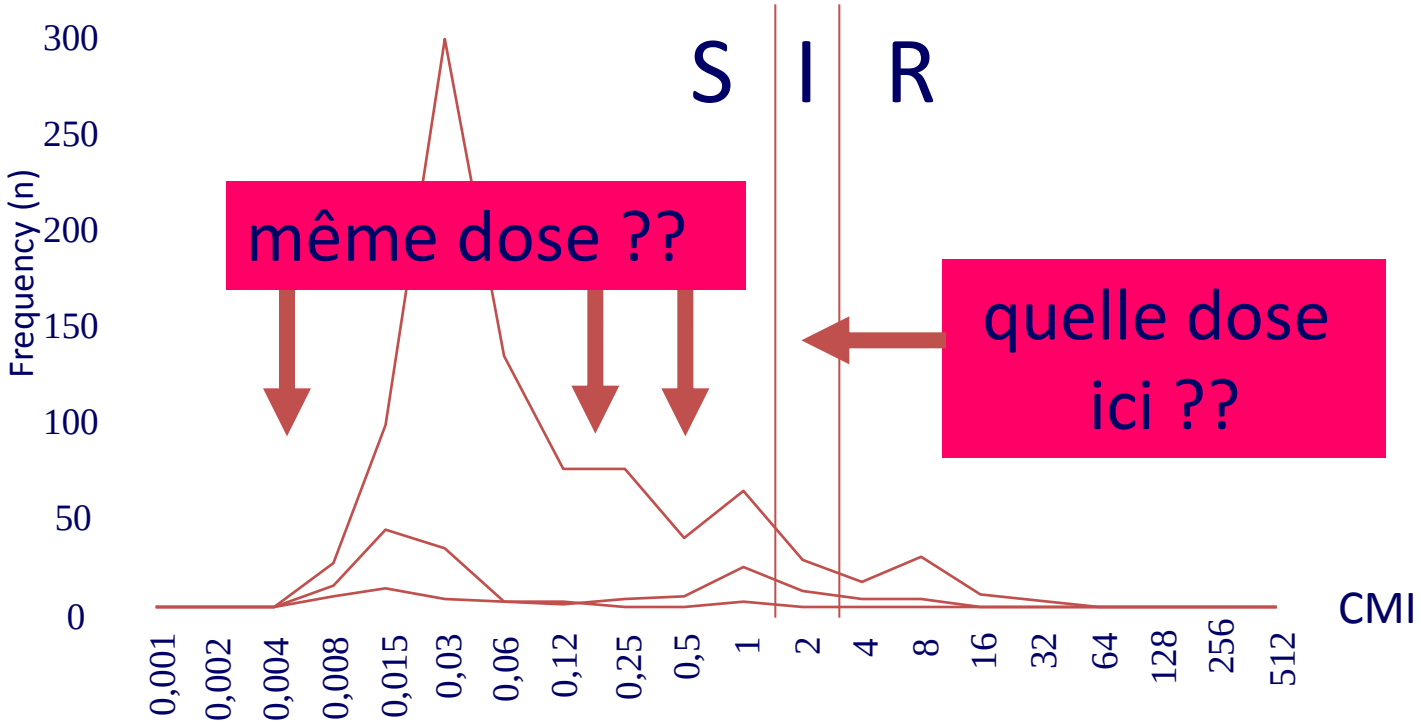
2017



Globalement 33% de retard

Traiter bien

Principe n°6 vite récupérer la CMI pour adapter éventuellement le traitement



Direct E-Test (AB Biodisk) of Respiratory Samples Improves Antimicrobial Use in Ventilator-Associated Pneumonia

2007

Emilio Bouza,[1] María V. Torres,[1] Celina Radice,[1] Emilia Cercenado,[1] Roberto de Diego,[2] Carlos Sánchez-Carrillo,[1] and Patricia Muñoz[1]

Table 3. Outcome of 250 episodes of ventilator-associated pneumonia (VAP).

Outcome	E-test group (n = 167)	Control group (n = 83)	P
Fever, mean days ± SD	4.61 ± 5.06	7.84 ± 6.24	<.01
Antibiotic therapy, mean days ± SD	15.72 ± 9.47	18.92 ± 10.92	.02
Defined daily doses of antibiotic therapy, mean ± SD	31.43 ± 24.47	42.72 ± 34.13	.01
Median cost, in €, of antibiotic per episode (IQR)	666 (236–1360)	984 (437–1601)	.03
Percentage of adequate days of antibiotic therapy	95.22	76.26	<.01
Percentage of adequate defined daily doses of antibiotic therapy	91.28	68.26	<.01

Diagnostic Microbiology and Infectious Disease 73 (2012) 107–110

Contents lists available at SciVerse ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Bacteriology

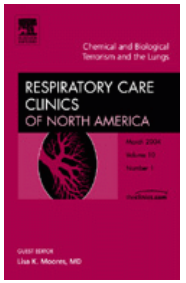
Direct testing of bronchoalveolar lavages from ventilator-associated pneumonia patients ☆,☆☆,★,★★,★★★

2012

Alexandre Boyer [a,b,c,*], José Medrano [a], Fatima Mzali [b,d], Claude-Charles Balick-Weber [a], Emilie Bessède [e], Walter Picard [a], Benjamin Clouzeau [a], Cécile M Bébéar [e], Frédéric Vargas [a], Gilles Hilbert [a], Anne Marie Rogues [b,c], Didier Gruson [a]

Tailoring Empirical Antimicrobial Therapy in Subjects With Ventilator-Associated Pneumonia With a 10-Hour E-Test Approach

2018



Alexandre Boyer MD PhD, Julien Goret MD, Benjamin Clouzeau MD, Antoine Romen MD, Renaud Prevel MD, Edouard Lhomme MD, Frédéric Vargas MD PhD, Gilles Hilbert MD PhD, Cecile Bébéar MD PhD, Didier Gruson MD PhD, and Fatima M'Zali PhD

Lecture CMI H24

par référent bactério et classement R, I, S

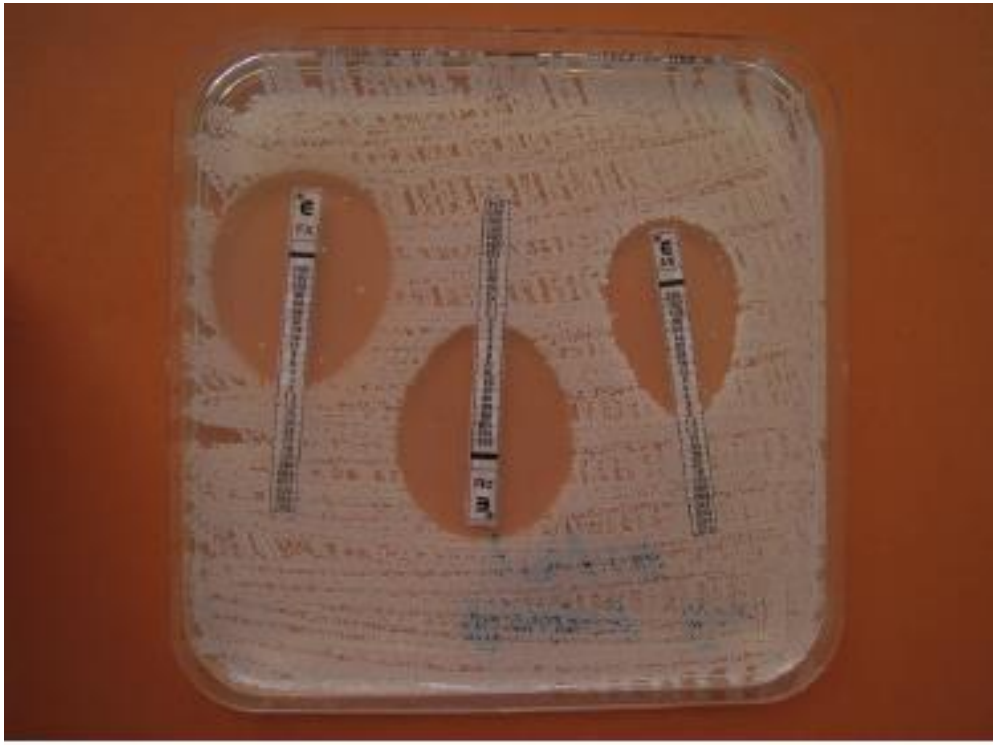
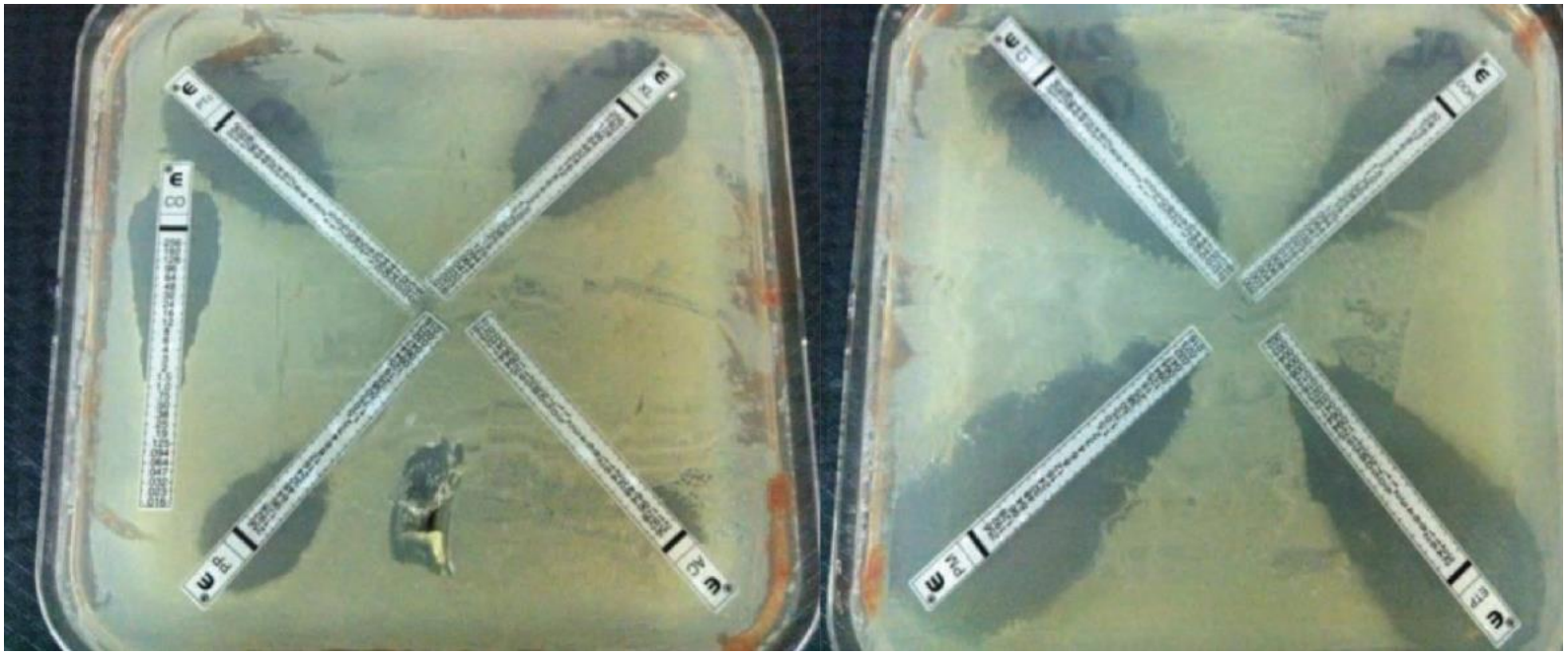


Fig. 1. Example of a monomicrobial VAP.

Lecture CMI H10 (possible dans 64% des PAVM)

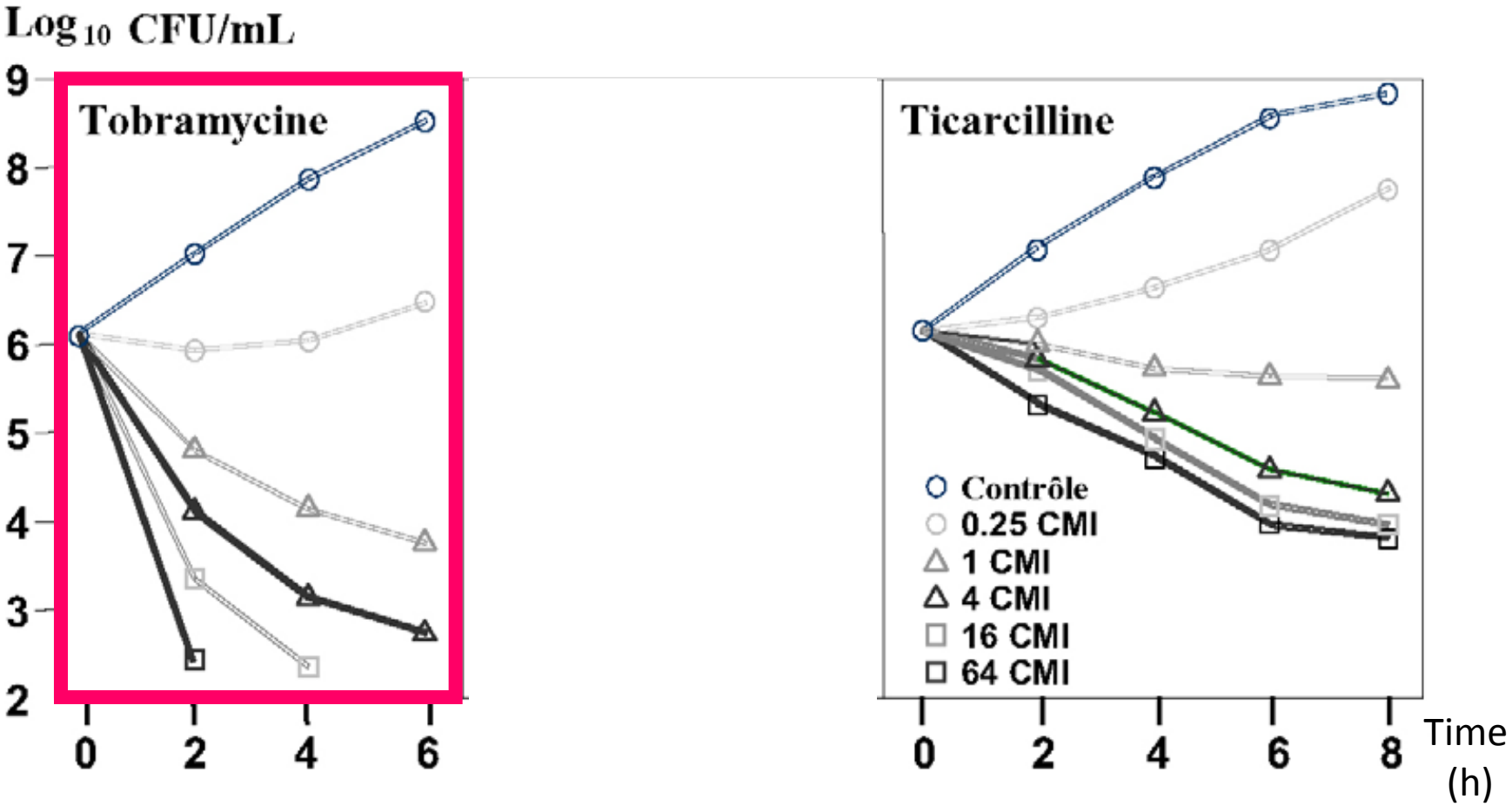


Traiter bien

Principe n°7 respecter les grands principes PK-PD

selon les familles d’ATB

ATB concentration-dépendants



Concept de forte monodose, < 5jours

- Haute dose pas plus toxique car la fixation sur les cellules du tubule rénal proximal est saturable ce qui les protège en cas de fortes concentrations
- De plus, effet post antibiotique et résistance adaptative

2007

George L Drusano University of Florida , Gainesville

Infectious Diseases, Applied Mathematics

M.D.

48.02

2011

aucune recommandation n'établit la façon de monitorer les aminosides en réanimation pour s'adapter à une balance bénéfice risque modifiée

Recommandations actuelles

1ère dose sur 30' IV lente dans 250 cc de G5%

Gentamycine: 7-8mg/kg

Amikacine: 20-30 mg/kg/j

ne doit pas être systématique, mais réservé à certaines situations. **En cas de traitement ≤ à 3 jours, aucun dosage n'est nécessaire chez les patients pour lesquels aucune modification des paramètres pharmacocinétiques n'est attendue.**

Dosage des concentrations pic 30 minutes après la fin de la perfusion sur une autre voie que la voie de passage

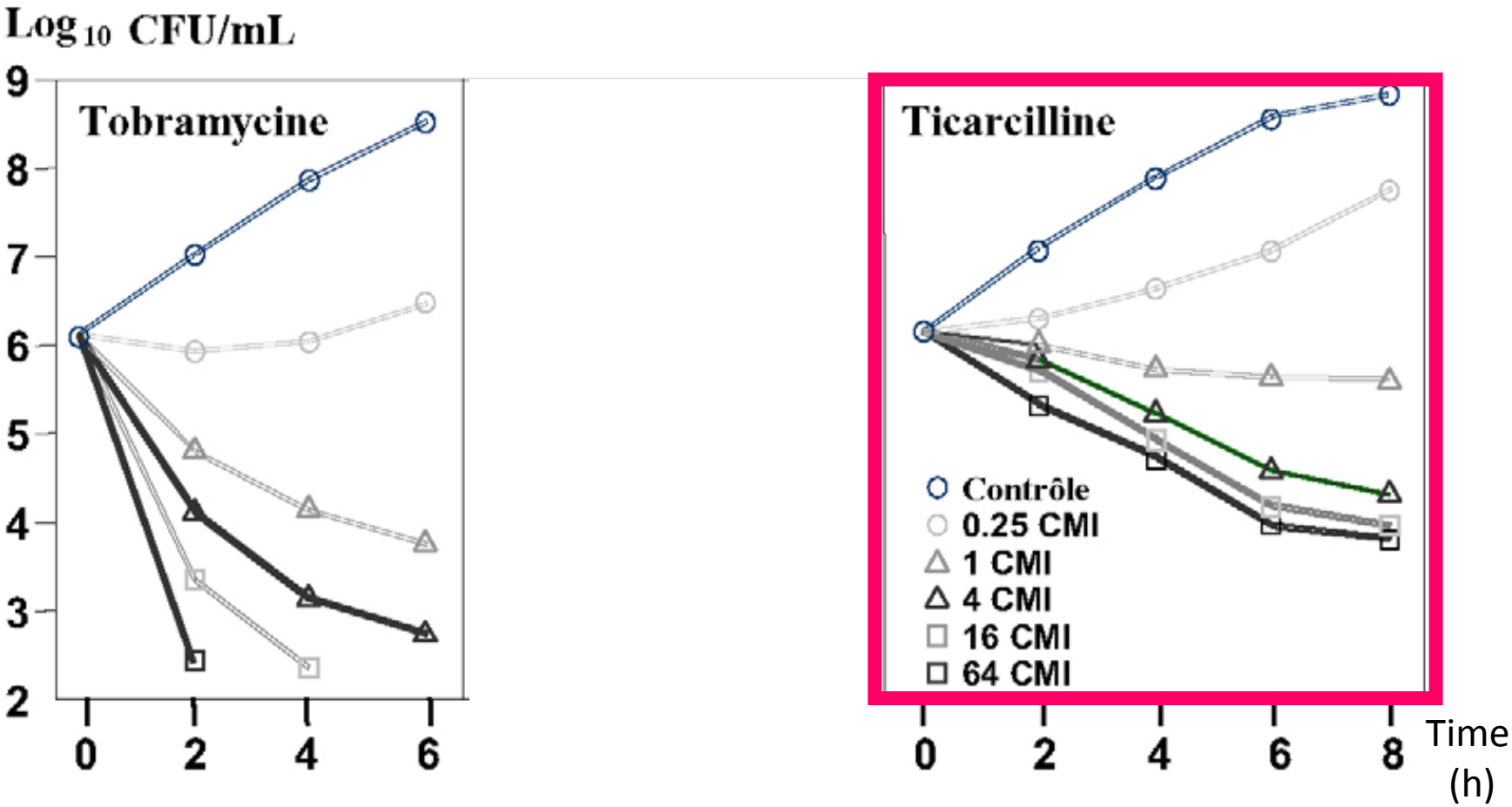
Objectifs:

- avant CMI

Tableau 1 : Objectifs de concentrations

	Pic (Cmax) en mg/l	Résiduelle (Cmin) en mg/l
Gentamicine, nétilmicine, tobramycine	30 à 40	< 0,5
Amikacine	60 à 80	< 2,5

ATB temps-dépendants



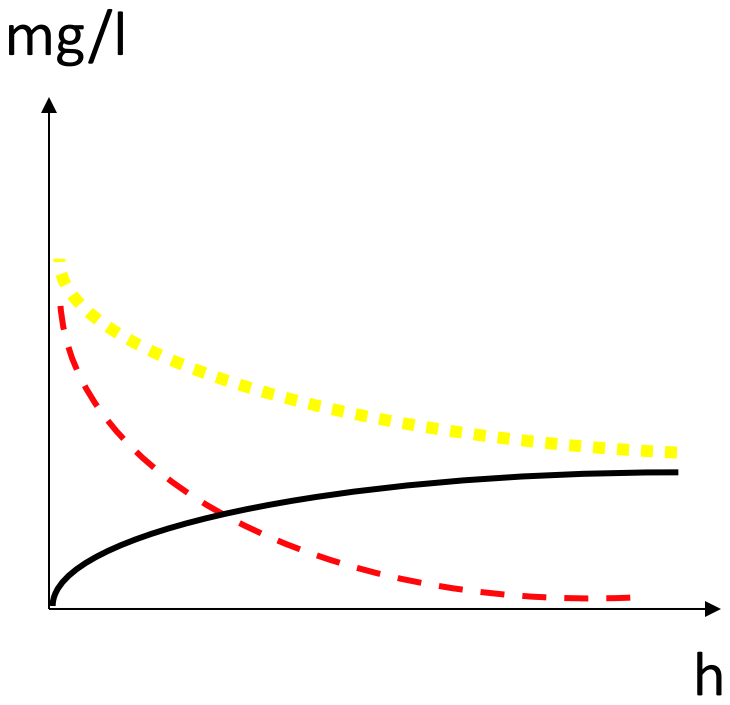
Peu d'EPA, ½ vie d'élimination courte

Δt > 4xCMI = 100% du temps

- Perfusion continue à Conc = 4 à 8 x CMI
- Fractionnement important des doses /4h
- Perfusion prolongée
- Antibiotique à demi-vie longue = ceftriaxone

D'autant plus que bactérie I (point critique PK/PD pour les BL 8 µg/ml) et que terrain à risque PK (réa, infections sévères, inoculum lourd, matériel étranger, neutropéniques, immunodéprimés)

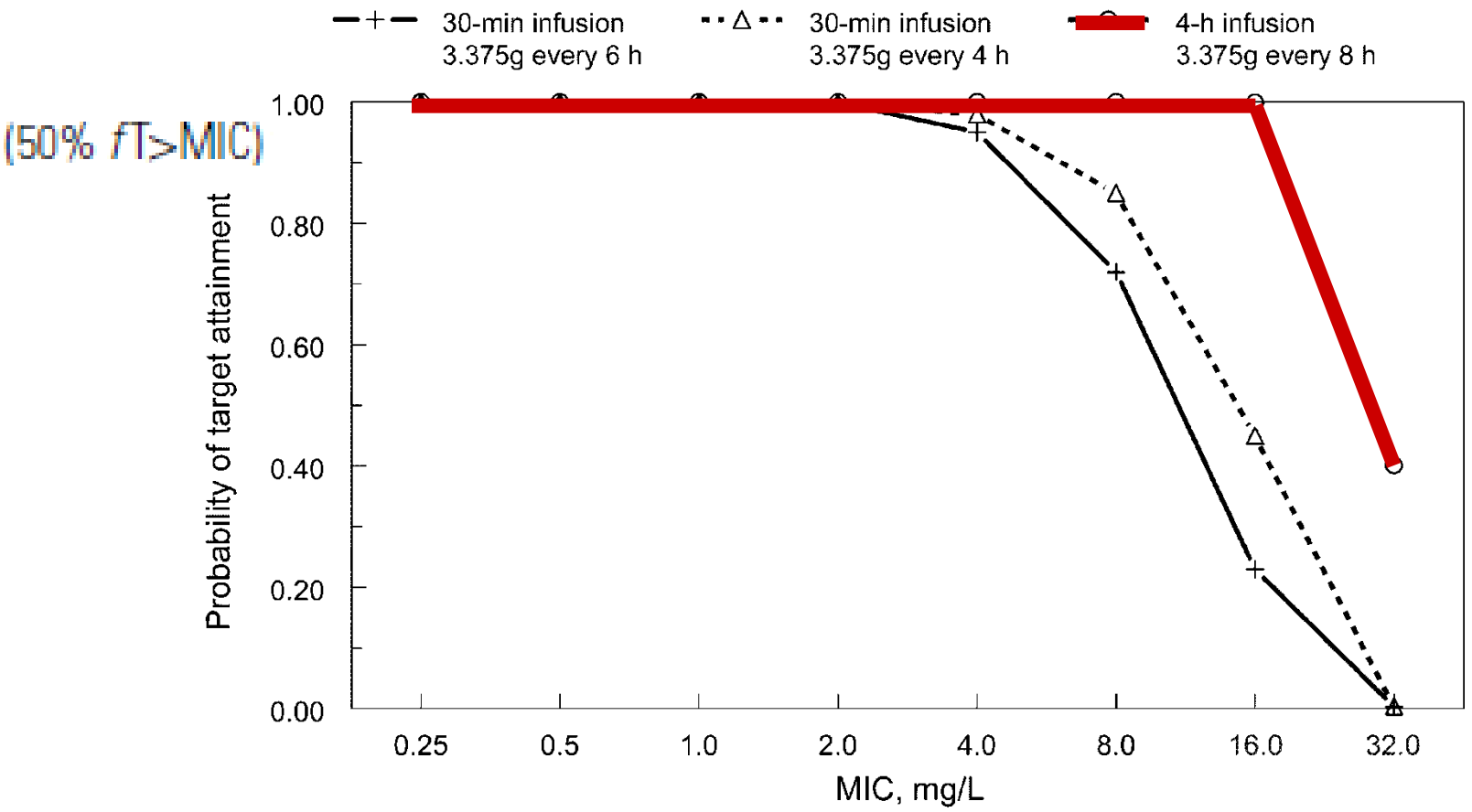
Si perfusion continue, faire une dose de charge



- Réduire le délai pour C>CMI
- Minimiser le risque de sous dosage si Vd augmentée
- Favoriser la rapidité de la diffusion extravasculaire

Lodise
2007

Piperacillin-Tazobactam for *Pseudomonas aeruginosa* Infection: Clinical Implications of an Extended-Infusion Dosing Strategy



Lodise
2007

Piperacillin-Tazobactam for *Pseudomonas aeruginosa* Infection: Clinical Implications of an Extended-Infusion Dosing Strategy

30-min infusion
3.375g every 6 h
or
30-min infusion
3.375g every 4 h

vs

4-h infusion
3.375g every 8 h

Overall
n = 194

APACHE II <17

Extended Infusion
n = 41
14-day mortality[C]: 12.2%
Median LOS (range)[a,c]:
21 (3-98) days

APACHE II ≥17

Intermittent Infusion
n = 38
14-day mortality[C]: 31.6%
Median LOS (range)[a,c]:
38 (6-131) days

Difference in 14 day mortality: *P* = .04
Difference in median LOS: *P* = .02

Extended Infusion
n = 61
14-day mortality: 6.6%
Median LOS (range)[a]:
18 (4-159) days

Interm…

14-day mortality: 3.7%
Median LOS (range)[a]:
18 (3-144) days

Difference in 14 day mortality: *P* = .5
Difference in median LOS: *P* = .5

…ion

14-day mortality[C]: 12.2%
Median LOS (range)[a,c]:
21 (3-98) days

Intermittent Infusion
n = 38
14-day mortality[C]: 31.6%
Median LOS (range)[a,c]:
38 (6-131) days

Difference in 14 day mortality: *P* = .04
Difference in median LOS: *P* = .02

Continuous versus Intermittent β-Lactam Infusion in Severe Sepsis

A Meta-analysis of Individual Patient Data from Randomized Trials

Jason A. Roberts[1,2,3,4], Mohd-Hafiz Abdul-Aziz[2,5], Joshua S. Davis[6,7], Joel M. Dulhunty[1,2,8], Menino O. Cotta[1,2,3,4], John Myburgh[9,10], Rinaldo Bellomo[11,12], and Jeffrey Lipman[1,2]

AJRCCM

2016

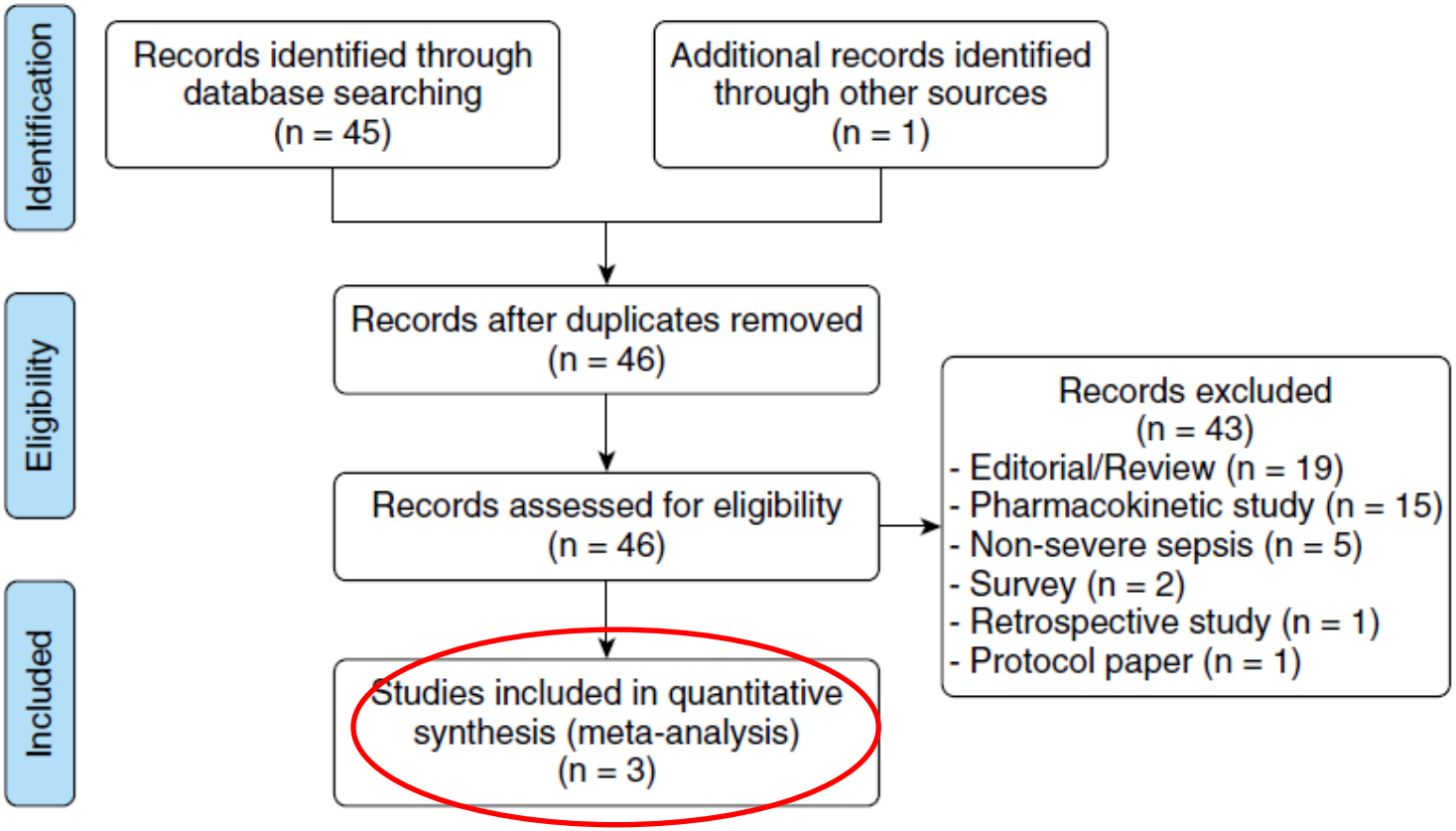


Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart for identification of included studies.

Continuous Infusion of Beta-Lactam Antibiotics in Severe Sepsis: A Multicenter Double-Blind, Random… Trial

Joel M. Dulhunty,[1] …
Charudatt Shirwadk… …en A. R. W… …[7] David L… …[4] Charles Gomersall,[5] …Lipman[1]

…fectious disease, 2013

A Multicent… …Contin… …ntermittent β-Lactam I…

Joel M. Dulhunty[1,2] …[4,5], Steven … Bellomo[8,9], …
Charles Gomersall[1] … Eastwood[8], … vid L. Paterson[15,16], …
Therese Starr[1,2], Sa… …the BLING I… …ICS Clinical Trials Group*

2015

Mohd H. Abdul-A…
Helmi Sulaiman
Mohd-Basri Mat-I…
Vineya Rai
Kang K. Wong
Mohd S. Hasan
Azrin N. Abd Rah…
Janattul A. Jamal…
Steven C. Wallis
Jeffrey Lipman
Christine E. Staat…
Jason A. Roberts

…nfusio… …sis (BLISS): …, two-c… …belled …ontroll… …tinuous …ittent I… …usion …l patie… …sepsis

…d (2016)

Continuous versus Intermittent β-Lactam Infusion in Severe Sepsis

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Jason A. Roberts[1,2,3,4], Mohd-Hafiz Abdul-Aziz[2,5], Joshua S. Davis[6,7], Joel M. Dulhunty[1,2,8], Menino O. Cotta[1,2,3,4], John Myburgh[9,10], Rinaldo Bellomo[11,12], and Jeffrey Lipman[1,2]

AJRCCM

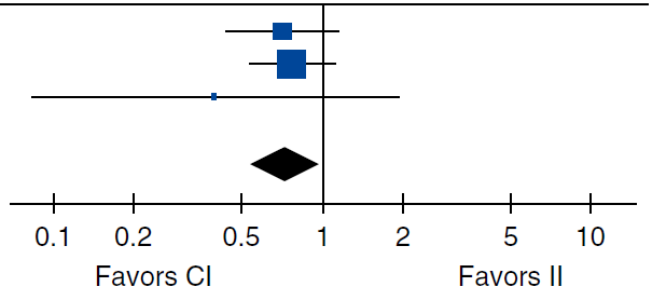
2016

Mortalité J30

Study or Subgroup	CI Events	CI Total	II Events	II Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abdul-Aziz 2016	20	70	28	70	33.3%	0.71 [0.45, 1.14]
Dulhunty 2015	39	212	52	220	60.7%	0.78 [0.54, 1.13]
Dulhunty 2013	2	30	5	30	5.9%	0.40 [0.08, 1.90]
Total (95% CI)		**312**		**320**	**100.0%**	**0.73 [0.55, 0.98]**
Total events	61		85			

Heterogeneity: $Chi^2 = 0.69$, df = 2 (P = 0.71); $I^2 = 0\%$

Test for overall effect: Z = 2.11 (P = 0.03)

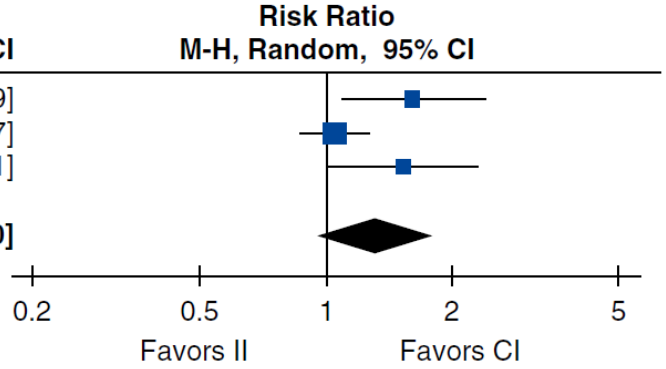


Clinical cure (7-14j après ATB)

Study or Subgroup	CI Events	CI Total	II Events	II Total	Weight	Risk Ratio M-H, Random, 95% CI
Abdul-Aziz 2016	39	70	24	70	28.8%	1.63 [1.10, 2.39]
Dulhunty 2015	111	212	109	220	44.0%	1.06 [0.88, 1.27]
Dulhunty 2013	23	30	15	30	27.2%	1.53 [1.02, 2.31]
Total (95% CI)		**312**		**320**	**100.0%**	**1.32 [0.97, 1.80]**
Total events	173		148			

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 5.56$, df = 2 (P = 0.06); $I^2 = 64\%$

Test for overall effect: Z = 1.78 (P = 0.07)



Principe n°8 ne pas oublier le contrôle de la source

Impact of Source Control in Patients With Severe Sepsis and Septic Shock

María Luisa Martínez, MD[1]; Ricard Ferrer, MD, PhD[2,3]; Eva Torrents, MD[1];
Raquel Guillamat-Prats, PhD[3]; Gemma Gomà, RN[1]; David Suárez, MSc, PhD[4];
Luis Álvarez-Rocha, MD[5]; Juan Carlos Pozo Laderas, MD, PhD[6]; Ignacio Martín-Loeches, MD, PhD[7];
Mitchell M. Levy, MD, FCCP, FCCM[8]; Antonio Artigas, MD, PhD[1,3]; for the Edusepsis Study Group

2016

5. Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup: Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013; 41:580–637

control be undertaken within 12 hours of diagnosis (5), up from 6 hours in the previous guidelines. This increase was based on a recent retrospective study in 106 patients with sep-

21. Boyer A, Vargas F, Coste F, et al: Influence of surgical treatment timing on mortality from necrotizing soft tissue infections requiring intensive care management. *Intensive Care Med* 2009; 35:847–853

off times (21). Although it is reasonable to assume that rapid

Influence of surgical treatment timing on mortality from necrotizing soft tissue infections requiring intensive care management

Boyer

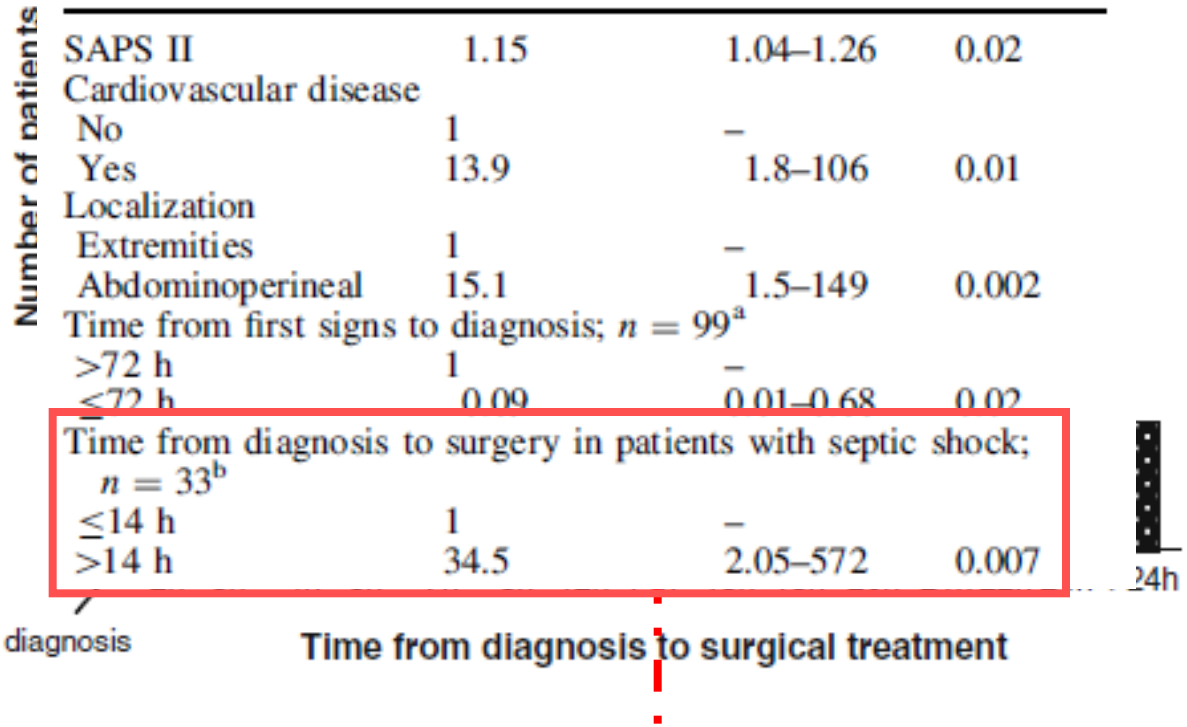
2009

33 patients avec fasciites en choc septique

6

Table 4 Results of multivariate analysis of hospital mortality in patients with severe NSTI

Variables	Adjusted OR	95% CI	*P* value
SAPS II	1.15	1.04–1.26	0.02
Cardiovascular disease			
No	1	–	
Yes	13.9	1.8–106	0.01
Localization			
Extremities	1	–	
Abdominoperineal	15.1	1.5–149	0.002
Time from first signs to diagnosis; $n = 99$[a]			
>72 h	1	–	
≤72 h	0.09	0.01–0.68	0.02
Time from diagnosis to surgery in patients with septic shock; $n = 33$[b]			
≤14 h	1	–	
>14 h	34.5	2.05–572	0.007



Conclusion et messages importants (et simples) dans le choc septique

- Faire le diagnostic d'infection rapidement
  - Évaluer la gravité avec le quickSOFA
- Administrer des ATB aussi vite que possible

- Documenter l'infection juste avant les ATBs sans perdre de temps

- Appeler le chirurgien et le convaincre

- Ne pas se tromper de cible microbiologique
  - Associations (…à Aminosides)
  - First dose supremacy
  - Pas de délai 2nde dose
- Tenir compte de CMI
  - PK-PD simple