III^{ème} Cours d'Automne en Infectiologie

Les Pensières, Veyrier-du-Lac, 11-13 septembre 2017

Actualités dans les Infections des Voies Respiratoires : Pneumonies

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Quels Facteurs Prédictifs de BMR pour les PAC et les HCAP ?

- Tous pts hospitalisés CAP ou HCAP
- Rétrospective jan 2010 Dec 2011
- Taux de résistance aux anti infectieux
- Analyse multivariée
- 521 pts : 50,5 CAP et 49,5 HCAP
- BMR chez 20 pts (3,8%)
  - CAP : 1,9%
  - HCAP : 5,9%

- BMR non associé à :
  - Facteurs de risque HCAP :
    - OR 1,95; [95%CI], 0,66-5,80, P = 0,23
  - Hémodialyse, perfusions à domicile, HAD, hospitalisation ≥ 48 h (90j)
- Facteurs indépendants de BMR :
  - Colonisation/infection P. aerugionosa :
    - OR 7,43; 95% CI, 2,24 - 24,61; *P* < 0,001
  - ABT < 90 j :
    - OR 2,90; 95% CI, 1,13 - 7,45; *P* =0,027
  - Mutation d'un long séjour :
    - OR 4,19; 95% CI, 1,55 - 11,31; *P* = 0,005
  - Durée d'hospitalisation (< 90 j ou 180 j)
    - *P* = 0,013 et *P* = 0,002, respectivement

Gross AE Antimicrob Agents Chemother 2014;9:5262-5268 doi:10.1128/AAC.02582-14

Association Between Hospitalization With CAP Laboratory-Confirmed Influenza Pneumonia and Prior Receipt of Influenza Vaccination

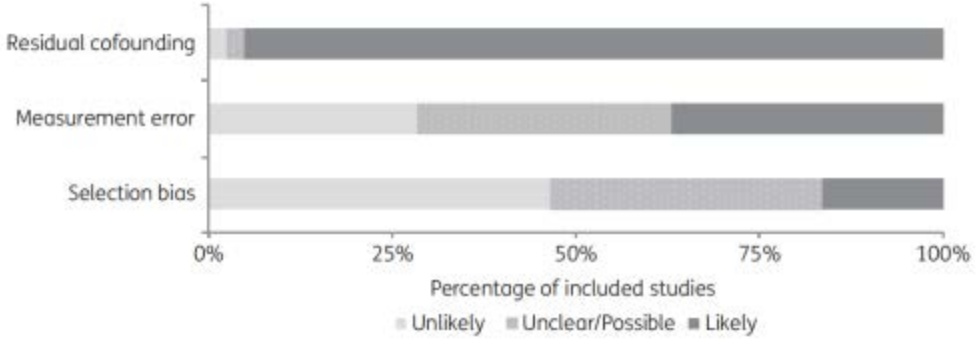
- Cas-contrôle, prospective, observationnelle, multicentrique, jan 2010-jun 2012, 4 centres US
  - Pts hospitalisés pour CAP
  - Data EPIC 6 mois pts avec grippe confirmée et vérification statut vaccinal
  - Exclusion pts hospitalisation récente, longs séjours et ID
  - Régression logistique OR
  - Comparaison taux de vaccination chez les pts influenza + et – hospitalisés pur CAP
  - EV = (1-OR ajusté) x 100%
- 2767 pts CAP; 162 (5,9%) grippe documentée

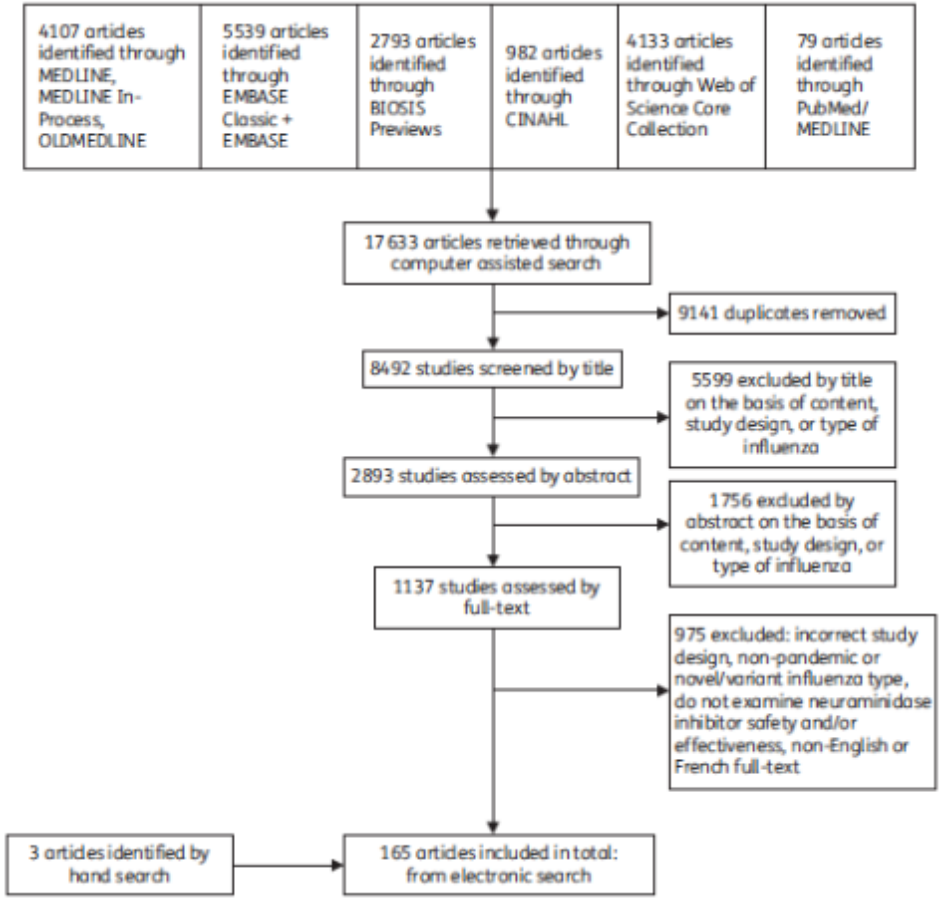
	Cases vaccinated No/Total No (%)	Controls not vaccinated No/Total No (%)	Adjusted Odds Ratio (95% CI)	Estimated Vaccine Effectiveness % (95% CI)
Overall estimate	28/162 (17)	766/2605 (29)	0,43 (0,28 to 0,68)	56,7 (31,9 to 72,5)
Included self-reported vaccination	56/190 (29)	1241/3270 (38)	0,52 (0,37 to 0,75)	47,5 (25,3 to 63,2)
Influenza season definition				
≥4% Positive tests per week	28/154 (18)	579/1563 (37)	0,41 (0,26 to 0,65)	59,1 (35,3 to 74,1)
≥5% Positive tests per week	28/153 (18)	523/1458 (36)	0,40 (0,25 to 0,63)	60,1 (36,8 to 74,8)
2010-2012 Season	28/156 (18)	721/2300 (31)	0,44 (0,28 to 0,69)	56,4 (31,2 to 72,3)
Hospitalization <7 d	23/136 (17)	624/2071 (30)	0,41 (0,25 to 0,68)	58,9 (32,3 to 75,0)
Hospitalization < 14 d	26/154 (17)	710/2379 (30)	0,43 (0,27 to 0,68)	57,3 (31,7 to 73,2)
Independent XRay confirmation	24/139 (17)	700/2389 (29)	0,43 (0,27 to 0,71)	56,6 (29,2 to 73,4)
Controls positive for other viruses	28/162 (17)	368/1196 (31)	0,37 (0,23 to 0,61)	62,8 (39,5 to 77,1)
Controls negative for all viruses	28/162 (17)	398/1409 (28)	0,46 (0,29 to 0,74)	53,8 (25,5 to 71,4)
Excluded pts with antiviral use	27/155 (17)	750/2546 (29)	0,44 (0,28 to 0,70)	56,2 (30,4 to 72,4)
Propensity score–adjusted analysis	28/162 (17)	766/2605 (29)	0,45 (0,29 to 0,72)	54,9 (28,5 to 71,5)

Grijalva CG JAMA 2015;314(14):1488-1497. doi:10.1001/jama.2015.12160

Safety and Effectiveness of Neuraminidase Inhibitors in Situations of Pandemic and/or Novel/Variant Influenza: a Systematic Review of the Literature, 2009–15

- 165 études
- 95% observationnelles
- Faible qualité méthodologique
  - Absence d'ajustement pour les variables confondantes
  - Manque de puissance
- Critères d'évaluation :
  - Mortalité, pneumonie, hospitalisation, transmission secondaire, gravité (admission rea ou décès),
  - durée de la fièvre, durée de la maladie,
  - Délai de mise sous tt par INA





Boikos C J Antimicrob Chemother 2017; 72: 1556–1573 doi:10.1093/jac/dkx013

Safety and Effectiveness of Neuraminidase Inhibitors in Situations of Pandemic and/or Novel/Variant Influenza: a Systematic Review of the Literature, 2009–15

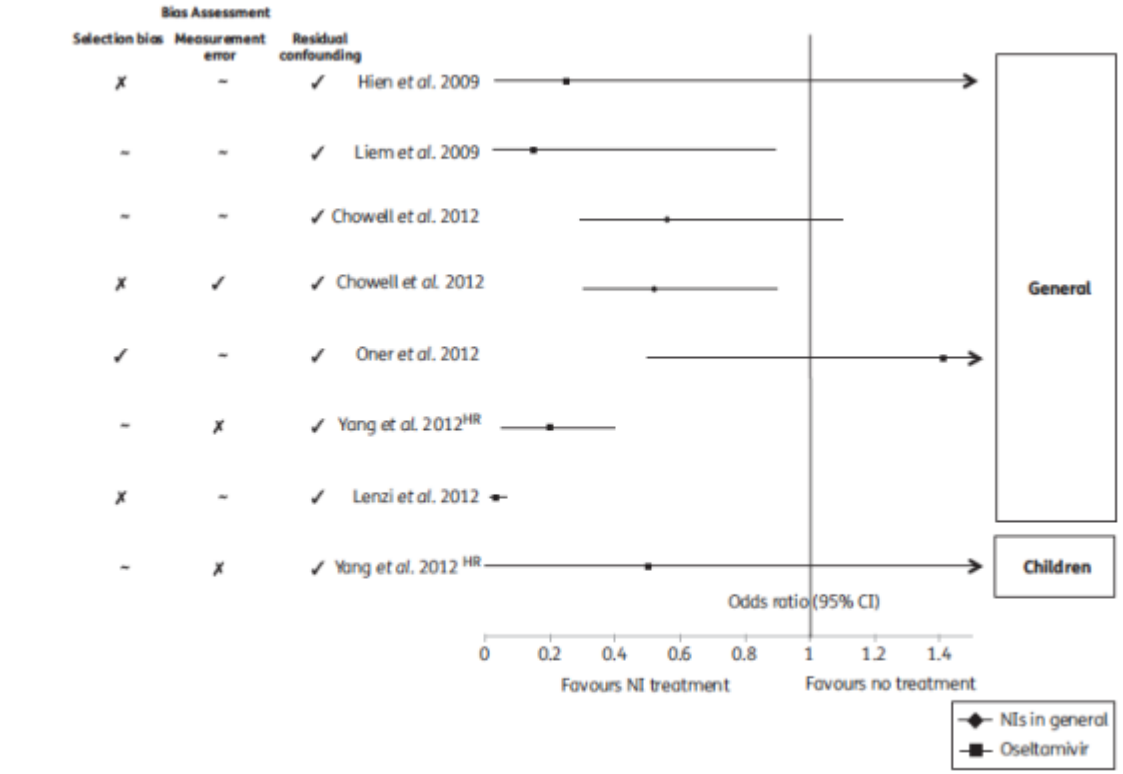


Figure 4. Odds or hazard of death comparing NI treatment to no treatment in the context of pandemic or novel/variant influenza. Unless otherwise noted, effect measures presented represent ORs. All estimates are adjusted [for at least 1 covariate (RCTs were also evaluated but none reported EMs of interest)]. GRADE Bias assessment scores are provided for each study.

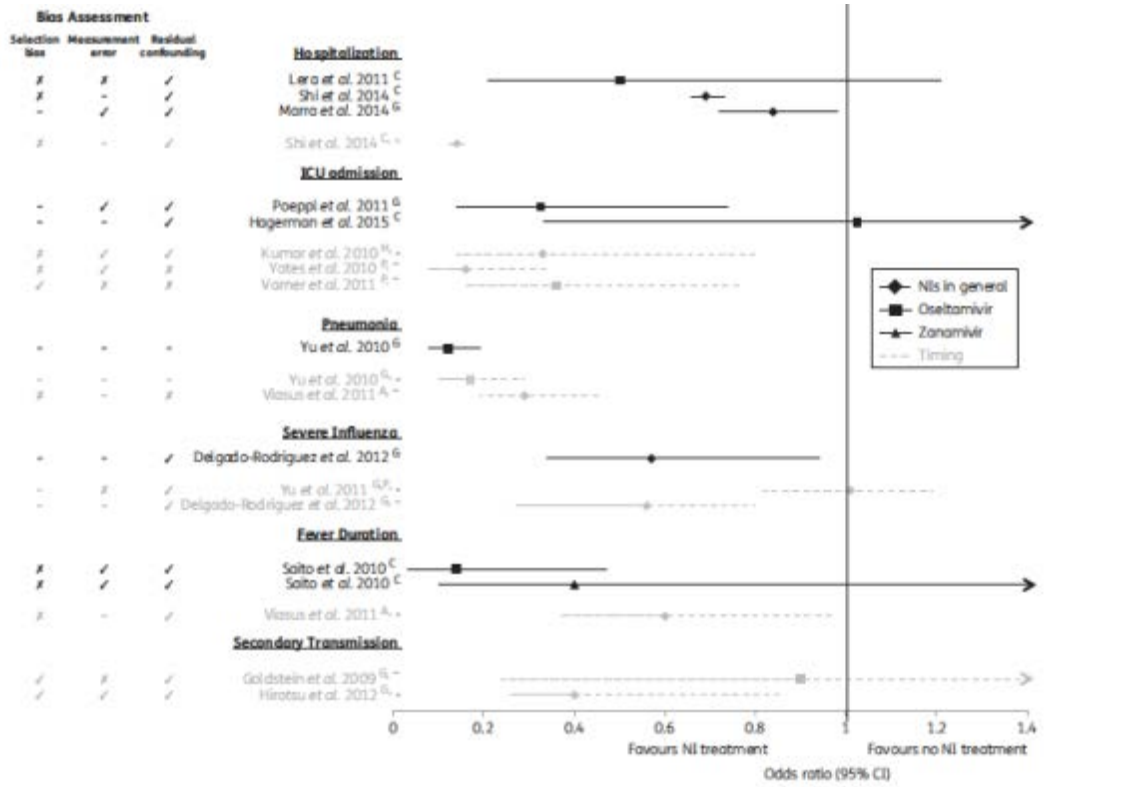


Figure 5. Odds of the outcome of interest comparing NI treatment with no treatment (black); odds of outcome of interest comparing NI administration within 48 h of symptom onset to > 48 h of symptom onset (grey). All outcomes are adjusted for at least 1 covariate or are RCTs. All EMs are ORs. GRADE Bias assessment scores are provided for each study: [A], adults; [G], general; [H], high risk; [P], pregnant women; [C], children; [E], elderly; [*], compared with NI administration >48 h; [°], compared with no NI treatment; ~, unclear comparator (either >48 h or no treatment).

Boikos C J Antimicrob Chemother 2017; 72: 1556–1573 doi:10.1093/jac/dkx013

Safety and Effectiveness of Neuraminidase Inhibitors in Situations of Pandemic and/or Novel/Variant Influenza: a Systematic Review of the Literature, 2009–15

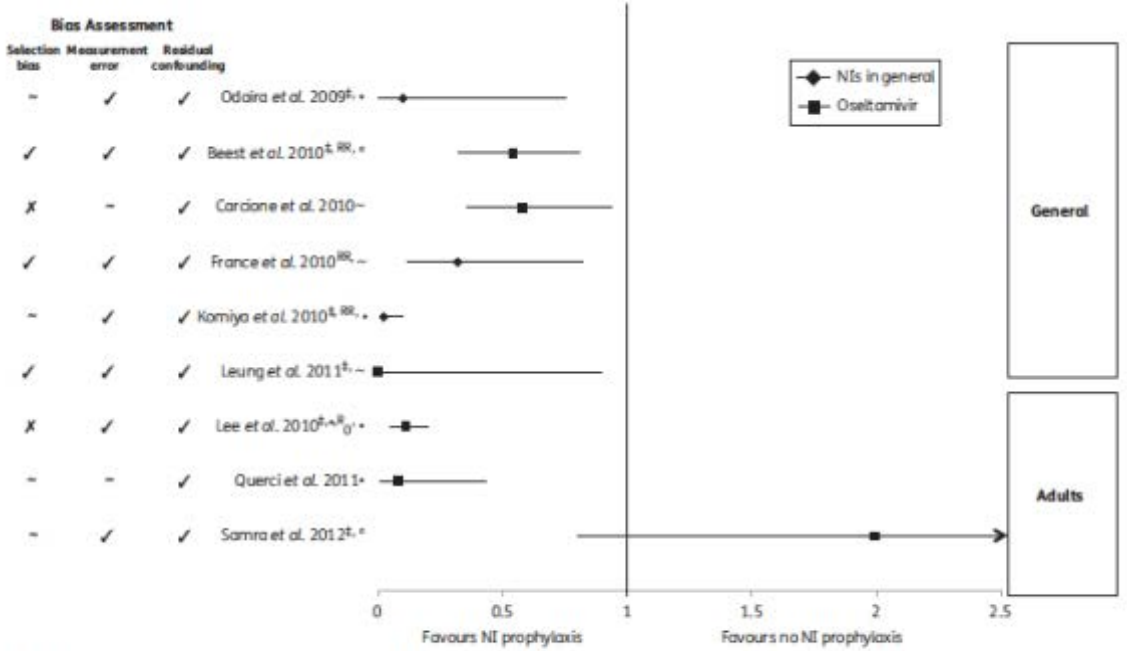


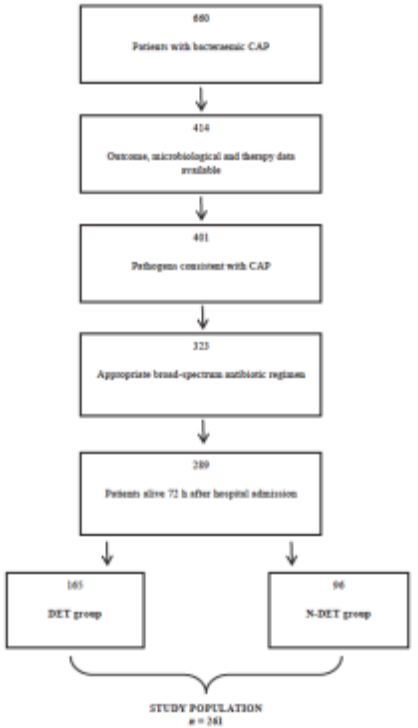
Figure 6. Odds (or risk) of influenza infection comparing NI prophylaxis to no prophylaxis; unless otherwise noted effect measures presented represent ORs. GRADE Bias assessment scores are provided for each study. ‡, unadjusted; *, 95% credible interval; RR, risk ratio; R_0, reproductive number; ^, post-exposure prophylaxis; °, pre-exposure prophylaxis; ~, timing of prophylaxis relative to exposure unclear.

- Études en population générale, avec ajustements pour les estimations, les INA apparaissent :
- Mortalité : efficacité probable, en particulier si administration < 48 h
- Pneumonie : Probablement efficaces réduction des pneumonies
- Réduction transmission secondaire : efficace en pxie
- Sécurité d'utilisation : en population générale et chez la femme enceinte et enfants : données limitées. Peu de données chez les sujets à risque élevé.

Boikos C J Antimicrob Chemother 2017; 72: 1556–1573 doi:10.1093/jac/dkx013

De-Escalation Therapy Among Bacteraemic Patients with CAP

- Analyse secondaire database PAC, 600 PAC, 35 pays (2001-2013)
- Désescalade :
  - Substitution ABT appropriée spectre étroit vs ABT appropriée initiale large spectre
  - < 7 j après admission
  - Sur documentation microbiologique
- Critère principal : mortalité 30j
- 261 pts PC + bactériémie inclus
- Desescalade : 165 pts (63,2%)



30 day mortality : multivariate analysis			
	RR	95% CI	P
Model intercept	0,05	0,02 – 0,12	<0,01
De-escalation	0,78	0,47 – 1,27	0,32
PSI class IV – V	1,01	1,01 – 1,02	<0,01
Macrolide therapy	1,18	0,71 – 1,95	0,53
Need for ICU	2,07	1,17 – 3,68	0,01
Severe sepsis	1,02	0,59 – 1,75	0,94

Clinical failure : multivariate analysis			
	RR	95% CI	P
Model intercept	0.08	0.04 – 0.16	<0.01
De-escalation	0.89	0.63 – 1.27	0.54
PSI class IV – V	1.01	1.00 – 1.02	0.05
Macrolide therapy	0.97	0.66 – 1.43	0.89
Need for ICU	4.08	2.39 – 6.97	<0.01
Severe sepsis	1.70	0.98 – 2.96	0.06

Carugati M Clin Microbiol Infect 2015; 21: 936.e11–936.e18 http://dx.doi.org/10.1016/j.cmi.2015.06.015

De-Escalation versus Continuation of Empirical Antimicrobial Therapy in CAP

- Database 82 hôpitaux académiques, japon
- Etude juillet 2010-mars 2013
- Mortalité toutes causes J15
- 35 858 pts identifiés, 6 588 exclus
  - Desescalade : 1258 (11,3%)
  - Poursuite : 8973 (80,4%)
  - Escalade : 928 (8,3%)

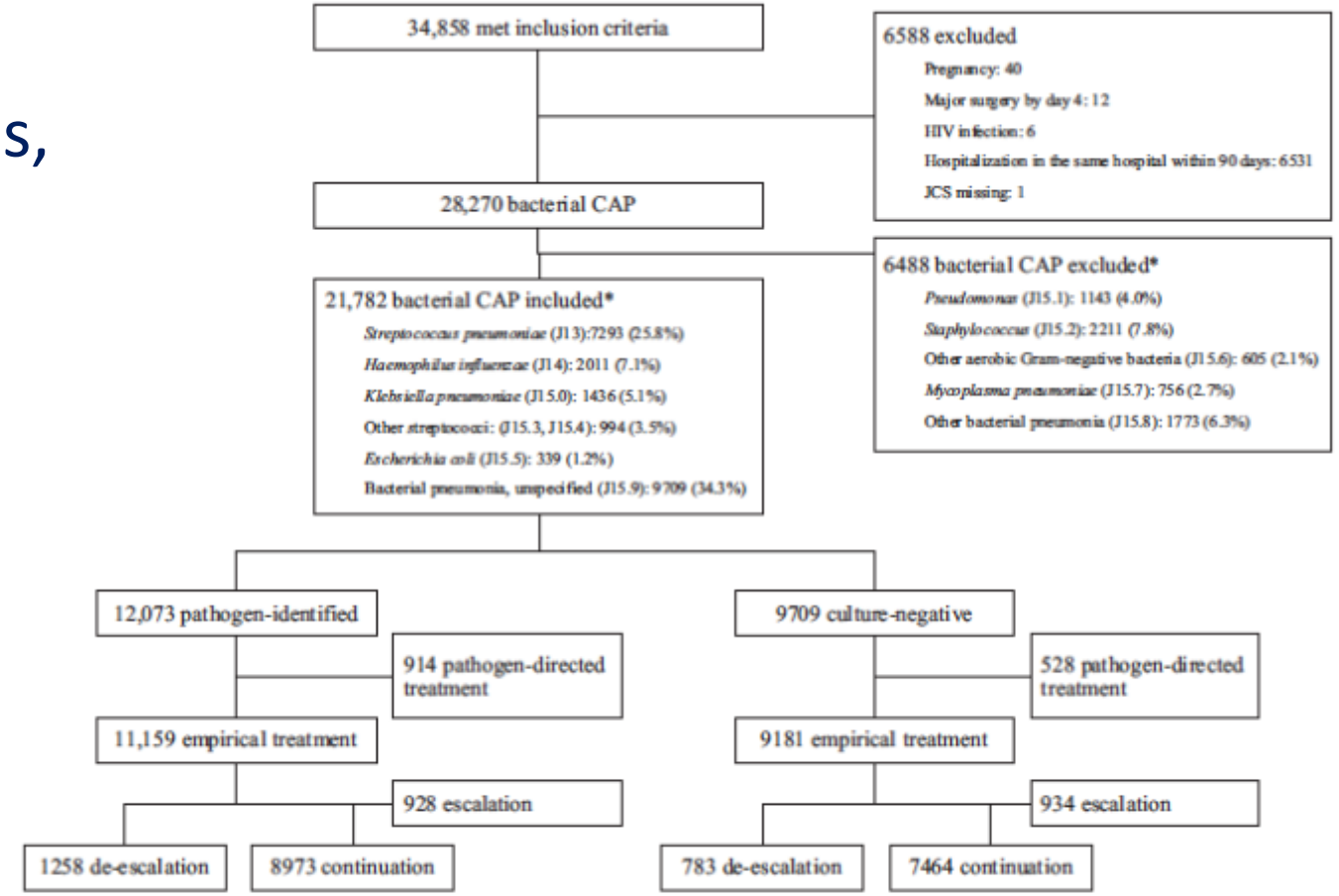


Figure 1 **Patient selection.** Abbreviations: CAP, community-acquired pneumonia; HIV, human immunodeficiency virus; JCS, Japan Coma Scale. * The causative pathogen is followed by the corresponding diagnosis codes according to the International Classification of Diseases, Tenth Revision.

Yamane H Journal of Infection (2016) 73, 314e325 http://dx.doi.org/10.1016/j.jinf.2016.07.001

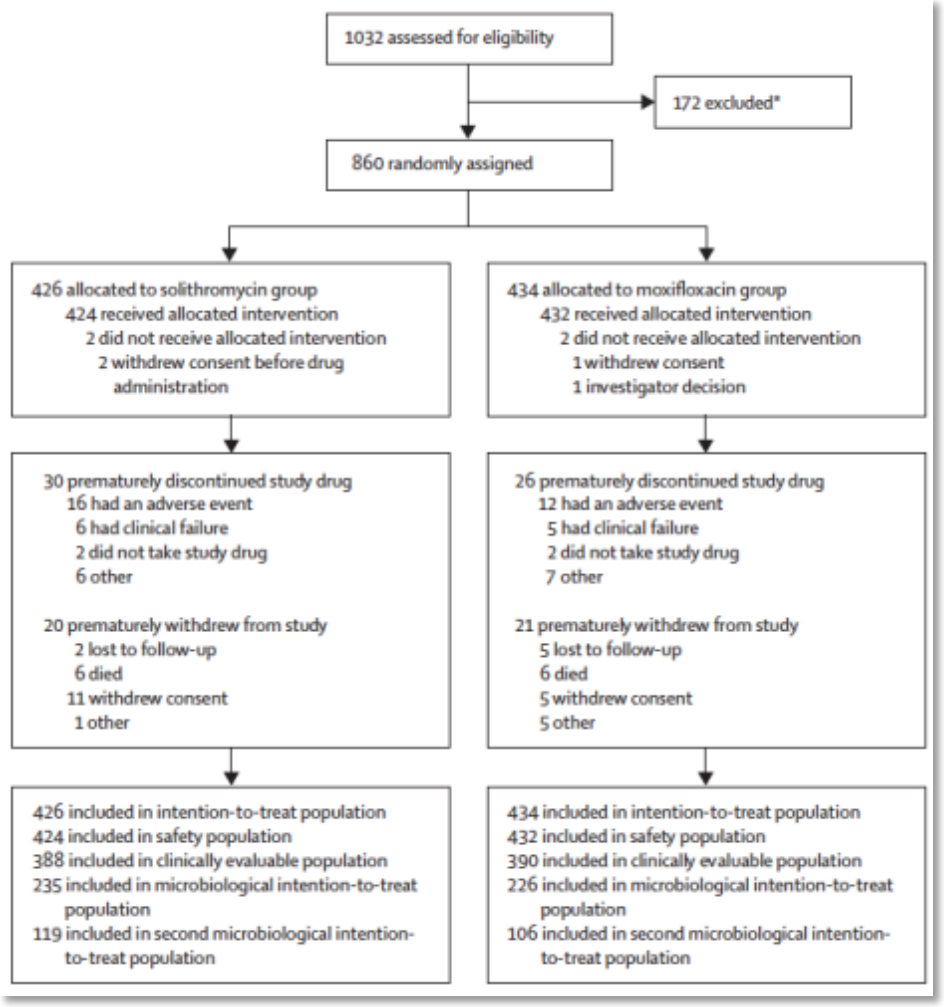
De-Escalation versus Continuation of Empirical Antimicrobial Therapy in CAP

- Database 82 hôpitaux académiques, japon
- Etude juillet 2010-mars 2013
- Mortalité toutes causes J15
- Modifications 1-4 j après admission, PAC documentées
- 35 858 pts identifiés, 6 588 exclus
  - Désescalade : 1258 (11,3%)
  - Poursuite : 8973 (80,4%)
  - Escalade : 928 (8,3%)

- CAP documentée :
  - Mortalité J15 :
    - Désescalade : 5,3%
    - Poursuite : 4,3%
    - Différence : 1,0% [95% CI, 1,7% - 3,7 %]
  - Mortalité intra hospitalière :
    - Désescalade : 8,0%
    - Poursuite : 8,8%
    - Différence : 0,8% [95% CI, 4,3% - 2,7%].
- CAP non documentée :
  - Mortalité J15 : Désescalade non inférieure à poursuite
  - Mortalité intra hospitalière : non-infériorité non démontrée

Yamane H Journal of Infection (2016) 73, 314e325 http://dx.doi.org/10.1016/j.jinf.2016.07.001

Efficacy and Safety of Oral Solithromycin *vs* Oral Moxifloxacin for Treatment of CAP



	Solithromycin group (n=426)	Moxifloxacin group (n=434)
(Continued from previous column)		
PORT score*		
Mean (SD)	71·7 (13·4)	71·2 (13·3)
Median (min–max)	71·0 (48–108)	69·0 (51–112)
PORT risk class*		
I	1 (<1%)	0
II	209 (49%)	223 (51%)
III	168 (39%)	173 (40%)
IV	48 (11%)	38 (9%)
CURB-65 score†		
0	135/416 (32%)	138/429 (32%)
1	175/416 (42%)	166/429 (39%)
2	97/416 (23%)	110/429 (26%)
3	8/416 (2%)	14/429 (3%)
4	1/416 (<1%)	1/429 (<1%)
Met SIRS criteria‡	231 (54%)	262/429 (60%)

Barrera CM. Lancet Infect Dis 2016;16:421-30

Efficacy and Safety of Oral Solithromycin *vs* Oral Moxifloxacin for Treatment of CAP

	Solithromycin group	Moxifloxacin group	Difference (95% CI)
Early clinical response			
Intention-to-treat population	333/426 (78·2%)	338/434 (77·9%)	0·29% (–5·5 to 6·1)
PORT II score	168/213 (78·9%)	175/217 (80·6%)	–1·77% (–9·8 to 6·3)
PORT III or IV score	165/213 (77·5%)	163/217 (75·1)	2·35% (–6·2 to 10·9)
Age <65 years	211/271 (77·9%)	240/297 (80·8%)	–2·95% (–10·0 to 4·1)
Age 65–74 years	70/93 (75·3%)	54/74 (73·0%)	2·30% (–12·3 to 16·9)
Age ≥75 years	52/62 (83·9%)	44/63 (69·8%)	14·03% (–2·1 to 30·2)
History of COPD or asthma	44/62 (71·0%)	43/64 (67·2%)	3·78% (–13·9 to 21·5)
Clinically evaluable population	326/403 (80·9%)	330/407 (81·1%)	–0·19% (–5·8 to 5·5)
Short-term follow-up			
Intention-to-treat population	360/426 (84·5%)	376/434 (86·6%)	–2·13% (–7·1 to 2·8)
PORT II score	183/213 (85·9%)	193/217 (88·9%)	–3·02% (–9·8 to 3·2)
PORT III or IV score	177/213 (83·1%)	183/217 (84·3%)	–1·23% (–8·7 to 6·2)
Age <65 years	223/271 (82·3%)	258/297 (86·9%)	–4·58% (–10·9 to 1·7)
Age 65–74 years	84/93 (90·3%)	65/74 (87·8%)	2·48% (–8·3 to 13·3)
Age ≥75 years	53/62 (85·5%)	53/63 (84·1%)	1·36% (–12·8 to 15·5)
History of COPD or asthma	57/62 (91·9%)	55/64 (85·9%)	6·00% (–6·5 to 18·5)
Clinically evaluable population	342/388 (88·1%)	356/390 (91·3%)	–3·14% (–7·7 to 1·4)
History of COPD or asthma	55/59 (93·2%)	53/59 (89·8%)	3·39% (–8·3 to 15·1)

Data are n/N (%). COPD=chronic obstructive pulmonary disease. PORT=Pneumonia Outcomes Research Team.

***Table 3*: Early clinical response rates and success at short-term follow-up**

Barrera CM. Lancet Infect Dis 2016;16:421-30

Efficacy and Safety of Oral Solithromycin *vs* Oral Moxifloxacin for Treatment of CAP

	Early clinical response rate*		Short-term follow-up success rate†	
	Solithromycin group	Moxifloxacin group	Solithromycin group	Moxifloxacin group
Streptococcus pneumoniae	21/28 (75%)	30/37 (81%)	25/28 (89%)	31/37 (84%)
With bacteraemia	3/5 (60%)	7/10 (70%)	3/5 (60%)	6/10 (60%)
Macrolide-resistant	5/7 (71%)	5/5 (100%)	7/7 (100%)	5/5 (100%)
Staphylococcus aureus	9/14 (64%)	5/7 (71%)	10/14 (71%)	4/7 (57%)
Haemophilus influenzae	33/37 (89%)	21/26 (81%)	27/37 (73%)	21/26 (81%)
Moraxella catarrhalis	10/11 (91%)	4/4 (100%)	9/11 (82%)	3/4 (75%)
Klebsiella pneumoniae	4/5 (80%)	1/3 (33%)	4/5 (80%)	2/3 (67%)
With bacteraemia	1/1 (100%)	0/1	1/1 (100%)	1/1 (100%)
Legionella spp	4/7 (57%)	2/3 (67%)	6/7 (86%)	2/3 (67%)
Mycoplasma pneumoniae	17/18 (94%)	18/22 (82%)	16/18 (89%)	19/22 (86%)

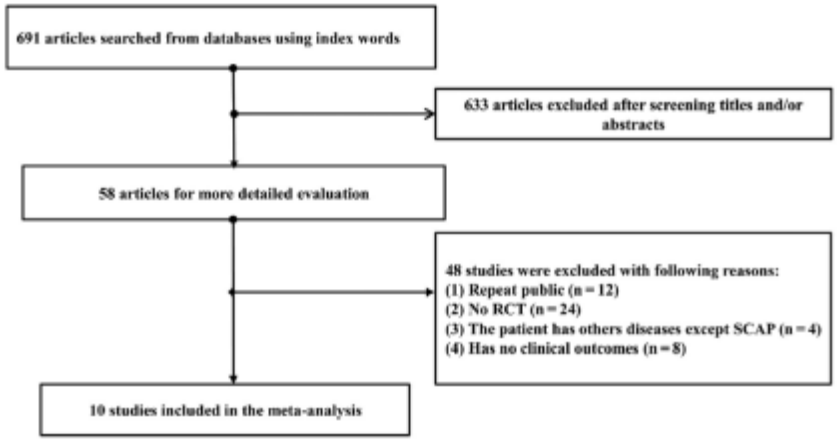
Data are n/N (%). *At day 4. †5–10 days after end of treatment.

***Table 4*: Early clinical response rates and success at short-term follow-up by key pathogen in the second microbiological intention-to-treat population (mITT-2)**

Critère Principal « Réponse clinique précoce »
solithromyine *vs* moxifloxacine : 333 (78,2%) vs 338 (77,9%) : différence 0,29, 95% CI – 5,5 à 6,1

Barrera CM. Lancet Infect Dis 2016;16:421-30

Efficacy of Corticosteroid Treatment for Severe CAP : A Meta-Analysis



In hospital mortality
RR 0,49 ; 95%CI : 0,29 to 0,85

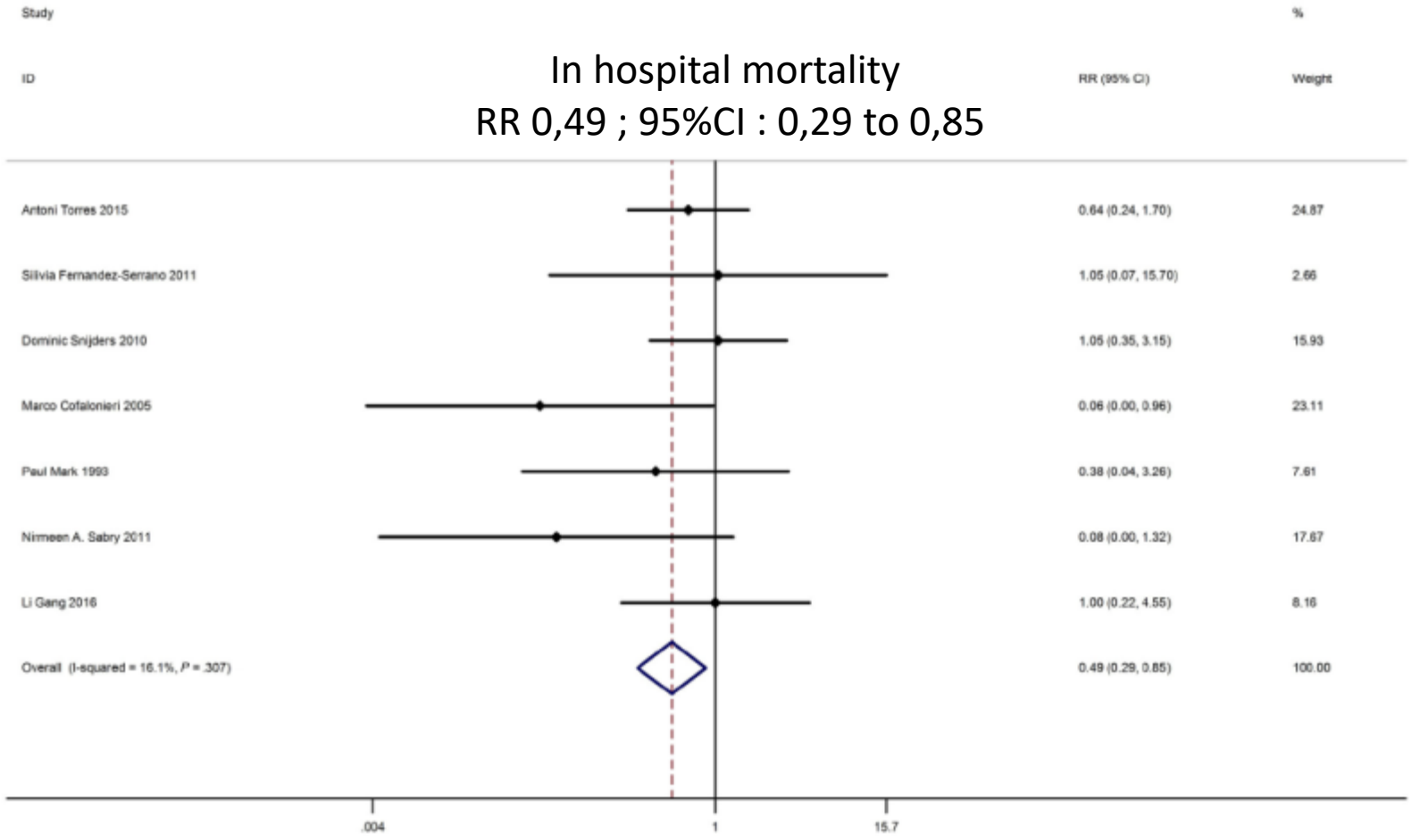


Fig. 2. Effect of corticosteroids vs placebo on in-hospital mortality for severe community-acquired pneumonia (CAP).

Wu WF American Journal of Emergency Medicine 2017 http://dx.doi.org/10.1016/j.ajem.2017.07.050

Efficacy of Corticosteroid Treatment for Severe CAP : A Meta-Analysis

Length of hospital stay
RR -4,21; 95%CI: -6,61 to -1,81

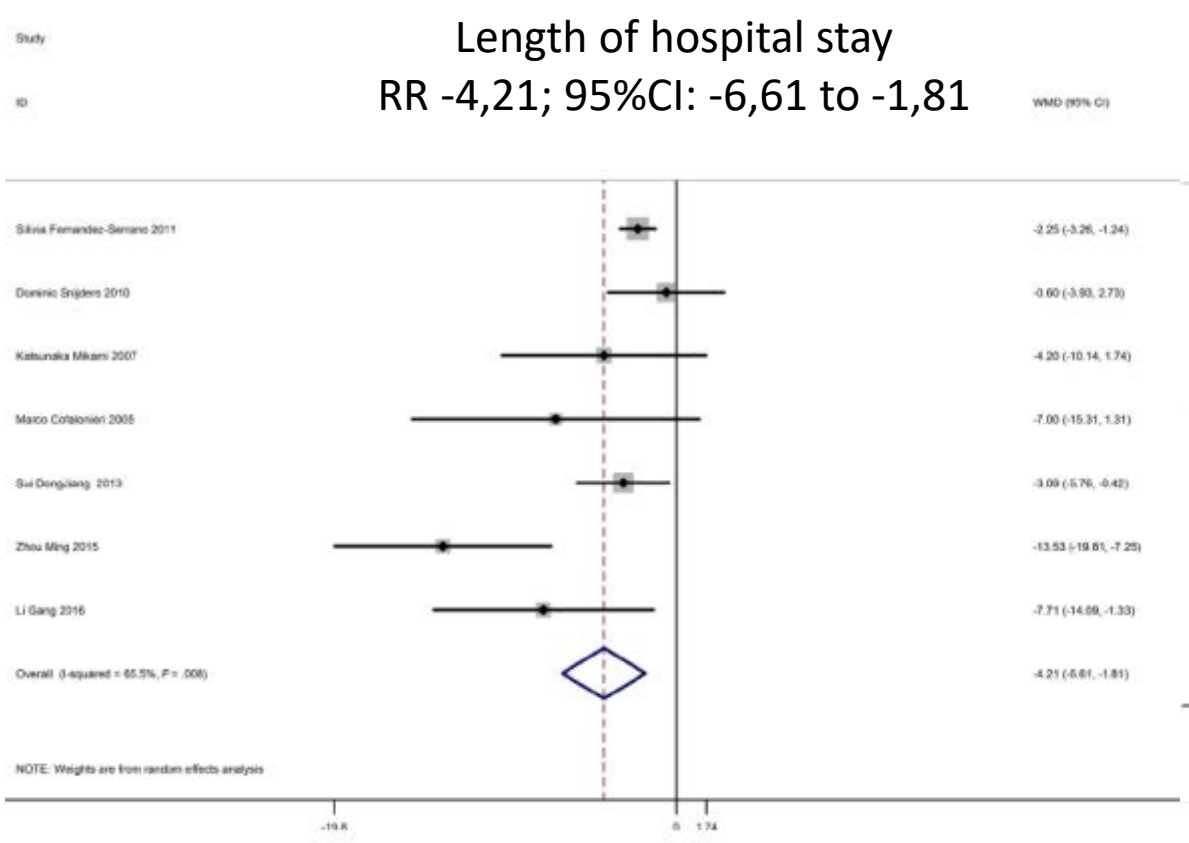


Fig. 4. Effect of corticosteroids vs placebo on length of hospital stay for severe community-acquired pneumonia (CAP).

Mechanical ventilation
RR -2,30; 95%CI: -6,09 to1,49

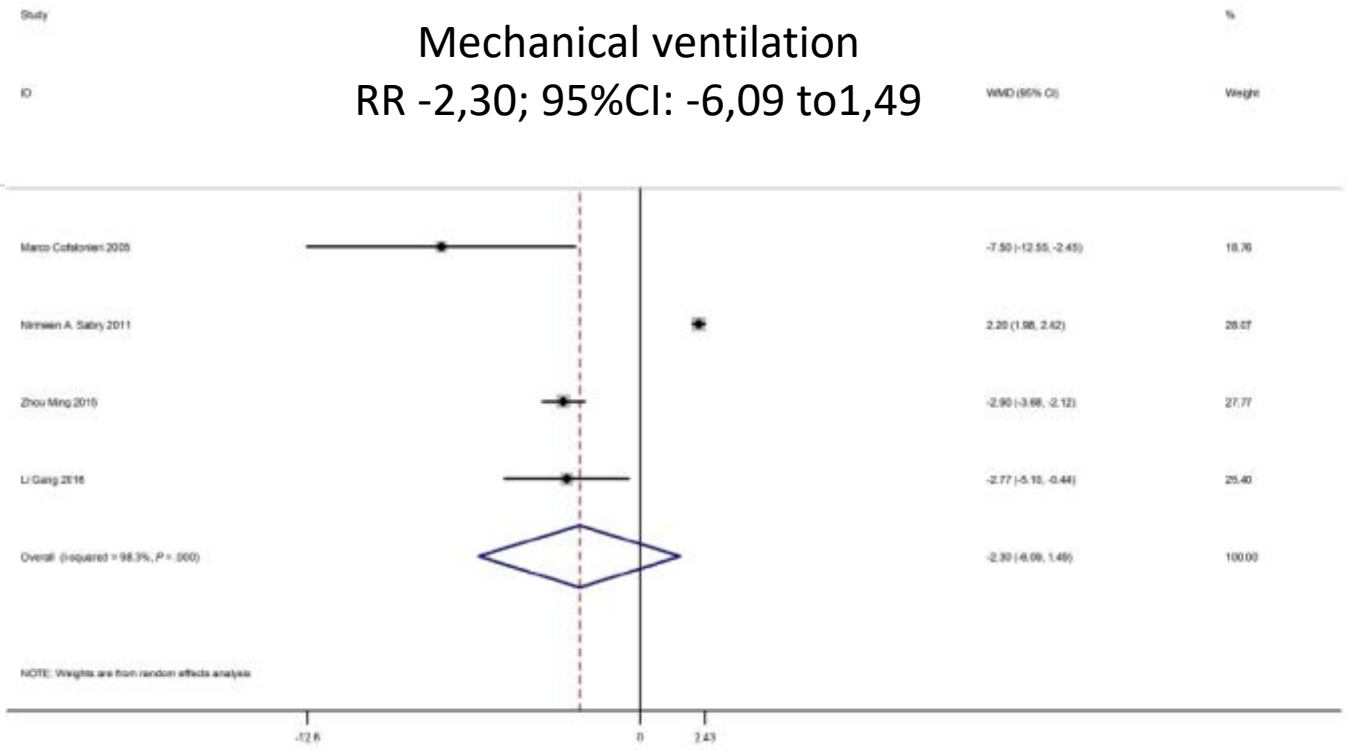


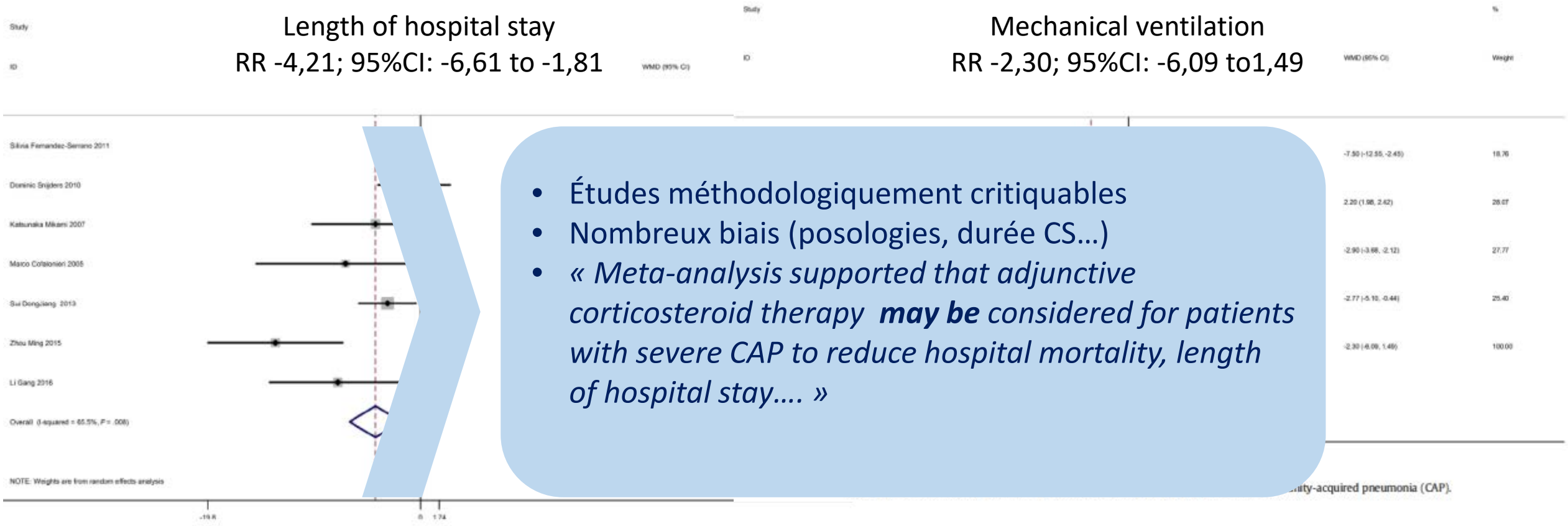
Fig. 5. Effect of corticosteroids vs placebo on mechanical ventilation time for severe community-acquired pneumonia (CAP).

Wu WF American Journal of Emergency Medicine 2017 http://dx.doi.org/10.1016/j.ajem.2017.07.050

Efficacy of Corticosteroid Treatment for Severe CAP : A Meta-Analysis

Length of hospital stay
RR -4,21; 95%CI: -6,61 to -1,81

Mechanical ventilation
RR -2,30; 95%CI: -6,09 to1,49



- Études méthodologiquement critiquables
- Nombreux biais (posologies, durée CS…)
- *« Meta-analysis supported that adjunctive corticosteroid therapy* ***may be*** *considered for patients with severe CAP to reduce hospital mortality, length of hospital stay…. »*

Fig. 4. Effect of corticosteroids vs placebo on length of hospital stay for severe community-acquired pneumonia (CAP).

Wu WF American Journal of Emergency Medicine 2017 http://dx.doi.org/10.1016/j.ajem.2017.07.050

Effect of Corticosteroids on Treatment Failure Among Hospitalized Patients With Severe CAP and High Inflammatory Response. A Randomized Clinical Trial

Torres A JAMA. 2015;313(7):677-686. doi:10.1001/jama.2015.88

CAP in Virologically Suppressed HIV-Infected Adult Patients A Matched Case-Control Study

- Étude cas-contrôle 2001-2016
  - Barcelone
  - Cas : 50 pts VIH+ ART, CD4 > 350/mm^3, CV indetectable
  - Contrôles : 100 pts VIH –
  - Appariement âge, sexe, comorbidités, même période
  - PAC à *S. pneumoniae*
- Cas :
  - Vaccination grippale : 14% vs 2%, P = 0,007
  - Vaccination pneumococcique : 10% vs 1%, P = 0,016
  - Co-infection VHB : 6% vs 0%, P = 0,36

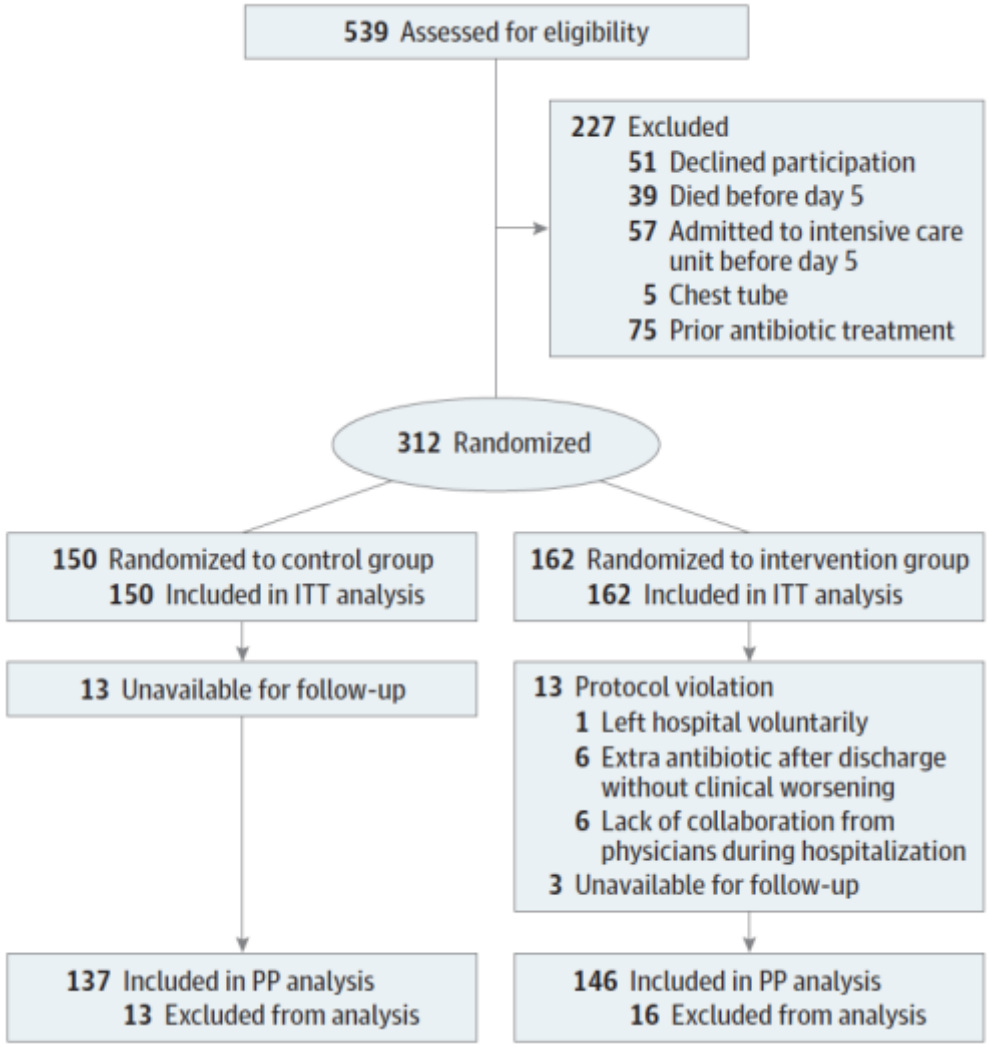
Clinical Outcomes			
Variables	Case Pts (HIV+) (n = 50)	Control Pts (HIV-) (n = 100)	P
ICU admission, No. (%)	9 (18)	27 (27)	.22
Mechanical ventilation, No. (%)	6 (12)	8 (8)	.43
LOS, median (IQR), d	7.0 (5.0; 11.0)	7.0 (4.0; 11.0)	.76
30-d mortality, No. (%)	0 (0)	0 (0)	.

PAC à *S. pneumoniae* chez les pts indetectable et avec CD4 > 350/mm^3
- Sévérité et pronostic comparable vs pts VIH –
- PEC = la même que pour la population générale

Cilloniz C Chest 2017; 152(2):295-303 http://dx.doi.org/10.1016/j.chest.2017.03.007

Duration of Antibiotic Therapy for CAP in the Era of Personalized Medicine. A Multicenter Randomized Clinical Trial

- Étude multicentrique, randomisée, non-infériorité
  - 4 hôpitaux universitaires, Espagne
  - Jan 2012 à aout 2013
  - 312 pts hospitalisés
  - But : validation durée de tt IDSA/ATS
- Randomisation j5
  - Gpe intervention :
    - Durée minimum de 5j
    - Arrêt à J5 si T < 37,8°C depuis 48h au moins et si signe clinique instabilité ≤ 1
  - Gpe contrôle :
    - Arrêt ABT à la discrétion du clinicien
- Critères évaluation :
  - Succès clinique J10 et J30,
  - Symptômes cliniques J5 et J10



Uranda AJS JAMA Intern Med. 2016;176(9):1257-1265. doi:10.1001/jamainternmed.2016.3633

Duration of Antibiotic Therapy for CAP in the Era of Personalized Medicine. A Multicenter Randomized Clinical Trial

Results for the primary study outcomes			
Outcome	Control group	Intervention group	P
Intent-to-Treat Analysis (n)	150	162	
Clinical success, n (%)			
At day 10	71 (48.6)	90 (56.3)	.18
At day 30	132 (88.6)	147 (91.9)	.33
CAP symptom questionnaire score, mean (SD)			
At day 5	24.7 (11.4)	27.2 (12.5)	.10
At day 10	18.6 (9.0)	17.9 (7.6)	.69
Per-Protocol Analysis			
Total No. of participants	137	146	
Clinical success, n (%)			
At day 10	67 (50.4)	86 (59.7)	.12
At day 30	126 (92.7)	136 (94.4)	.54
CAP symptom questionnaire score, mean (SD)			
At day 5	24.3 (11.4)	26.6 (12.1)	.16
At day 10	18.1 (8.5)	17.6 (7.4)	.81

Table 3. Clinical Success Rates at Days 10 and 30 Among Different Severity Groups Defined by PSI Class[a]

	No. (%) of Participants		
PSI Class	Control Group	Intervention Group	*P* Value
Clinical Success at Day 10			
PSI classes I-III			
Intent to treat	41/86 (47.7)	58/101 (57.4)	.18
Per protocol	39/80 (48.8)	58/94 (61.7)	.09
PSI classes IV-V			
Intent to treat	30/60 (50)	32/59 (54.2)	.64
Per protocol	28/53 (52.8)	28/50 (56)	.75
Clinical Success at Day 30			
PSI classes I-III			
Intent to treat	83/88 (94.3)	93/102 (91.2)	.41
Per protocol	80/82 (97.6)	89/95 (93.7)	.29
PSI classes IV-V			
Intent to treat	49/61 (80.3)	54/58 (93.1)	.04
Per protocol	46/54 (85.2)	47/49 (95.9)	.10

Uranda AJS JAMA Intern Med. 2016;176(9):1257-1265. doi:10.1001/jamainternmed.2016.3633

Duration of Antibiotic Therapy for CAP in the Era of Personalized Medicine. A Multicenter Randomized Clinical Trial

Results for the primary study outcomes			
Outcome	Control group	Intervention group	P
Intent-to-Treat Analysis (n)	150	162	
Clinical success, n (%)			
At day 10	71 (48.6)	90 (56.3)	.18
		147 (91.9)	.33
		(12.5)	.10
		9 (7.6)	.69
		146	
		(59.7)	.12
		(94.4)	.54
		26.6 (12.1)	.16
At day 10	18.1 (8.5)	17.6 (7.4)	.81

Table 3. Clinical Success Rates at Days 10 and 30 Among Different Severity Grou ...y PSI Class

PSI Class	No. (%) of Participants		P Value
	Control Group	Intervention Group	
Clinical Success at Day 10			
PSI classes I-III			
Intent to treat	41/86 (47.7)	58/101 (57.4)	.18
Per protocol	39/80 (48.8)	58/94 (61.7)	.09
PSI classes IV-V			
Intent to treat	30/60 (50)	32/59 (54.2)	.64
Per protocol	28/53 (52.8)	28/50 (56)	.75
Clinical Success at Day 30			
PSI classes I-III			
Intent to treat	83/88 (94.3)	93/102 (91.2)	.41
Per protocol	80/82 (97.6)	89/95 (93.7)	.29
PSI classes IV-V			
Intent to treat	49/61 (80.3)	54/58 (93.1)	.04
Per protocol	46/54 (85.2)	47/49 (95.9)	.10

« IDSA/ATS recommendations for shorter duration of antibiotic treatment based on clinical stability criteria can be safely implemented in hospitalized patients with CAP, leading to a significant reduction in treatment duration. »

Uranda AJS JAMA Intern Med. 2016;176(9):1257-1265. doi:10.1001/jamainternmed.2016.3633

Duration of Antibiotic Therapy for CAP in the Era of Personalized Medicine. A Multicenter Randomized Clinical Trial

Table 4. Results for Secondary Study Outcomes in the Per-Protocol Analysis[a]

Outcome	Control Group (n = 137)	Intervention Group (n = 146)	*P* Value
Time, median (IQR), d			
Taking antibiotics	10 (10-11)	5 (5-6.5)	<.001
Not taking antibiotics	21 (10-27)	25 (5-32)	.001
Taking intravenous antibiotics	2 (1-4)	3 (2-4)	.22
Until clinical improvement	12 (8-18)	12 (7-15)	.41
Return to normal activity	18 (9-25)	15 (10-21)	.36
Radiographic resolution at day 30	93 (73.2)	112 (81.2)	.12
In-hospital mortality	2 (1.5)	3 (2.1)	>.99
30-d Mortality	3 (2.2)	3 (2.1)	>.99
Recurrence by day 30	6 (4.4)	4 (2.8)	.53
Readmission by day 30	9 (6.6)	2 (1.4)	.02
In-hospital complications			
Pleural effusion	10 (7.3)	5 (3.4)	.15
Treatment failure[b]	2 (1.5)	3 (2.1)	>.99
Respiratory failure[c]	26 (19.0)	31 (21.2)	.64
Severe sepsis[d]	7 (5.1)	8 (5.5)	.89
Renal failure[e]	5 (3.7)	6 (4.1)	.85
ICU admission	2 (1.5)	1 (0.7)	.61
Use of invasive mechanical ventilation	2 (1.5)	1 (0.7)	.61
Use of noninvasive mechanical ventilation	3 (2.2)	2 (1.4)	.67
Need for vasopressors	2 (1.5)	3 (2.1)	>.99
Antibiotic adverse effects by day 30	18 (13.1)	17 (11.7)	.72
Time with antibiotic adverse effects, mean (SD), d	3 (2.8)	1.7 (2.1)	.24
Length of hospital stay, mean (SD), d	5.5 (2.3)	5.7 (2.8)	.69

Uranda AJS JAMA Intern Med. 2016;176(9):1257-1265. doi:10.1001/jamainternmed.2016.3633

Pneumonia Caused by Methicillin-Resistant *Staphylococcus aureus*: Does Vancomycin Heteroresistance Matter?

- Étude de cohorte rétrospective, comparative,2005-201
- Issue pneumonie SARM hVISA *vs* VSSA
- 87 pts, 29 hVISA *vs* 58 VSSA
- Critères d'évaluation :
  - Durée de la bactériémie associée,
  - Température,
  - Leucocytose,
  - Durée, d'hospitalisation, ICU, VM,
  - Échec vancomycine,
  - Mortalité liée au SARM

Multivariable logistic regression for risk factors associated with inpatient mortality

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
hVISA phenotype	2.55 (0.99–6.59)	3.95 (1.18–13.21)
PVL positive	1.39 (1.45–11.08)	6.63 (1.79–24.64)
ID consult	0.37 (0.15–0.94)	0.35 (0.11–1.13)
SOFA score	1.36 (1.14–1.65)	1.36 (1.08–1.70)

hVISA, heterogeneous vancomycin-intermediate S. aureus; PVL, Panton-Valentine leukocidin; ID consult, infectious disease consultation; SOFA, sequential organ failure assessment

Claeys KC Antimicrob Agents Chemother 60:1708 –1716. doi:10.1128/AAC.02388-15.

In Vivo Efficacy of Ceftolozane Against *P. aeruginosa* in a Rabbit Experimental Model of Pneumonia: Comparison with Ceftazidime, Piperacillin/Tazobactam and Imipenem

Pulmonary bacterial load and spleen and blood culture results for the different treatment groups and controls							
	Controls (n = 10)	Ceftolozane 1 g t.i.d. (n = 7)	Ceftolozane 2 g t.i.d. (n = 7)	Ceftazidime 2 g t.i.d. (n = 6)	TZP 4 g q.i.d. (n = 6)	Imipenem 1 g t.i.d. (n = 6)	P-value[a]
Pulmonary bacterial load (log10 CFU/g)[b]	6.3 ± 0.9	4.9 ± 0.3	3.6 ± 0.3	4.8 ± 0.2	5.5 ± 0.8	3.9 ± 0.3	10^{-6}
Spleen cultures positive/negative[c]	8/2	4/3	2/5	3/3	5/1	2/4	N/S
Blood cultures positive/negative[c]	2/8	0/7	0/7	1/5	1/5	0/6	N/S

a Quantitative variables were compared by one-way analysis of variance (ANOVA); proportions (percentages) were compared using Fisher's exact test.

b **Bacterial loads were significantly different for all antibiotics compared with the controls, except TZP**. Post-hoc Bonferroni test revealed no difference between the 1 g ceftolozane group and the ceftazidime, TZP or imipenem groups, whereas the **2 g ceftolozane group had a significantly lower bacterial load than both ceftazidime ($P < 0.05$) and TZP ($P < 0.01$) groups**.

c No difference was observed for spleen or blood cultures between the groups.

The MICs for *P. aeruginosa* PAO1 were 0.5 mg/L for ceftolozane, 1 mg/L for ceftazidime, 4 mg/L for TZP and 0.5 mg/L for imipenem.

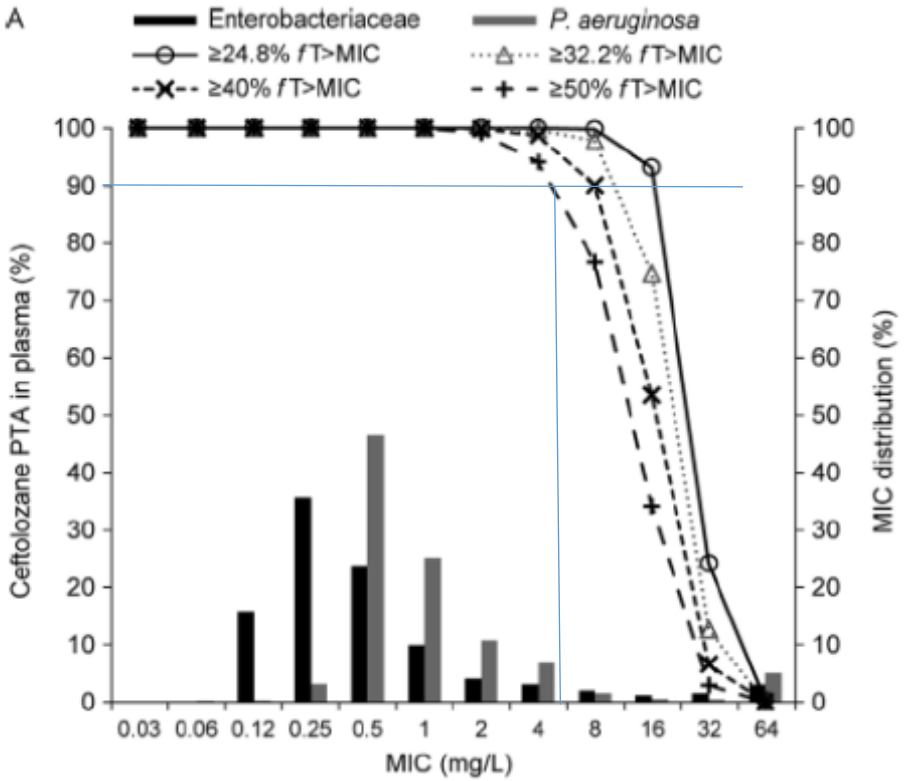
Bretonnière C International Journal of Antimicrobial Agents 44 (2014) 218–221 http://dx.doi.org/10.1016/j.ijantimicag.2014.04.017

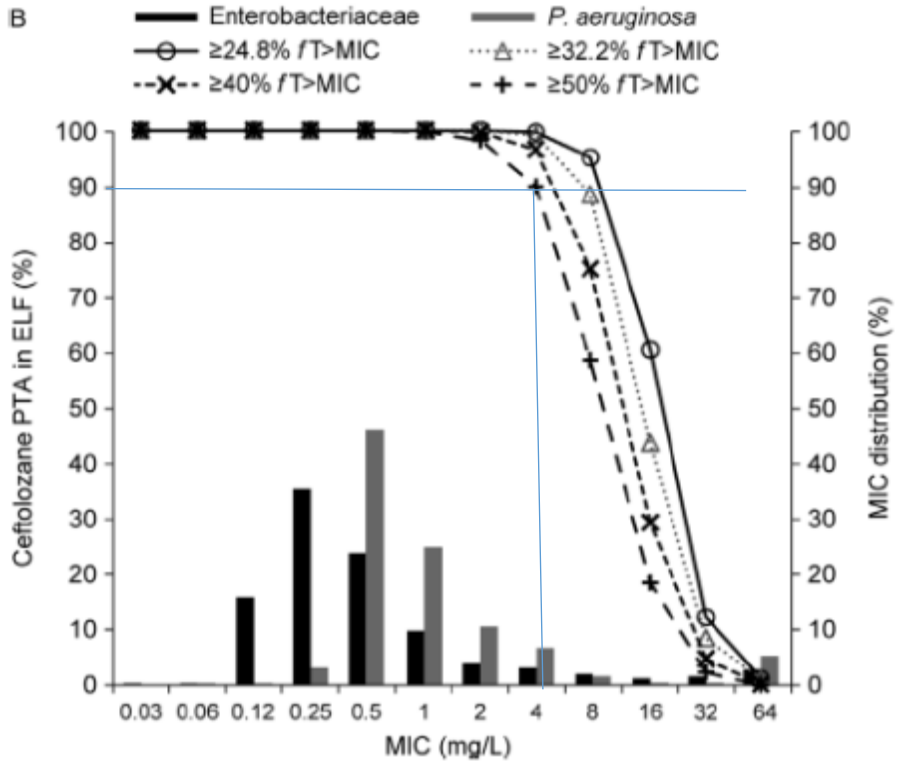
Ceftolozane/Tazobactam PK/PD-Derived Dose Justification for Phase 3 Studies in Patients With Nosocomial Pneumonia

- AMM = cUTIs et cIAIs (1,5 g/8h)
- Simulation de Monte Carlo pour déterminer les posologies de C/T pour les PAS
  - Probabilité <90% d'atteindre la cible
  - Tenant compte des CMIs des pathogènes impliqués dans les PAS
- Modèle PK film épithélial/plasma
- Mesure des concentrations P/T
  - Plasma et liquide de lavage broncho alvéolaire
  - Différents temps entre 0 et 8 h
  - 25 volontaires sains

Xiao AJ The Journal of Clinical Pharmacology 2016;56:56-66 DOI: 10.1002/jcph.566

Ceftolozane/Tazobactam PK/PD-Derived Dose Justification for Phase 3 Studies in Patients With Nosocomial Pneumonia

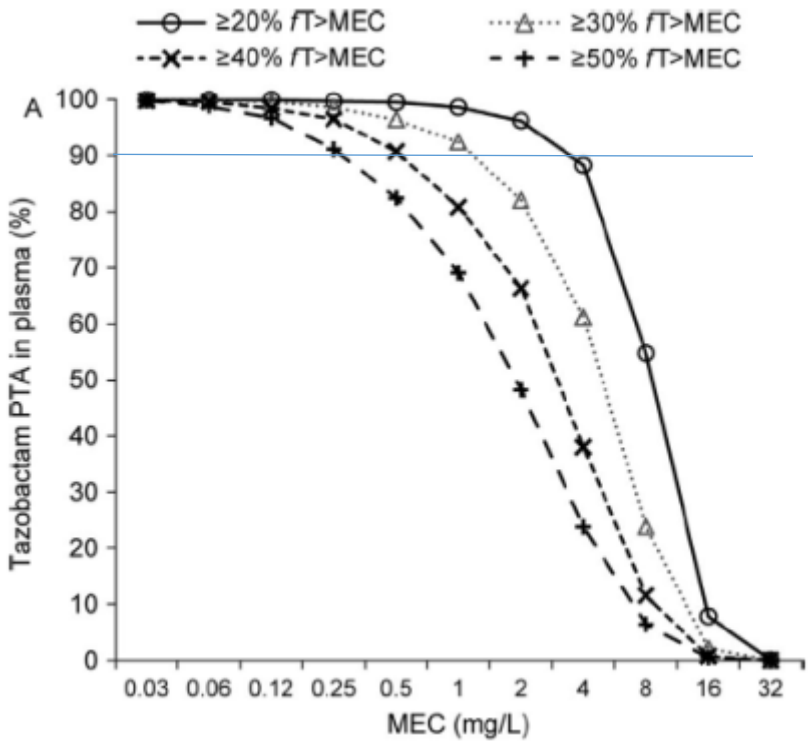


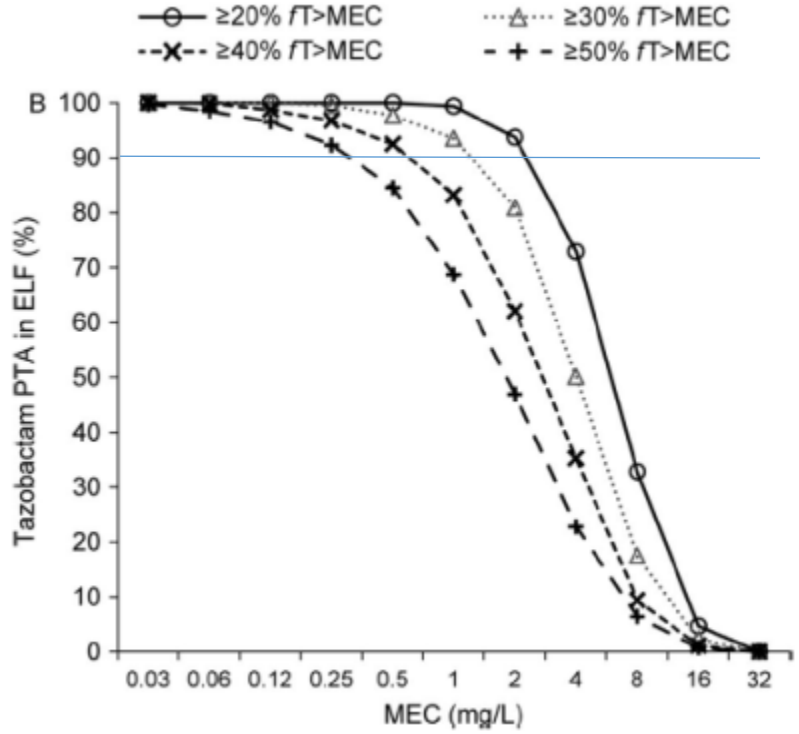


MIC distribution of *Enterobacteriaceae* and *P. aeruginosa* isolates from hospitalized patients with pneumonia from 2012 US/ European Union surveillance data7 and simulated PTA of ceftolozane in plasma (A) and ELF (B) in patients with normal renal function following 1.5 g ceftolozane/tazobactam administered as a 60-minute intravenous infusion every 8 hours.

Xiao AJ The Journal of Clinical Pharmacology 2016;56:56-66 DOI: 10.1002/jcph.566

Ceftolozane/Tazobactam PK/PD-Derived Dose Justification for Phase 3 Studies in Patients With Nosocomial Pneumonia





Simulated PTA of tazobactam in plasma (A) and ELF (B) in patients with normal renal function following 3 g ceftolozane/tazobactam administered as a 60-minute intravenous infusion every 8 hours

Xiao AJ The Journal of Clinical Pharmacology 2016;56:56-66 DOI: 10.1002/jcph.566

Ceftolozane/Tazobactam PK/PD-Derived Dose Justification for Phase 3 Studies in Patients With Nosocomial Pneumonia

- Because of the difference in sites of infection
- And an approximately 50% plasma-to-ELF penetration ratio to achieve a similar or better antibacterial effect (90% PTA) against pathogens with an MIC up to 8 mg/L
- a double of the current approved dose of ceftolozane/tazobactam for cUTI and cIAI is needed for the treatment of nosocomial pneumonia
- 3 g, 1.5 g, and 750 mg for nosocomial pneumonia in patients with normal renal function/mild renal impairment, moderate renal impairment, and severe renal impairment, respectively.

Xiao AJ The Journal of Clinical Pharmacology 2016;56:56-66 DOI: 10.1002/jcph.566

Impact of Bronchoalveolar Lavage Multiplex Polymerase Chain Reaction on Microbiological Yield and Therapeutic Decisions in Severe Pneumonia in Intensive Care Unit

- Objectif :
  - Comparer l'impact de la PCR multiplex *vs* culture conventionnelle
  - Sur le diagnostic microbiologique
  - Sur la décision thérapeutique
  - Dans les pneumonies sévères de réanimation
- Étude cas-contrôle rétrospective
  - 58 pts gpe contrôle : cultures LBA
  - 57 pts étude : PCR-M + culture LBA

Sircar M Journal of Critical Care 31 (2016) 227–232 http://dx.doi.org/10.1016/j.jcrc.2015.10.012

Short-Course *vs* Prolonged-Course Antibiotic Therapy for Hospital-Acquired Pneumonia in Critically Ill Adults (Review)

- 6 études comparatives retenues
- Patients sévères (HAP + VAP)
- 7-8 j vs 10-15 j ABT
- 1088 pts
- Hétérogénéité dans le critères de diagnostic des pneumonies

- VAP, analyse globale :
  - Augmentation nombre de jours sans ABT : - 4,2 j; [IC95% 2,26 à 5,78]
  - Réduction récurrence VAP due à BMR OR 0,44; [IC95% 0,21 à 0,95]
  - Sans impact sur la mortalité
- VAP à BGN NF
  - Récurrence supérieure si tt court : OR 2,18; [IC95% 1,14 à 4,16]
  - Sans impact sur la mortalité

Pugh R Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007577 DOI: 10.1002/14651858.CD007577.pub3.

Short-Course *vs* Prolonged-Course Antibiotic Therapy for Hospital-Acquired Pneumonia in Critically Ill Adults (Review)

- 6 études comparatives retenues
- Patients sévères (HAP + VAP)
- 7-8 j vs 10-15 j ABT
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- Hétérogénéité dar e c diagnostic des pne o

- VAP, analyse globale :
  - Augmentation nombre de jours sans ABT : - 4,2 j; [IC95% 2,26 à 5,78]
  - P due à BMR
  - 95]
  - té
  - t court : OR
  - té

- *Sur un faible nombre d'étude*
- *Et avec définitions hétérogènes*
- *TT court (7-8 j) peut réduire l'émergence de résistance*
- *Sans impact négatif sur l'issue et la mortalité*
- *POUR LES VAP A BGN NF*

Pugh R Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007577 DOI: 10.1002/14651858.CD007577.pub3.

Should short-course antibiotic therapy versus prolonged-course antibiotic therapy be used in critically ill patients with hospital-acquired pneumonia?

Patient or population: hospital-acquired pneumonia
Settings: intensive care
Intervention: short-course antibiotic therapy
Comparison: prolonged-course antibiotic therapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Prolonged-course antibiotic therapy	Short-course antibiotic therapy				
Mortality Follow-up: 28 days	175 per 1000	201 per 1000 (141 to 277)	OR 1.18 (0.77 to 1.8)	598 (3 studies)	⊕⊕⊕○ **moderate**[1]	-
Mortality NF-GNB Follow-up: 28 days	265 per 1000	255 per 1000 (123 to 450)	OR 0.95 (0.39 to 2.27)	179 (2 studies)	⊕⊕○○ **low**[1,2]	-
Mortality MRSA Follow-up: 28 days	238 per 1000	286 per 1000 (91 to 614)	OR 1.28 (0.32 to 5.09)	42 (1 study)	⊕⊕⊕○ **moderate**[1]	-
Recurrence of pneumonia Clinical and/or microbiological criteria	180 per 1000	237 per 1000 (171 to 318)	OR 1.41 (0.94 to 2.12)	733 (19 studies)	⊕⊕○○ **low**[1,3]	-
Recurrence of pneumonia NF-GNB Clinical and/or microbiological criteria	247 per 1000	417 per 1000 (272 to 577)	OR 2.18 (1.14 to 4.16)	176 (2 studies)	⊕⊕⊕○ **moderate**[1]	-
Recurrence of pneumonia MRSA Clinical and/or microbiological criteria	370 per 1000	479 per 1000 (66 to 920)	OR 1.56 (0.12 to 19.61)	49 (2 studies)	⊕⊕⊕○ **moderate**[1]	-
28-day antibiotic-free days Follow-up: 28 days	The mean 28-day antibiotic free days in the intervention groups was **4.02 higher** (2.26 to 5.78 higher)			431 (2 studies)	⊕⊕○○ **low**[1,4]	-

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MRSA:** methicillin-resistant *Staphylococcus aureus*; **NF-GNB:** non-fermenting Gram-negative bacilli; **OR:** odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Low total number of events.
[2]Kollef et al. Multiple interventions (short versus prolonged duration, doripenem versus imipenem, extended versus standard infusion), protocol violations at several centres and premature cessation of study.
[3]Differences in duration of mechanical ventilation prior to episode of pneumonia and differences in bacterial aetiology.
[4]Presumed differences in administration of antibiotics (outside of context of study) between studies.

Pugh R Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007577 DOI: 10.1002/14651858.CD007577.pub3.

Analysis 1.3. Comparison 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic therapy for HAP, Outcome 3 28-day antibiotic-free days.

Review: Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults

Comparison: 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic therapy for HAP

Outcome: 3 28-day antibiotic-free days

Study or subgroup	Short course N	Mean(SD)[Days]	Prolonged course N	Mean(SD)[Days]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 NF-GNB							
Chastre 2003a	64	12 (7.4)	63	7.5 (5.4)		24.0 %	4.50 [2.25, 6.75]
Subtotal (95% CI)	**64**		**63**			**24.0 %**	**4.50 [2.25, 6.75]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.92 (P = 0.000089)							
2 MRSA							
Chastre 2003a	21	12.9 (7)	21	4.9 (5.7)		13.6 %	8.00 [4.14, 11.86]
Subtotal (95% CI)	**21**		**21**			**13.6 %**	**8.00 [4.14, 11.86]**
Heterogeneity: not applicable							
Test for overall effect: Z = 4.06 (P = 0.000049)							
3 Non NF-GNB/ MRSA							
Chastre 2003a	112	13.7 (7.5)	120	10 (4.6)		29.6 %	3.70 [2.09, 5.31]
Subtotal (95% CI)	**112**		**120**			**29.6 %**	**3.70 [2.09, 5.31]**
Heterogeneity: not applicable							
Test for overall effect: Z = 4.49 (P < 0.00001)							
4 Unspecified organism							
Fekih Hassen 2009	14	4.1 (1.9)	16	1.8 (1.6)		32.8 %	2.30 [1.03, 3.57]
Subtotal (95% CI)	**14**		**16**			**32.8 %**	**2.30 [1.03, 3.57]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.56 (P = 0.00037)							
Total (95% CI)	**211**		**220**			**100.0 %**	**4.02 [2.26, 5.78]**
Heterogeneity: $Tau^2 = 2.04$; $Chi^2 = 9.39$, df = 3 (P = 0.02); $I^2 = 68\%$							
Test for overall effect: Z = 4.48 (P < 0.00001)							
Test for subgroup differences: $Chi^2 = 9.39$, df = 3 (P = 0.02), $I^2 = 68\%$							

-10 -5 0 5 10

Favours prolonged course Favours short course

Pugh R Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007577 DOI: 10.1002/14651858.CD007577.pub3.

Analysis 1.10. Comparison 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic
Analysis 1.10. Comparison 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic
therapy for HAP, Outcome 10 Relapse of pneumonia.

Review: Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults

Comparison: 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic therapy for HAP

Outcome: 10 Relapse of pneumonia

Study or subgroup	Short course n/N	Prolonged course n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 NF-GNB					
Chastre 2003a	21/64	12/63		46.7 %	2.08 [0.92, 4.70]
Subtotal (95% CI)	**64**	**63**		**46.7 %**	**2.08 [0.92, 4.70]**
Total events: 21 (Short course), 12 (Prolonged course)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.75 (P = 0.080)					
2 MRSA					
Chastre 2003a	3/21	4/21		11.6 %	0.71 [0.14, 3.64]
Subtotal (95% CI)	**21**	**21**		**11.6 %**	**0.71 [0.14, 3.64]**
Total events: 3 (Short course), 4 (Prolonged course)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.41 (P = 0.68)					
3 Non NF-GNB/MRSA					
Chastre 2003a	9/112	7/120		29.8 %	1.41 [0.51, 3.92]
Subtotal (95% CI)	**112**	**120**		**29.8 %**	**1.41 [0.51, 3.92]**
Total events: 9 (Short course), 7 (Prolonged course)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.66 (P = 0.51)					
4 Unspecified organism					
Capellier 2012	6/116	2/109		11.9 %	2.92 [0.58, 14.78]
Subtotal (95% CI)	**116**	**109**		**11.9 %**	**2.92 [0.58, 14.78]**
Total events: 6 (Short course), 2 (Prolonged course)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.29 (P = 0.20)					
Total (95% CI)	**313**	**313**		**100.0 %**	**1.70 [0.97, 2.97]**
Total events: 39 (Short course), 25 (Prolonged course)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.88, df = 3 (P = 0.60); I^2 =0.0%					
Test for overall effect: Z = 1.86 (P = 0.063)					
Test for subgroup differences: Chi^2 = 1.88, df = 3 (P = 0.60), I^2 =0.0%					

0.005 0.1 1 10 200

Favours short course Favours prolonged course

Analysis 1.11. Comparison 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic therapy for HAP, Outcome 11 Subsequent infection due to resistant organism.

Review: Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults

Comparison: 1 Short (fixed)-course antibiotic therapy versus prolonged-course antibiotic therapy for HAP

Outcome: 11 Subsequent infection due to resistant organism

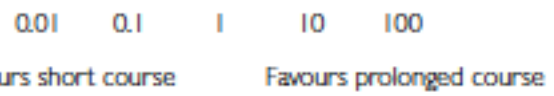
Study or subgroup	Short course n/N	Prolonged course n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Chastre 2003a	24/57	33/53		100.0 %	0.44 [0.21, 0.95]
Total (95% CI)	**57**	**53**		**100.0 %**	**0.44 [0.21, 0.95]**

Total events: 24 (Short course), 33 (Prolonged course)

Heterogeneity: not applicable

Test for overall effect: Z = 2.10 (P = 0.036)

Test for subgroup differences: Not applicable



Pugh R Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007577 DOI: 10.1002/14651858.CD007577.pub3.

Analysis 2.1. Comparison 2 Discontinuation of antibiotics according to Clinical Pulmonary Infection Score, Outcome 1 30-day mortality.

Review: Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults

Comparison: 2 Discontinuation of antibiotics according to Clinical Pulmonary Infection Score

Outcome: 1 30-day mortality

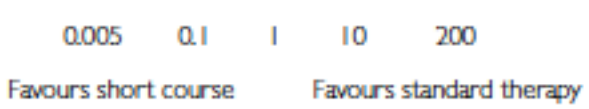
Study or subgroup	Short course therapy n/N	Standard therapy n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Singh 2000	5/39	13/42		100.0 %	0.33 [0.10, 1.03]
Total (95% CI)	**39**	**42**		**100.0 %**	**0.33 [0.10, 1.03]**

Total events: 5 (Short course therapy), 13 (Standard therapy)

Heterogeneity: not applicable

Test for overall effect: Z = 1.91 (P = 0.056)

Test for subgroup differences: Not applicable



Pugh R Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007577 DOI: 10.1002/14651858.CD007577.pub3.

Rapid Diagnosis of Infection in the Critically Ill, a Multicenter Study of Molecular Detection inBloodstream Infections, Pneumonia, and Sterile Site Infections

- Étude observationnelle
  - 6 services de réanimation, Europe
  - Oct 2013-juin 2014
  - Bactériémies, pneumonies, infection sites stériles,
- Résultats cultures conventionnelles vs PCR/spectrométrie de masse
- 529 patients :
  - 616 bactériémies, 185 pneumonies, 110 infections sites stériles
- 616 bactériémies : documentation
- 228 cas (37%) PCR/SP
- 68 cas (11%) cultures
- À 6 heures :
  - Sensibilité 81%
  - Specificité : 69%
  - VP : 97%
- Impact sur le tt : 57%

Vincent JL Crit Care Med 2015;43:2283–2291 DOI: 10.1097/CCM.0000000000001249

Rapid Diagnosis of Infection in the Critically Ill, a Multicenter Study of Molecular Detection inBloodstream Infections, Pneumonia, and Sterile Site Infections

TABLE 2. Bloodstream Infection Assay Performance

		Culture				
		+	−	Total	Sensitivity	81% (95% CI, 70–89%)
Polymerase chain reaction/ electrospray ionization-mass spectrometry	+	55	173	228	Specificity	69% (95% CI, 65–73%)
	−	13	384	397	Positive predictive value	24% (95% CI, 19–30%)
	Total	68	557	625	Negative predictive value	97% (95% CI, 94–98%)

Vincent JL Crit Care Med 2015;43:2283–2291 DOI: 10.1097/CCM.0000000000001249

Rapid Diagnosis of Infection in the Critically Ill, a Multicenter Study of Molecular Detection inBloodstream Infections, Pneumonia, and Sterile Site Infections

TABLE 3. Assay Performance in Samples From Lower Respiratory Tract and Sterile Fluid and Tissue Infections

		Culture				
Lower respiratory tract		+	–	Total	Sensitivity	84% (95% CI, 74–91%)
PCR/ESI-MS	+	68	49	117	Specificity	53% (95% CI, 43–63%)
	–	13	55	68	PPV	58% (95% CI, 40–67%)
	Total	81	104	185	NPV	81% (95% CI, 70–89%)
Sterile fluid and tissue		+	–	Total	Sensitivity	85% (95% CI, 72–93%)
PCR/ESI-MS	+	45	33	78	Specificity	42% (95% CI, 29–56%)
	–	8	24	32	PPV	58% (95% CI, 46–69%)
	Total	53	57	110	NPV	75% (95% CI, 57–89%)

PPV = positive predictive value, NPV = negative predictive value.

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Clinical Failure With and Without Empiric Atypical Bacteria Coverage in Hospitalized Adults With CAP : A Systematic Review and Meta-Analysis

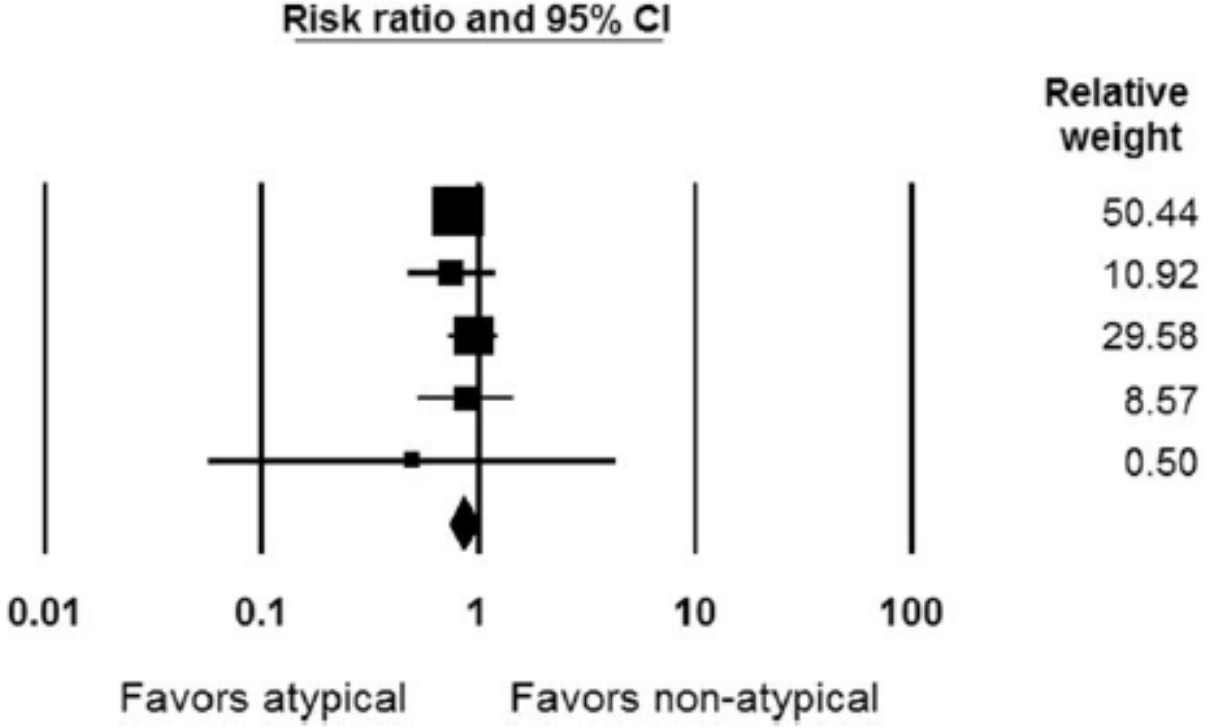
- PubMed, EMBASE, Cochrane..
- 1105 études identifiées
- 910 screenées
- 5 études contrôlées randomisées CAP hospitalisées
- 2011 pts

- Réduction risque d'échec clinique si atypiques couverts :
  - RR = 0,851 [95% CI, 0,732–0,99; P = 0,037]
- Mortalité NS
  - RR = 0,549 [95% CI, 0,259–1,165, P = 0,118]
- Échec bacteriologique NS
  - RR = 0,816 [95% CI, 0,523–1.272, P = 0,369]
- Diarrhée NS
  - RR = 0,746 [95% CI, 0,311–1.790, P = 0,512]
- Arret pour EI NS
  - RR = 0,83 [95% CI, 0,542–1.270, P = 0,39]

Eljaaly K BMC Infectious Diseases (2017) 17:385 DOI 10.1186/s12879-017-2495-5

Clinical Failure With and Without Empiric Atypical Bacteria Coverage in Hospitalized Adults With CAP : A Systematic Review and Meta-Analysis

Study name	clinical failure / Total		Statistics for each study			
	Atypical	non-atypical	Risk ratio	Lower limit	Upper limit	p-Value
Garin 2014.	97 / 289	120 / 291	0.814	0.658	1.007	0.057
Petitpretz 2001.	27 / 200	37 / 208	0.759	0.481	1.198	0.236
Norrby 1998.	75 / 314	76 / 305	0.959	0.726	1.265	0.765
Leophonte 2004.	24 / 167	25 / 153	0.880	0.525	1.473	0.625
Kalbermatter 2000.	1 / 28	4 / 56	0.500	0.059	4.266	0.526
	224 / 998	262 / 1013	0.851	0.732	0.990	0.037



Eljaaly K BMC Infectious Diseases (2017) 17:385 DOI 10.1186/s12879-017-2495-5

Clinical Failure With and Without Empiric Atypical Bacteria Coverage in Hospitalized Adults With CAP : A Systematic Review and Meta-Analysis

Study name	clinical failure / Total		Statistics for each study		Risk ratio and 95% CI	Relative weight
	Atypical	non-atyp	Risk ratio			
Garin 2014.	97 / 289	120 / 29	814			50.44
Petitpretz 2001.	27 / 200	37 / 208	759			10.92
Norrby 1998.	75 / 314	76 / 305	59			29.58
Leophonte 2004.	24 / 167	25 / 153	0			8.57
Kalbermatter 2000.	1 / 28	4 / 56	00			0.50
	224 / 998	262 / 101	351			

- *Oui…. Mais*
- *Études*
  - *Limitées en nombre*
  - *Anciennes > 10 ans*
  - *Avec ABT rétirés du marché témafloxacine*
  - *Monothérapie inappropriée : ciprofloxacine*
- *Promotion inappropriée des quinolones (5/6 études)*

Eljaaly K BMC Infectious Diseases (2017) 17:385 DOI 10.1186/s12879-017-2495-5

Clinical Failure With and Without Empiric Atypical Bacteria Coverage in Hospitalized Adults With CA… …ematic Review and Meta-Analysis

Study name	clinical failure / Total	Statistics for ea…		Relative weight
	Atypical non-aty…	Risk …		
Garin 2014.	97 / 289	12…		50.44
Petitpretz 2001.	27 / …			10.92
Norrby 1998.	7…			29.58
Leophonte 2004. 2…				8.57
Kalbermatter 2000.1…				0.50
	224 …			

Savoir faire analyse critique de l'impériale Cochrane

…marché témafloxacine

…ple inappropriée : ciprofloxacine

…on inappropriée des quinolones (5/6 …tudes)

Eljaaly K BMC Infectious Diseases (2017) 17:385 DOI 10.1186/s12879-017-2495-5

Severe Varicella-Zoster Virus Pneumonia: a Multicenter Cohort Study

- Étude observationnelle jan 1995-jan 2015
  - Pts admis pour pneumonie à VZV
  - 29 services de réanimation
- Résultats : 102 pts
  - Age moyen : 39 ans
  - ID: 53 (52%)
  - 50% : VM dans les 48h suivant admission en réanimation
  - VM : 14 j (7-21)
  - Mortalité
    - réanimation : 17%
    - hospitalière : 24%
  - Corticoïdes :
    - Durée VM, séjour en réanimation, surinfection supérieurs
    - Sans bénéfice sur la mortalité

Table 2 Characteristics of the pulmonary involvement ($n = 102$)

Variables	
Pulmonary symptoms ($n = 102$)	
Temperature, °C	39.2 (38.7–39.9)
Dyspnea	96 (94%)
Cough	45 (44%)
Hemoptysis	9 (9%)
Chest pain	10 (10%)
Acute respiratory failure at ICU admission	69 (68%)
Chest X-ray at ICU admission ($n = 97$, 95%)	
Normal	1 (1%)
Unilateral alveolar opacities	7 (8%)
Bilateral alveolar opacities	23 (24%)
Unilateral interstitial pattern	1 (1%)
Bilateral interstitial pattern	68 (75%)
Lung CT scan ($n = 31$, 30%)	
Normal	0 (0%)
Ground glass opacities	11 (39%)
Nodules	14 (50%)
Consolidations	14 (50%)
Interlobular septal thickening	2 (8%)
Pleural effusion	8 (29%)
Fiberoptic bronchoscopy ($n = 35$, 35%)[a]	
Inflammatory mucosa	6 (43%)
Vesicular lesions on bronchial mucosa	6 (43%)
Normal	2 (14%)
Bronchoalveolar lavage ($n = 29$, 28%)	
Diffuse intra-alveolar hemorrhage[b]	5 (29%)
Cell count/μL ($n = 11$, 38%)	300,000 (215,000–675,000)
Macrophages, % of total cells	50 (22–65)
Lymphocytes, % of total cells	7.5 (5–20)
Neutrophils, % of total cells	31 (5–63)
Eosinophils, % of total cells	0 (0–2)
Siderophages, % of total cells	0 (0–5)
Virus identified by PCR in the BAL (24 samples)	23 (96%)

Table 3 ICU management and outcome data

Variables	
VZV-related treatment	
Acidovir	102 (100%)
Acidovir dose, mg/8 h	10 (10–10)
Steroids	10 (10%)
Immunoglobulins	1 (1%)
Systemic antibiotics at ICU admission	62 (61%)
Primary source of bacterial co-infection ($n = 40$, 39%)	
Lung	24 (60%)
Bloodstream	8 (20%)
Skin	4 (10%)
Other	4 (10%)
Life-sustaining therapies	
Non-invasive mechanical ventilation	29 (28%)
Invasive mechanical ventilation	52 (51%)
Vasopressors	36 (35%)
Renal replacement therapy	24 (24%)
ARDS criteria according to the Berlin definition ($n = 42$, 41%)	
Mild ARDS	8 (19%)
Moderate ARDS	10 (24%)
Severe ARDS	24 (57%)
Other interventions	
Neuromuscular blockers	26/52 (50%)
Prone positioning	14/52 (28%)
Veno-venous ECMO	7/52 (13%)
Outcome data	
ICU length of stay (days)	8 (4–16.75)
Hospital length of stay (days)	14 (9–33)
ICU mortality	17 (17%)
Hospital mortality	24 (24%)

Mirouse A Critical Care 2017; 21:137 DOI 10.1186/s13054-017-1731-0

Severe Varicella-Zoster Virus Pneumonia: a Multicenter Cohort Study

Table 4 Multivariate analysis of factors associated with the need for invasive mechanical ventilation during ICU stay

Variable	OR (CI 95%)	*p*
SOFA score at day 1 (per point increment)	1.90 (1.33–2.70)	<0.001
Oxygen flow at ICU admission, L/min (per L/min increment)	1.25 (1.08–1.45)	0.004
Early bacterial co-infection	14.94 (2.00–111.8)	0.009

Results are presented for the imputed data
Candidate predictors were: age, any comorbidity, underlying immunosuppression, SOFA score at day 1, oxygen flow at ICU admission, alveolar consolidation on chest X-ray, antibiotics at ICU admission, and early bacterial co-infection
CI confidence interval, *ICU* intensive care unit, *OR* odds ratio, *SOFA* Sequential Organ Failure Assessment

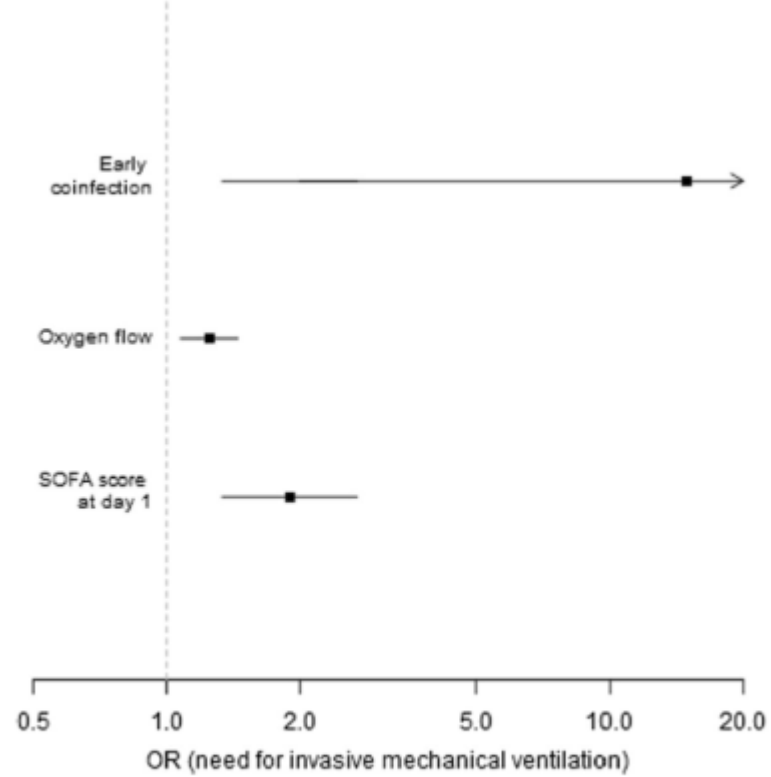


Fig. 2 Risk factors associated with the need for invasive mechanical ventilation in patients with VZV pneumonia. *OR* odds ratio, *SOFA* Sequential Organ Failure Assessment

Co-infections bactériennes :

- Poumon : (n = 24, 60%)
- Bactériémie : (n = 8, 20%)
- Peau : (n = 4, 10%)
- Principale bactérie : *Staphylococcus aureus* (n = 12, 30%).

Mirouse A Critical Care 2017; 21:137 DOI 10.1186/s13054-017-1731-0

Severe Varicella-Zoster Virus Pneumonia: a Multicenter Cohort Study

Table 5 Characteristics of patients who received steroids ($n = 10$) compared to matched controlled patients ($n = 60$) who did not received steroids[a]

	No steroid use ($n = 60$)	Steroids use ($n = 10$)	p
Demographics			
Age, years	43 (34–56)	48 (35.5–60.75)	0.60
Male gender	38 (63%)	5 (50%)	0.49
Co-morbidities	55 (92%)	9 (90%)	1.00
Underlying immunosuppression	33 (55%)	7 (70%)	0.50
Year of ICU admission	2009 (2006–2012)	2010 (2008–2012)	0.48
Time (days) from dyspnea onset to ICU admission	2 (1–3)	2 (1–3.25)	0.79
Parameters at ICU admission			
Temperature, °C	39.1 (38.25–39.7)	39.4 (38.85–40.8)	0.22
Respiratory rate, breaths/min	30 (26.5–38.5)	35 (32–35)	0.34
Oxygen flow, L/min	10 (5–15)	8.5 (1.5–15)	0.55
Hemoptysis	6 (10%)	0 (0%)	0.58
PaO_2:FiO_2 ratio, mmHg	105 (75.5–174.5)	86 (80.5–210)	1.00
SOFA score at day 1	5 (4–9)	7 (5–7.75)	0.55
ICU management			
Invasive mechanical ventilation	36 (60%)	9 (90%)	0.08
Time (days) from ICU admission to intubation	1 (1–2)	1 (1–1)	0.30
ARDS criteria according to the Berlin definition	31 (52%)	7 (70%)	0.33
Length of invasive mechanical ventilation, days	13.5 (7–17.25)	28 (13–53)	0.06
Bacterial superinfection	26 (43%)	8 (80%)	0.04
Outcome data			
ICU length of stay, days	10 (4–17)	32 (10.75–69.5)	0.01
Hospital length of stay, days	16.5 (10–32.25)	40.5 (21.25–74)	0.02
ICU mortality	12 (20%)	2 (20%)	1.00
Hospital mortality	15 (25%)	6 (60%)	0.06

Values are shown as n (%) or median (25^{th}–75^{th} percentiles)

[a]Patients who received steroids were matched in a 1:6 ratio to a control group of patients who did not receive steroids. Matched controls were screened from the current cohort with the following four matching criteria: age, year of ICU admission, SOFA score at day 1, and ARDS criteria according to the Berlin definition

ARDS acute respiratory distress syndrome, *ICU* intensive care unit, PaO_2:FiO_2 ratio of arterial oxygen partial pressure to fractional inspired oxygen, *SOFA* Sequential Organ Failure Assessment

Mirouse A Critical Care 2017; 21:137 DOI 10.1186/s13054-017-1731-0

Time to Blood Culture Positivity as A Predictor of Clinical Outcomes and Severity in Adults with Bacteremic Pneumococcal Pneumonia

- Objectif : évaluer l'association entre délai de positivité des hémocultures et issue des PAC à SP bactériémiques
- Étude prospective, 278 pts, 2003-2015
- Age médian : 62
- PSI IV-V : 51%
- Mortalité : 8% < 21j post admission

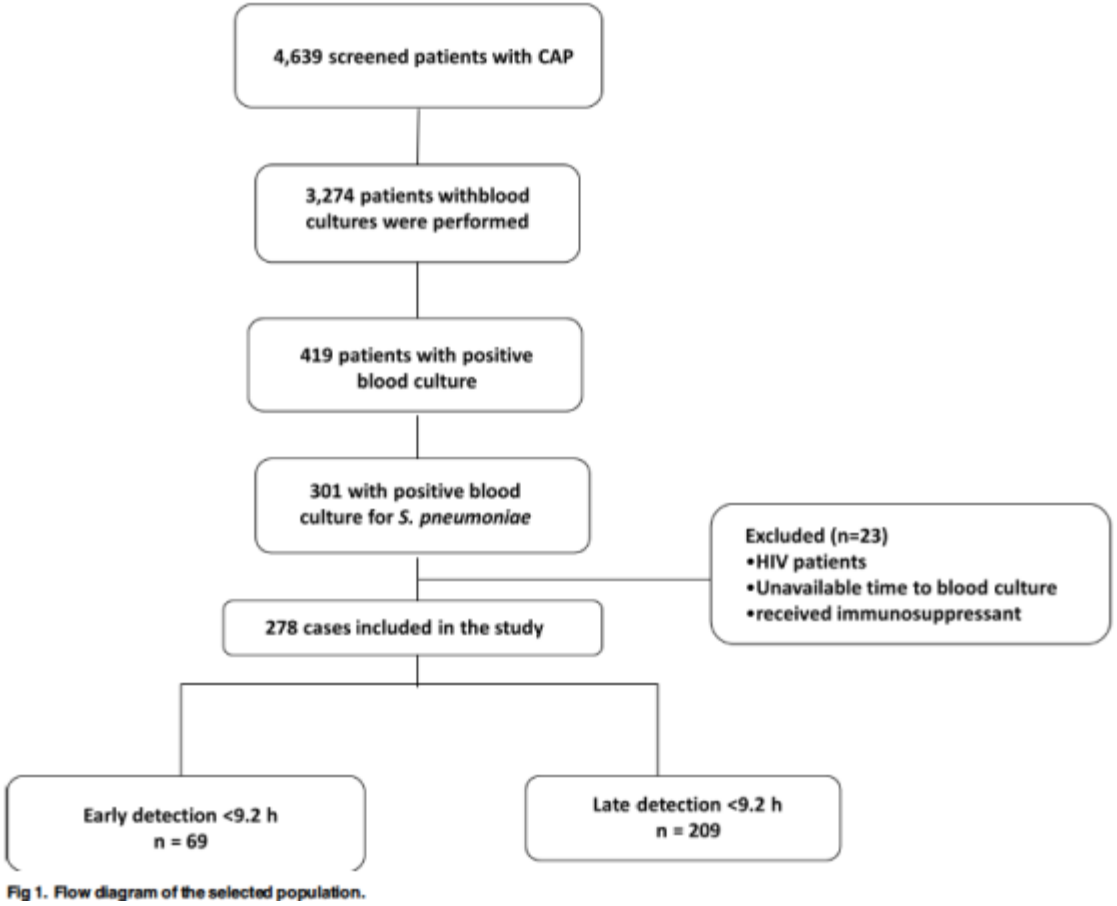


Fig 1. Flow diagram of the selected population.

Cilloniz C PLoS ONE 12(8): e0182436. https://doi.org/10.1371/journal.pone.0182436

Time to Blood Culture Positivity as A Predictor of Clinical Outcomes and Severity in Adults with Bacteremic Pneumococcal Pneumonia

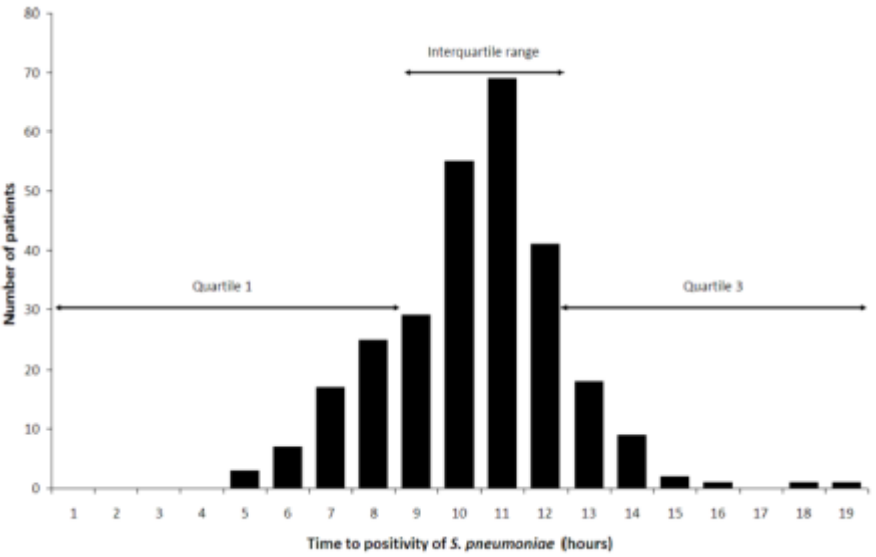


Fig 2. Time to positivity of S. Pneumoniae in blood culture.

Table 2. Clinical outcomes.

Variables	Cohort of patients	Early detection <9.2 h	Late detection ≥9.2 h	P Value
	n = 278	n = 69	n = 209	
Length of hospital stay (days), median (IQR)	9 (5; 14)	12 (8; 18)	8 (5; 12)	**<0.001**
Length of hospital stay, ≥9 days, n (%)	139 (52)	47 (71)	92 (46)	**<0.001**
In-hospital mortality, n (%)	19 (7)	10 (15)	9 (4)	**0.010**
30-day mortality, n (%)	21 (8)	10 (15)	11 (5)	**0.018**
ICU admission, n (%)	87 (31)	27 (39)	60 (29)	0.60
Length of ICU stay (days), mean (IQR)	5 (3; 9)	5.5 (4; 21.5)	5 (3; 7)	0.16
ICU mortality, n (%)[a]	8 (9)	4 (15)	4 (7)	0.24
Mechanical ventilation, n (%)				**0.018**
Not ventilated	216 (83)	44 (70)	172 (88)	**0.029**
Non-invasive	21 (8)	8 (13)	13 (7)	0.82
Invasive	22 (8)	11 (18)	11 (6)	**0.007**

Abbreviations: ICU = intensive care unit; IQR = interquartile range. Percentages calculated on non-missing data.

[a] 87 patients in the overall cohort, 27 patients in the early detection group and 60 patients in the late detection group were used to calculate the percentages.

Cilloniz C PLoS ONE 12(8): e0182436. https://doi.org/10.1371/journal.pone.0182436

Time to Blood Culture Positivity as A Predictor of Clinical Outcomes and Severity in Adults with Bacteremic Pneumococcal Pneumonia

Table 3. Significant simple and multiple linear regression analyses to predict length of hospital stay.

Variable	Simple			Multiple[ab]		
	β	95% CI	P Value	β	95% CI	P Value
Chronic respiratory disease	2.74	-0.45 to 5.93	0.092	-	-	-
C-reactive protein ≥15 mg/dL	1.68	0.92 to 3.06	0.090	-	-	-
PSI risk class IV-V	4.67	1.62 to 7.72	0.003	3.97	1.14 to 6.81	0.006
Pleural effusion	3.74	-0.21 to 7.69	0.064	-	-	-
ARDS	16.42	10.7 to 22.1	<0.001	15.58	10.1 to 21.0	<0.001
Acute renal failure	4.18	1.02 to 7.35	0.010	-	-	-
Septic shock	5.96	1.03 to 10.9	0.018	-	-	-
Mechanical ventilation	8.40	5.98 to 10.8	<0.001	-	-	-
Early detection (time to positivity <9.2 h)	6.74	3.24 to 10.24	<0.001	5.20	1.81 to 8.52	0.002

Abbreviations: β = unstandardized beta coefficient; ARDS = acute respiratory distress syndrome; CI = confidence interval; OR = odds ratio; PSI = pneumonia severity index.

Data are shown as estimated βs (95% CIs) of the explanatory variables in the model. Regression coefficients represent the mean change in the response variable for one unit of change in the predictor variable while holding other predictors in the model constant.

The P value is based on the null hypothesis that all βs relating to an explanatory variable equal zero (no effect).

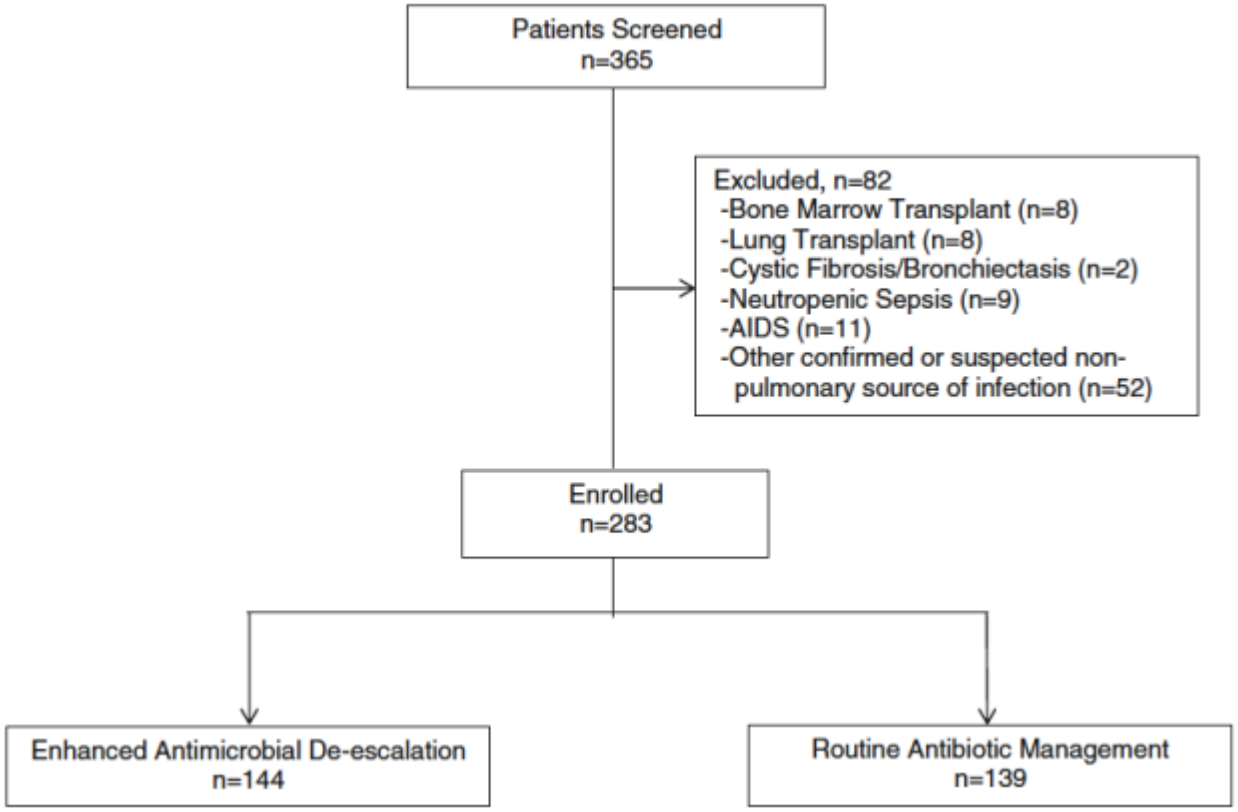
[a] Adjusted R^2 coefficient of determination = 0.18.

[b] Patients' predicted length of hospital stay is equal to 4.49 + 3.97 (PSI) + 15.58 (ARDS) + 5.20 (time to positivity <9.2 h) days. Patients' days of length of hospital stay increased 3.97 in case of PSI risk class IV-V, increased 15.58 in case of ARDS and increased 5.20 if time to positivity <9.2 h.

Cilloniz C PLoS ONE 12(8): e0182436. https://doi.org/10.1371/journal.pone.0182436

Enhanced Antimicrobial de-Escalation for Pneumonia in Mechanically Ventilated Patients: A Cross-over Study

- Étude prospective, cross-over
- 2 services de réanimation
- Groupe désescalade renforcée
  - Ré-évaluation quotidienne résultats microbiologique et prescription ABT
  - Désescalade en fonction résultats microbiologiques et évolution clinique
- *vs* groupe contrôle
  - Décisions déterminées en staff incluant réanimateurs « certifiés » et un pharmacien « clinique » spécialisé en réanimation
- 238 pts sous VM
  - 144 (50,9%) gpe desescalade
  - 139 (49,1%) gpe contrôle



Trupka T Critical Care 2017; 21:180 DOI 10.1186/s13054-017-1772-4

Enhanced Antimicrobial de-Escalation for Pneumonia in Mechanically Ventilated Patients: A Cross-over Study

	Enhanced antibiotic de-escalation (n = 144)	Routine antibiotic management (n = 139)	*P* value
Early failure of initial antibiotics	40 (27.8)	33 (23.7)	0.438
Antibiotics de-escalated*	70/104 (67.3)	70/106 (66.0)	0.845
Deterioration post de-escalation*	8/70 (11.4)	6/70 (8.6)	0.573
Total antibiotic days	7.0 (4.0, 8.8)	7.0 (4.0, 9.0)	0.616
Mortality	51 (35.4)	35 (25.2)	0.061
ICU length of stay	6.0 (3.0, 12.0)	6.0 (4.0, 12.0)	0.935
Hospital length of stay	11.0 (6.0, 22.0)	12.0 (6.0, 20)	0.918
Ventilator days	4.5 (2.0, 9.0)	4.0 (2.0, 9.0)	0.953
Secondary pneumonia	12 (8.3)	12 (8.6)	0.928
Secondary pneumonia due to antibiotic-resistant pathogen	9 (6.3)	6 (4.3)	0.468

Values expressed as median (interquartile range) and number (percent). *ICU* intensive care unit.
*The percentages were derived from the subgroups of patients who did not have failure of initial antibiotics

Trupka T Critical Care 2017; 21:180 DOI 10.1186/s13054-017-1772-4

Enhanced Antimicrobial de-Escalation for Pneumonia in Mechanically Ventilated Patients: A Cross-over Study

	Enhanced antibiotic de-escalation (n = 144)	Routine antibiotic management (n = 139)	*P* value
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- *La mise en place d'un programme renforcé de désescalade*
- *Dans un service de réanimation déjà habitué à la pratique de l'ABT stewardship et à la désescalade*
- *S'avère sans gain supplémentaire*

Trupka T Critical Care 2017; 21:180 DOI 10.1186/s13054-017-1772-4

Frequency, Associated Factors and Outcome of Multi-Drug-Resistant Intensive Care Unit-Acquired Pneumonia Among Patients Colonized with Extended-Spectrum β-Lactamase-Producing *Enterobacteriaceae*

- Étude observationnelle, prospective, 6 ans mars 2009/mars 2015
- Monocentrique, réa médicale CHU 850 lits
- Objectifs :
  - Principal : déterminer chez les porteurs d'EBLSE, la prévalence, les FDR associés et l'ilmpact des pneumonies à EBLSE.
  - Secondaire : déterminer les facteurs associés aux pneumonies acquises en réanimation dues à des bactéries carbapenem-R.
- Inclusion de tous les pts colonisés à l'admission en réanimation ayant présenté une pneumonie
- Recueil de toutes les données de ces pts
- 6303 pts admis, 597 colonisés EBLSE
  - 481 (81%) VM
  - 111 pts P acquise en réanimation, dont 54 EBLSE

Table 1 Multivariable analysis of factors associated with ESBL-PE pneumonia among 111 patients with ESBL-PE colonization

Associated factors	AOR	95% CI	*p*
SAPS2 > 43	2.81	1.16–6.79	0.022
>2 days amoxicillin/clavulanic acid in ICU	0.24	0.08–0.71	0.010
Colonization with *E.cloacae* or *K. pneumoniae*	10.96	2.93–41.0	<0.0001

Razazi K Ann Intensive Care 2017;7:61 DOI 10.1186/s13613-017-0283-4

Frequency, Associated Factors and Outcome of Multi-Drug-Resistant Intensive Care Unit-Acquired Pneumonia Among Patients Colonized with Extended-Spectrum β-Lactamase-Producing *Enterobacteriaceae*

Table 2 Outcome associated with nosocomial pneumonia, according to aetiology ($n = 111$)

Variables	ESBL− ($n = 63$)	ESBL+ ($n = 48$)	*p* value
Septic shock	21 (33%)	25 (52%)	0.047
SOFA at ICUAP onset	4 [2–9]	7 [4–10]	0.037
Bacteraemia	5 (8%)	7 (15%)	0.26
Appropriate initial first-line antimicrobial therapy[a]	48 (76%)	37 (77%)	0.91
Appropriate 1st beta-lactam	46 (73%)	31(65%)	0.34
Resolution of infection[b]	49 (78%)	35 (73%)	0.31
LOS in ICU, all patients	25 [18–41]	33 [19–60]	0.09
LOS in ICU, survivors only	25 [22–41]	40 [27–80]	0.017
LOS in hospital, all patients	41 [23–70]	42 (20–84)	0.81
LOS in hospital, survivors only	57 [40–75]	62 [46–121]	0.29
Death in ICU	24 (38%)	28 (58%)	0.034
Death in hospital	27 (43%)	32 (67%)	0.013

LOS length of stay

[a] First-line antibiotic administered within the first 24 h following ICUAP was deemed appropriate if the isolated pathogen was susceptible to at least one drug administered (including aminoglycosides alone)

[b] Resolution of clinical signs and symptoms of pneumonia without documented microbiologic persistence and alive at day seven

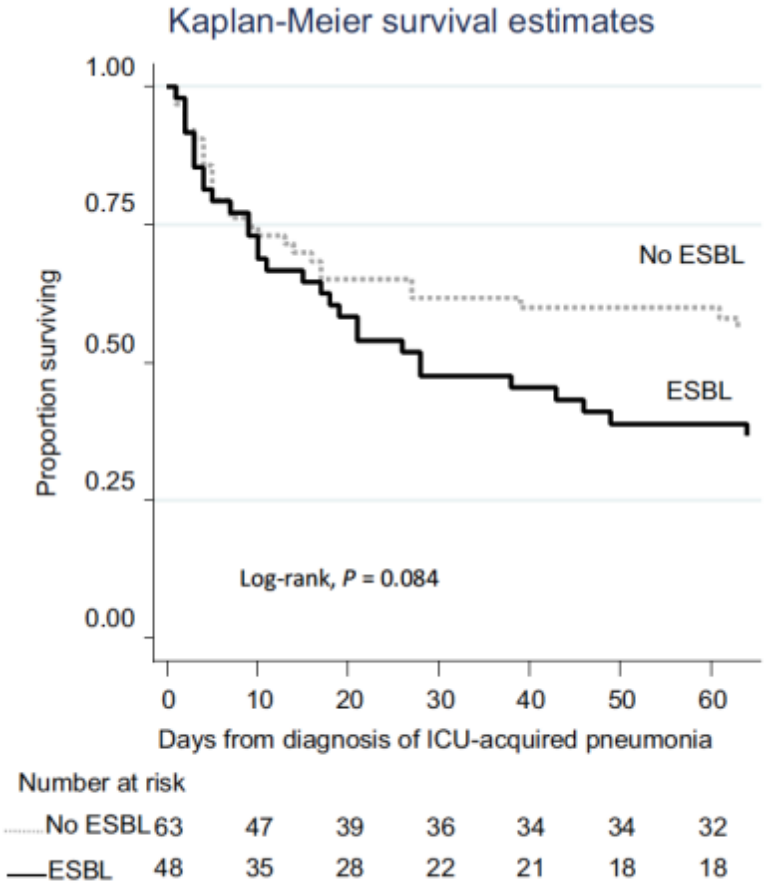

Fig. 1 Sixty-day survival in patients with ESBL carriage and ICU-acquired pneumonia

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Table 3 Cox regression (bivariable and multivariable) analyses of variables associated with death at sixty days

Variables	Bivariable analysis		Multivariable analysis	
	HR (95% CI)	*p* value	aHR (95% CI)	*p* value
SAPS2 > 43	1.76 (1.03–3.00)	0.038	1.93 (1.12–3.34)	0.018
Chronic pulmonary disease	1.68 (0.93–3.04)	0.086	–	
Liver cirrhosis	1.89 (0.86–4.17)	0.11	–	
Ab < 3 mo., broad-sp. > 10 d	2.21 (1.31–3.71)	0.003	–	
C3G < 3 mo	1.64 (0.93–2.90)	0.087	–	
Carbapenem < 3 mo	2.59 (1.11–6.06)	0.03	–	
Charlson > 2	1.75 (1.04–2.95)	0.034	–	
ESBL colonization at admission	1.56 (0.92–2.63)	0.10	–	
Septic shock associated with nosocomial pneumonia	2.86 (1.68–4.85)	0.0001	2.81 (1.66–4.78)	<0.0001
VAP	0.48 (0.24–0.96)	0.037	0.48 (0.24–0.98)	0.04
ESBL-PE ICUAP	1.57 (0.93–2.64)	0.091	1.15 (0.65–2.05)	0.64
ICU-acquired infection before ICUAP	0.51 (0.28–0.95)	0.033	0.52 (0.28–0.97)	0.04
Others antibiotics between colonization and pneumonia	1.49 (0.89–2.52)	0.13	–	
Appropriate empirical antimicrobial therapy[a]	1.05 (0.56–1.95)	0.88	0.66 (0.34–1.27)	0.22

Ab antibiotic, *broad-sp.* broad-spectrum, *3GC* third-generation cephalosporin; *iBL* beta-lactamase inhibitor, *mo* month, *VAP* ventilator-associated pneumonia, *ICUAP* ICU-acquired pneumonia, *<3 mo* within 3 months before ICU admission, *HR (95% CI)* hazard ratio interquartile range (25–75%)

[a] Antibiotic treatment was considered adequate if one or more antibiotics initiated for ICUAP were active against the causative microorganism on the basis of the antibiotic susceptibility profile of the strain

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IFN-α2a or IFN-β1a in Combination with Ribavirin to Treat Middle East Respiratory Syndrome Coronavirus Pneumonia: A Retrospective Study

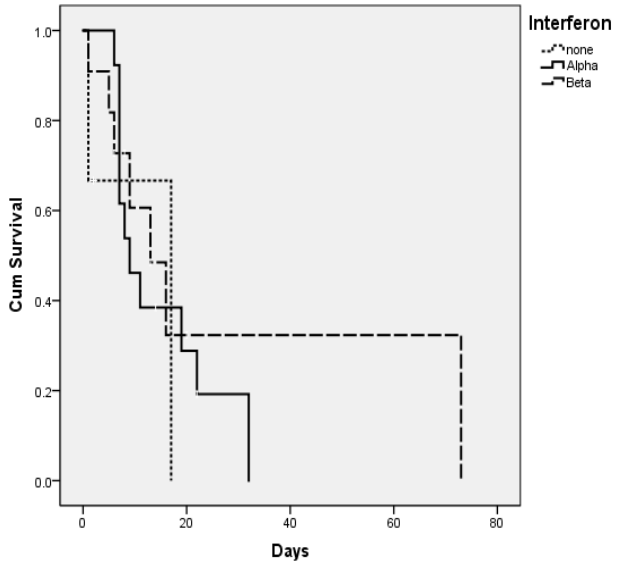
- Étude rétrospective
- Arabie Saoudite, Jeddah
- 1er avril 2014 – 30 juin 2014
- Infection MERS-CoV confirmée par RT-PCR
- RT-PCR plasmatique réalisée chez 19/32 pts; positive pour 10/19 pts
- Traitement :
  - IFN- α2a (180 mg sous-cutanée 1/semaine) ou IFN- β1a (44 mg sous-cutanée 3/semaine)

  +
  - Ribavirine (dose de charge 2 g PO) 600 mg/12h PO
- 32 cas confirmés

Risk factors for mortality in patients with MERS-CoV infection

Variable	OR	95%CI	P
Age (≥50 vs < 50 years)	26.1	3.58 – 190.76	0.001
Diabetes mellitus	15.74	2.46 – 100.67	0.004
Oxygen requirement (yes vs no)	0.32	0.9 – 1.1	0.07
Creatinine (>110 vs ≤110 μM)	2.33	0.73 – 7.4	0.15
IFN-α treatment	0.16	0.02 – 1.38	0.09
IFN-β treatment	0.28	0.03 – 2.33	0.24

Survival of patients with MERS CoV infection who received interferon α2a, interferon β1a, and no interferon



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