Rechutes, récidives, secondes pneumonies: quelles définitions?

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Vendredi 31 janvier 2025 – *Maison de la Réanimation, Paris*

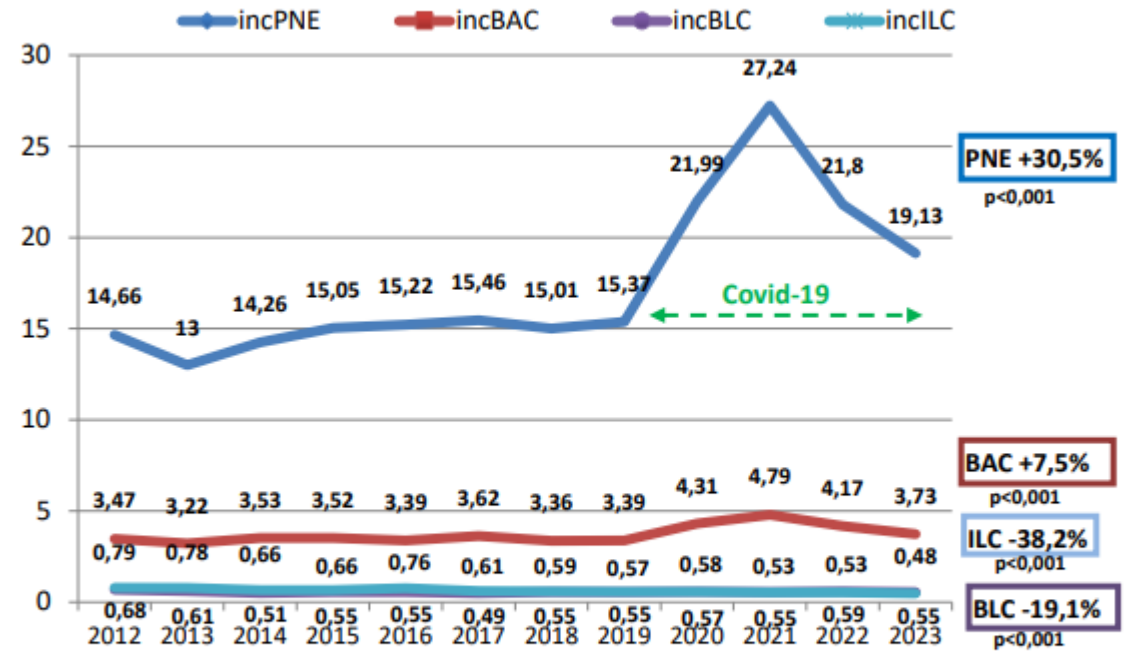
Liens d’intérêt

- lecture fees from MSD, Shionogi, and a travel grant from Pfizer

En France

- Infection nosocomiale la plus fréquente en réanimation

Figure 6 - Evolution des taux d'incidence de 2012 à 2023 sur l'ensemble du réseau



incPNE — *incidence des pneumonies liées à l'intubation pour 1000 j d'intubation*
incBAC — *incidence des bactériémies pour 1000 j d'hospitalisation en réanimation*
incBLC — *incidence des bactériémies liées aux CVC jusqu'à 2018, liées aux CC depuis 2019 pour 1000 j de cathétérisme*
incILC — *incidence des infections liées aux CVC jusqu'à 2018, liées aux CC depuis 2019 pour 1000 j de cathétérisme*

Attributable mortality of ventilator-associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies

Wilhelmina G Melsen, Maroeska M Rovers, Rolf H H Groenwold, Dennis C J J Bergmans, Christophe Camus, Torsten T Bauer, Ernst W Hanisch, Bengt Klarin, Mirelle Koeman, Wolfgang A Krueger, Jean-Claude Lacherade, Leonardo Lorente, Ziad A Memish, Lee E Morrow, Giuseppe Nardi, Christianne A van Nieuwenhoven, Grant E O'Keefe, George Nakos, Frank A Scannapieco, Philippe Seguin, Thomas Staudinger, Arzu Topeli, Miquel Ferrer, Marc J M Bonten

www.thelancet.com/infection **Vol 13 August 2013**

	Total number of patients	RRR VAP (95% CI)	RRR mortality (95% CI)	Attributable mortality (95% CI*)
All studies	6284	0·30 (0·21 to 0·38)	0·04 (–0·06 to 0·12)	13% (–0·14 to 0·38)
Trauma	1159	0·40 (0·25 to 0·52)	–0·08 (–0·45 to 0·19)	0% (–1·06 to 0·45)
Medical	3314	0·32 (0·17 to 0·43)	–0·01 (–0·14 to 0·11)	0% (–0·41 to 0·29)
Surgical	1560	0·26 (0·04 to 0·43)	0·18 (–0·01 to 0·33)	69% (0·08 to 3·60)
APACHE <20				
Unadjusted	1588	0·31 (0·10 to 0·47)	0·00 (–0·26 to 0·20)	0% (–0·94 to 0·72)
Adjusted†	1521	0·34 (0·14 to 0·49)	–0·03 (–0·31 to 0·18)	0% (–0·97 to 0·77)
APACHE 20–29	1176	0·28 (0·05 to 0·45)	0·10 (–0·12 to 0·27)	36% (–0·29 to 1·51)
APACHE ≥30	359	0·47 (0·08 to 0·70)	–0·03 (–0·39 to 0·23)	0% (–0·95 to 0·37)
SAPS 2 <35	364	0·45 (0·08 to 0·67)	–0·23 (–1·18 to 0·30)	0% (–4·48 to 0·82)
SAPS 2 35–58	723	0·38 (0·11 to 0·56)	0·18 (–0·07 to 0·38)	47% (–0·13 to 1·08)
SAPS 2 ≥58	377	0·35 (–0·05 to 0·60)	–0·12 (–0·50 to 0·16)	0% (–2·27 to 0·60)

RRR=relative risk reduction. VAP=ventilator-associated pneumonia. APACHE=acute physiology and chronic health evaluation. SAPS 2=simplified acute physiology score. *95% CI attributable mortality as estimated with bootstrap analyses. †Adjusted for trauma .

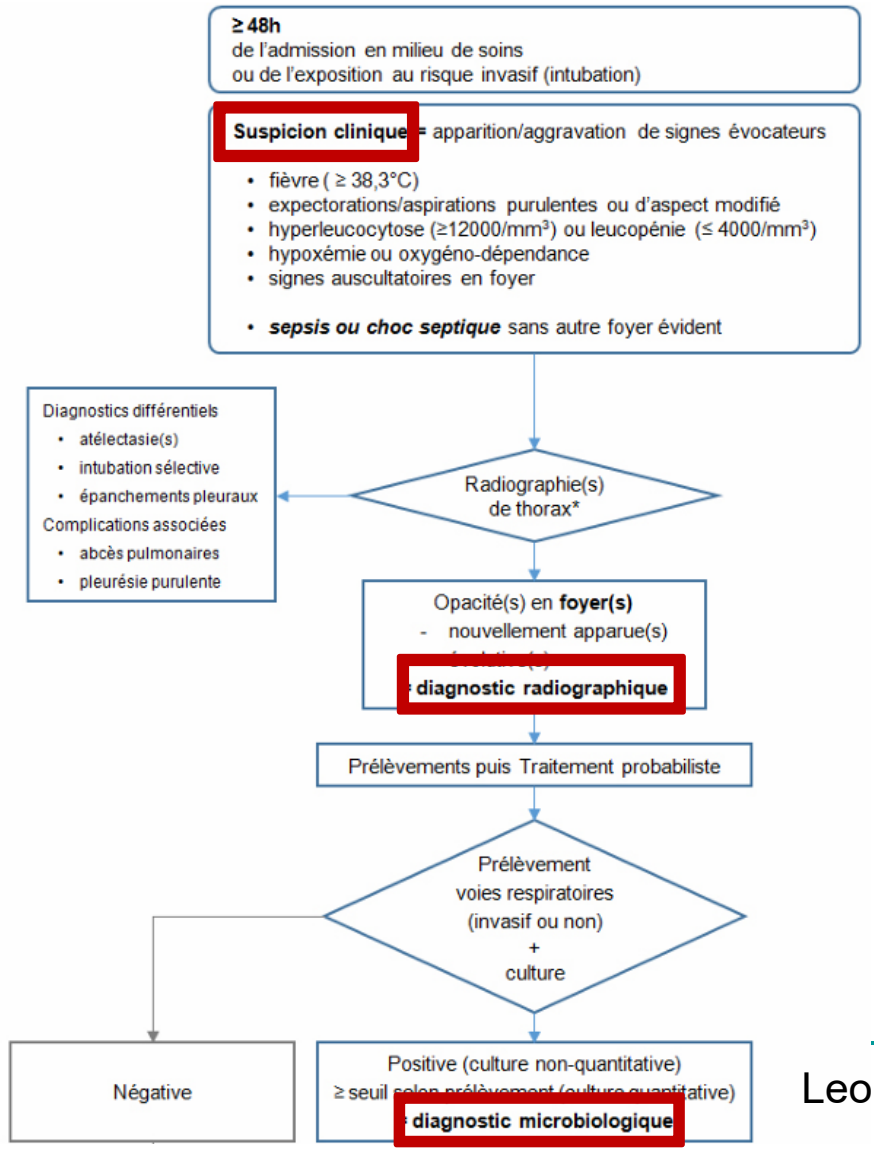
Table 2: **Results of primary analysis (random effects model)**

PAVM : autres impacts pronostiques

- Allongement de la durée de VM
- Allongement de la durée de séjour
- Cout médico-économique majeur

Muscedere CID 2010
Kollef ICHE 2012
Zimlichman Jama intern med 2013

Diagnostic



Leone et al RFE SFAR/SRLF 2017

2ème épisode: Critères cliniques multiples exemple relapse

- Chastre JAMA 2003 PneumA At least 1 of the initial causal bacterial strains at significant concentration AND Fever AND Purulent secretions AND A new or persistent infiltrate on chest X ray OR Unexplained deterioration of blood gases (decrease PaO2/FiO2 >30%) OR Unexplained hemodynamic instability (>30% dose vasopressor or introduction) OR Concomitant and even imposing an urgent change of antibiotic treatment
- Khollef LID 2019: Initial causal bacteria at significant concentration AND Recurrence of signs or symptoms of pneumonia OR New radiological evidence of pneumonia OR Antibiotic received AND After the test of cure for the treatment of pneumonia
- Capellier G et al. PLoS One 2012: A positive quantitative culture (same initial bacterial species regardless of its susceptibility profile) AND Radio-clinical suspicion of VAP OR Worsening SOFA (+2 points from baseline) AND ≥ 4 days of antibiotic treatment for preceding VAP episode

2ème épisodes: définitions multiples

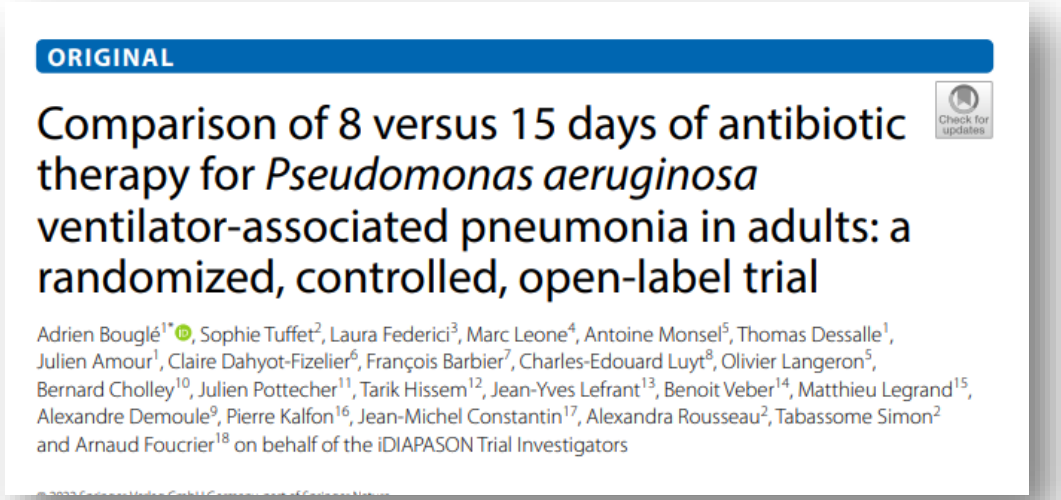
- Grande variabilité des définitions et des entités de récurrence:
  - Fréquence entre 8 et 80%

Relapse:
délais différents :
+4 jours début ATB
+2 jours fin ATB
Après amélioration clinique

Persistent:
délais différents (étalés/période ATB)

Superinfection:
Aussi appelé « new infection »
-3 délais différents :
+3 jours début ATB
Durant période ATB
Après amélioration clinique

Chastre et al JAMA 2003
Cappelier et al Plos One 2012
Luyt et al AIC 2020
Decavèle et al J Crit Care 2021
Collado-Iledo AIC 2024



ORIGINAL

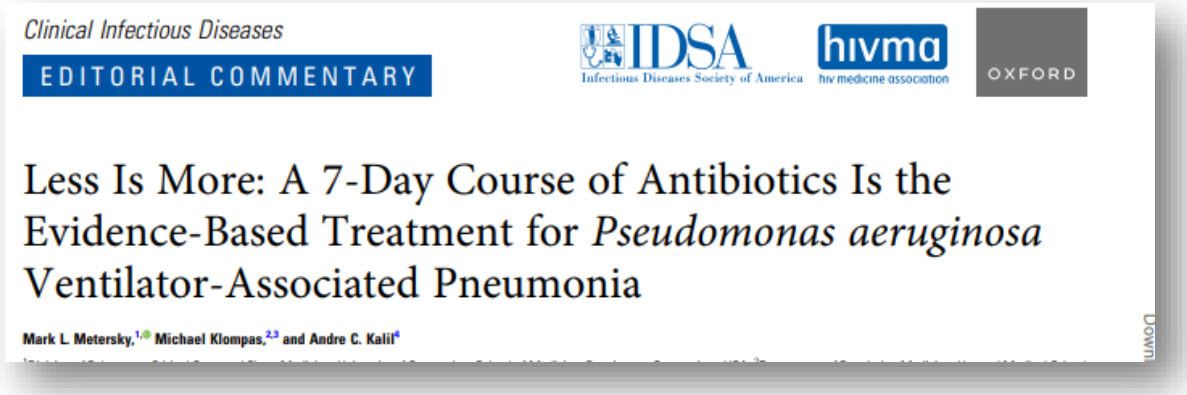
Comparison of 8 versus 15 days of antibiotic therapy for *Pseudomonas aeruginosa* ventilator-associated pneumonia in adults: a randomized, controlled, open-label trial

Adrien Bouglé[1*], Sophie Tuffet[2], Laura Federici[3], Marc Leone[4], Antoine Monsel[5], Thomas Dessalle[1], Julien Amour[1], Claire Dahyot-Fizelier[6], François Barbier[7], Charles-Edouard Luyt[8], Olivier Langeron[5], Bernard Cholley[10], Julien Pottecher[11], Tarik Hissem[12], Jean-Yves Lefrant[13], Benoit Veber[14], Matthieu Legrand[15], Alexandre Demoule[9], Pierre Kalfon[16], Jean-Michel Constantin[17], Alexandra Rousseau[2], Tabassome Simon[2] and Arnaud Foucrier[18] on behalf of the iDIAPASON Trial Investigators

Table 2 Primary outcome and its components, according to study group

Outcome or event	15-day group (*N* = 98)	8-day group (*N* = 88)	Difference (90% CI)
Death or PA-VAP recurrence rate at day 90 during hospitalization in the ICU in ITT population—no. (%)	25/98 (25.5)	31/88 (35.2)	9.7% (− 1.9–21.2%)
Death or PA-VAP recurrence rate at day 90 during hospitalization in the ICU in PP population—no. (%)	22/80 (27.5)	29/72 (40.3)	12.8% (− 0.4–25.6%)
PA-VAP recurrence rate during hospitalization in the ICU in ITT population—no. (%)	9/98 (9.2)	15/88 (17)	7.9% (− 0.5–16.8%)

PA-VAP, pseudomonas aeruginosa ventilator-associated pneumonia; ICU, Intensive Care Unit; PP, per protocol; ITT, intention-to-treat



- Nombre de jours à risque de rechute plus élevé :x4 dans Diapason
- Etude Pneuma : 1,5 rechute /100 jours à risque (dans bras 8 ou 15)
- -> biais d'immortalité

Facteurs de risques de 2ème épisode

- Facteurs de risque:
  - COVID 19
  - Précèdent épisode avec un non fermentant
  - Résistance +/-
  - SDRA / ventilation mécanique prolongée
  - Gravité initiale
- Facteurs protecteurs:
  - Quinolone pour ttt *pseudomonas*

Plaquette AJRCCM 2013
Combes CCM2007
Cappelier et al Plos One 2012
Luyt et al AIC 2020
Gragueb-Chatti J Clin med 2022
Decavèle et al J Crit Care 2021

A consensus of European experts on the definition of ventilator-associated pneumonia recurrences obtained by the Delphi method: the RECUVAP study

Under review

Méthodes DELPHI

- Delphes oracle le la Grèce antique

Nasa et al World J Methodol 2021

Méthodes Delphi

- 1ère mise en application contemporaine : militaire (RAND 1953)

MEMORANDUM
RM-727/1-ABRIDGED
JULY 1962

AN EXPERIMENTAL APPLICATION OF THE DELPHI METHOD TO THE USE OF EXPERTS

Norman Dalkey and Olaf Helmer

SUMMARY

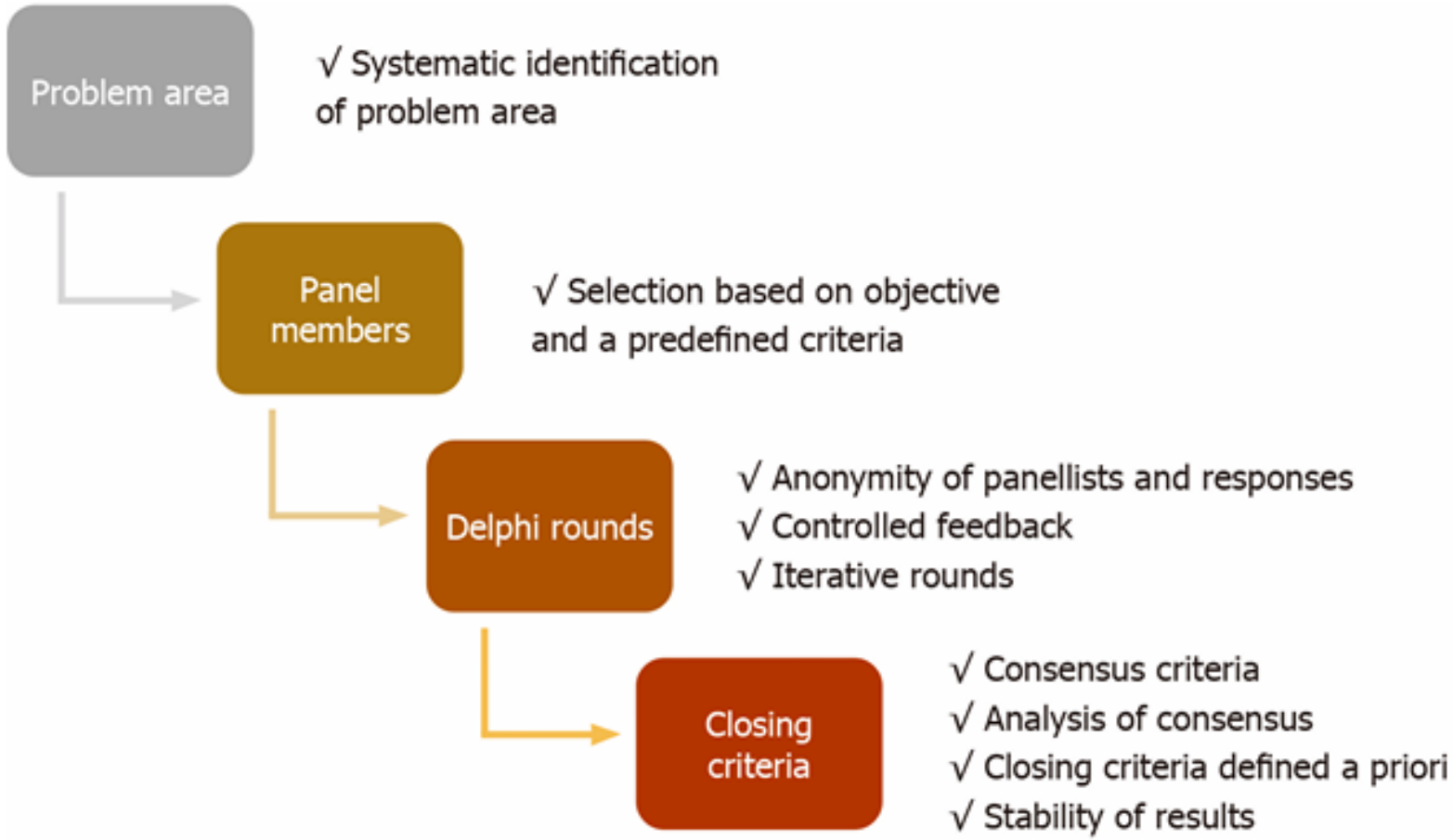
This paper gives an account of an experiment in the use of the so-called DELPHI method, which was devised in order to obtain the most reliable opinion consensus of a group of experts by subjecting them to a series of questionnaires in depth interspersed with controlled opinion feedback.

CONFIDENCE-OF-DESTRUCTION ESTIMATES

	Respondent						
Response	1	2	3	4	5	6	7
Primary (50% confidence)	125	50	150	300	200	1000	5000
10% and 90% confidence	75–200	25–150	100–175	250–800	70–500	—	2500–10000

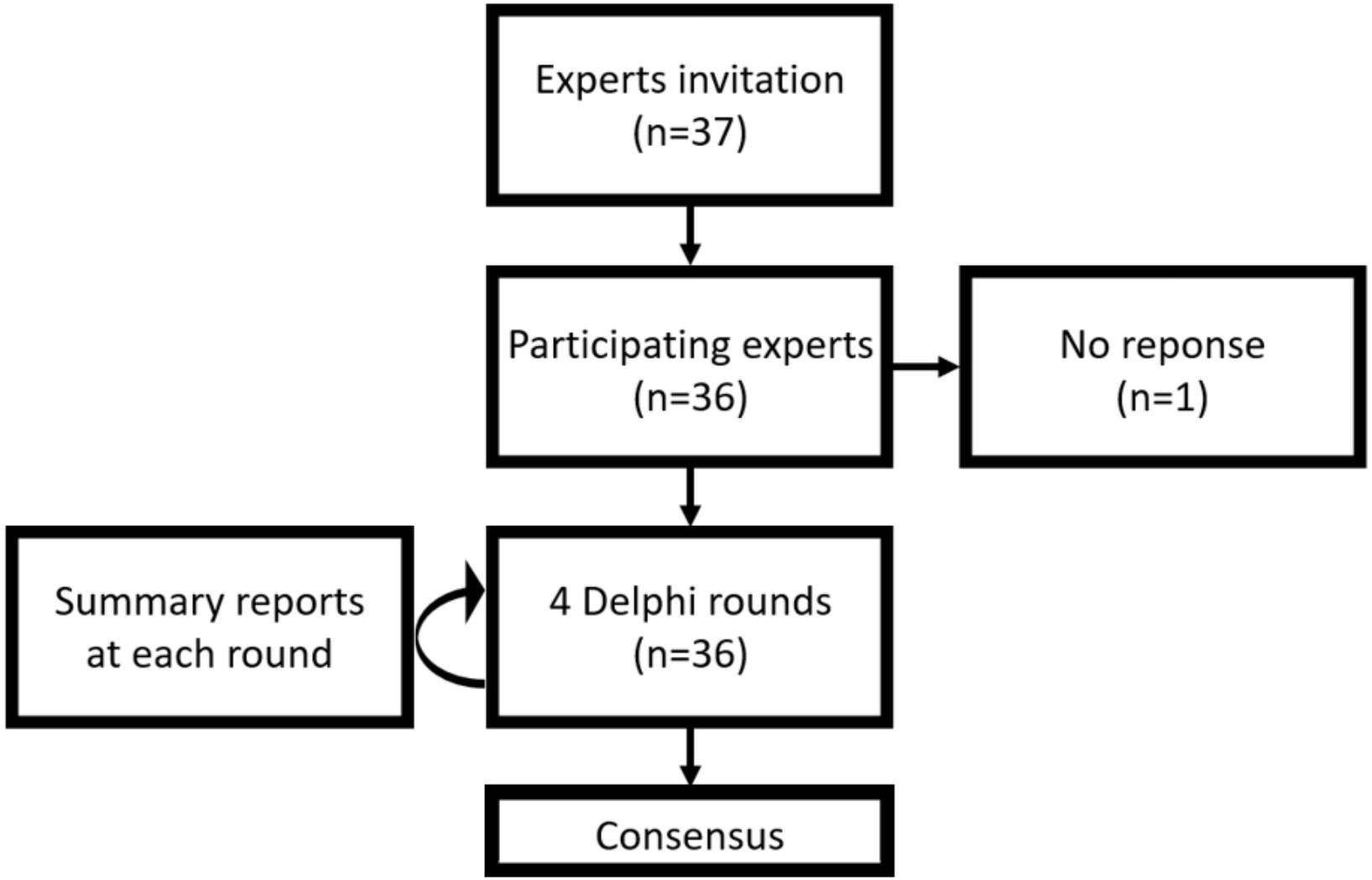
Dalkey et al Manag Sci 1963

Methodes DELPHI

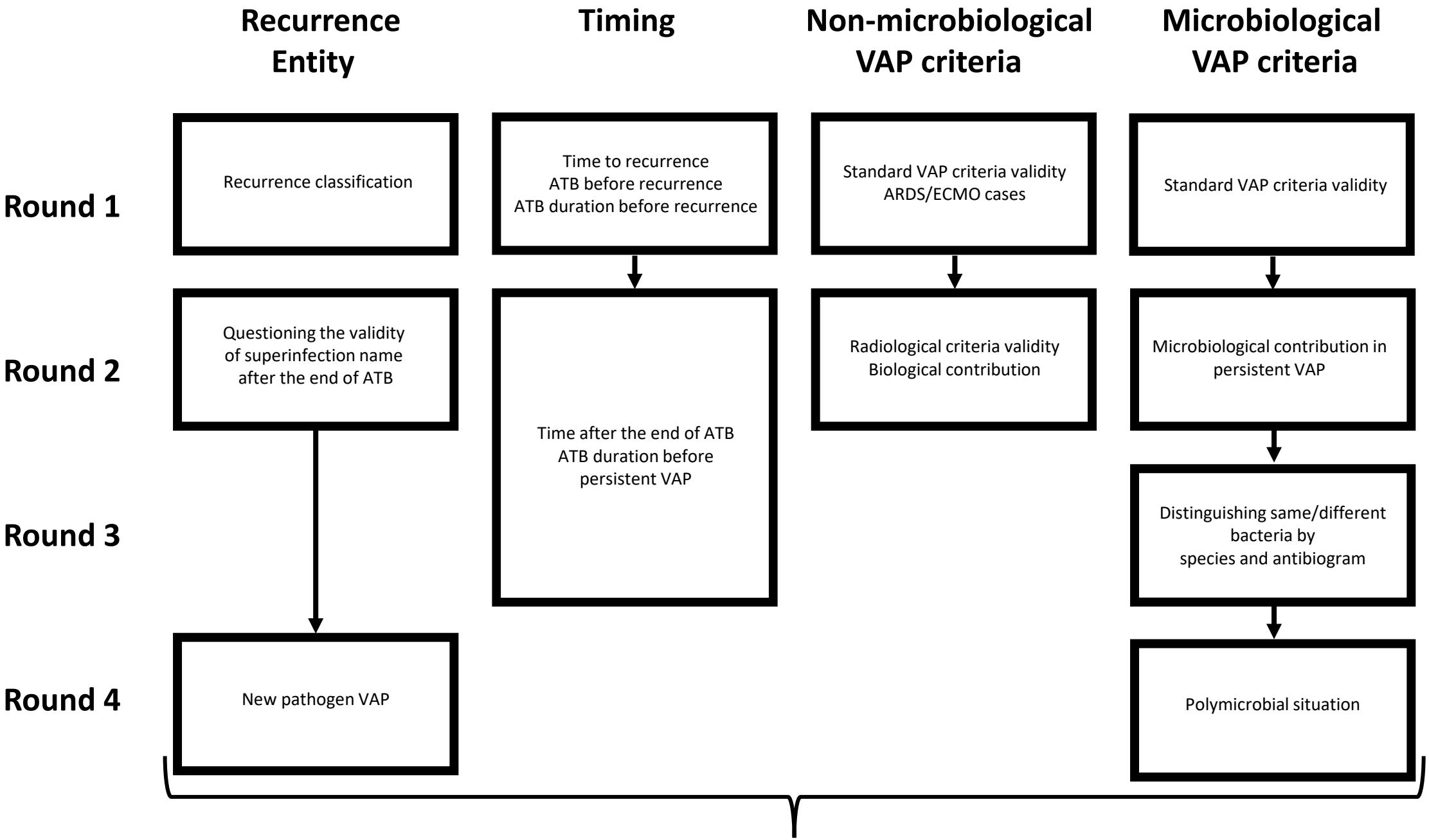


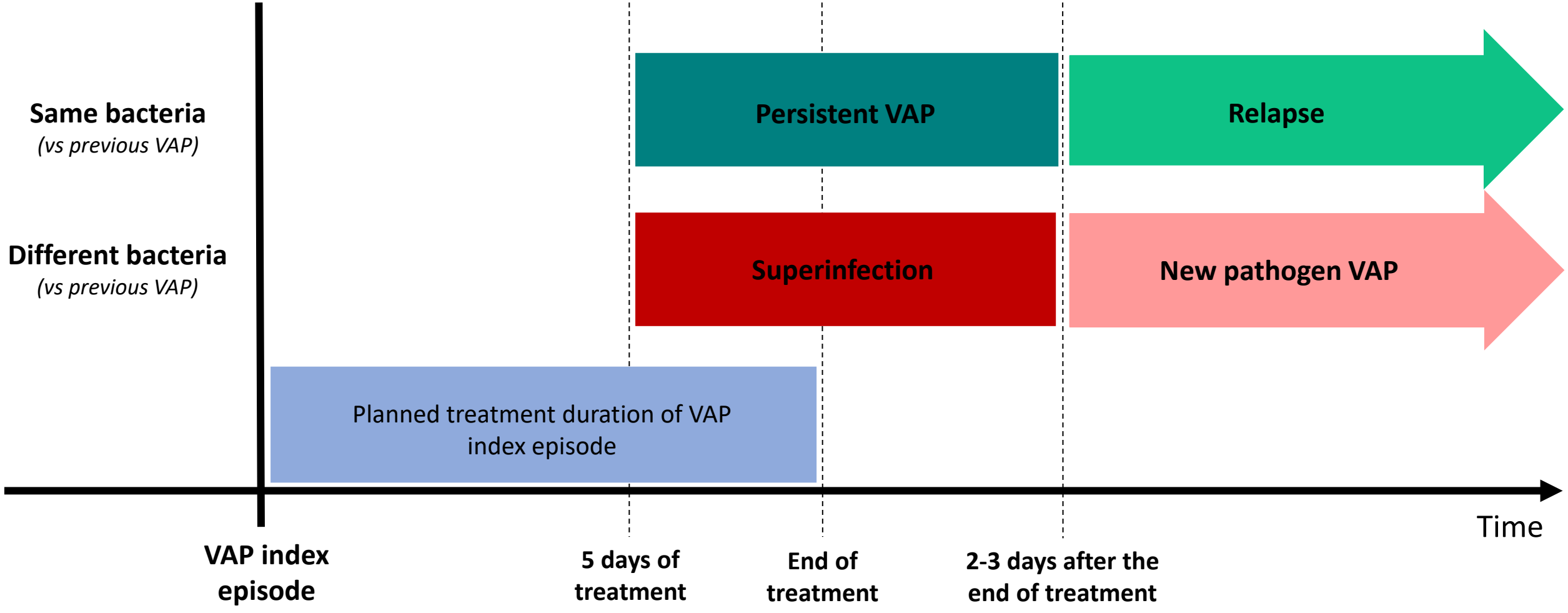
Nasa et al World J Methodol 2021

Méthodes DELPHI



Antoine Gaillet[1,2*], Charles-Edouard Luyt[3*], Jean-Francois Timsit[4], Karim Asehnoune[5], Francois Barbier[6], Matteo Bassetti[7], Lila Bouadma[4], Adrien Bouglé[8], Jean Chastre[3], Andrew Conway Morris[9], Jan J De Waele[10,11], François Dépret[12], George Dimopoulos[13], Stephan Ehrmann[14], Santiago Ewig[15], Muriel Fartoukh[16], Arnaud Foucrier[17], José Garnacho-Montero[18], Sami Hraiech[19], Marc Leone[20], Demosthenes Makris[21], Ignacio Martin-Loeches[22,23], Dimitrios Matthaiou[24], Antoine Monsel[25], Philippe Montravers[26], Saad Nseir[27], José-Artur Paiva[28], Laurent Papazian[29], Garyfallia Poulakou[30], Pedro Póvoa[31,32,33], Jérôme Pugin[34], Alejandro H Rodriguez[35], Antoine Roquilly[5], Damien Roux[36], Anahita Rouzé[27], Fabio Silvio Taccone[37], Antoni Torres[23], Jean-Ralph Zahar[38], Emmanuel Weiss[17$], Keyvan Razazi[1,2$]


Recurrence Entity
Timing
Non-microbiological VAP criteria
Microbiological VAP criteria
Round 1
Round 2
Round 3
Round 4
Recurrence classification
Time to recurrence
ATB before recurrence
ATB duration before recurrence
Standard VAP criteria validity
ARDS/ECMO cases
Standard VAP criteria validity
Questioning the validity of superinfection name after the end of ATB
Time after the end of ATB
ATB duration before persistent VAP
Radiological criteria validity
Biological contribution
Microbiological contribution in persistent VAP
Distinguishing same/different bacteria by species and antibiogram
New pathogen VAP
Polymicrobial situation
Identification of 4 distinct VAP clinical entities


Same bacteria
(vs previous VAP)
Different bacteria
(vs previous VAP)
Persistent VAP
Relapse
Superinfection
New pathogen VAP
Planned treatment duration of VAP index episode
Time
VAP index episode
5 days of treatment
End of treatment
2-3 days after the end of treatment

	Persistent VAP	Relapse	Superinfection	New pathogen VAP
Usual clinical criteria necessary	Yes			
Evolution according to previous VAP episode	Absence of clinical cure throughout the planned duration of AAT	Partial or complete resolution of the initial clinical signs of the previous VAP	Regardless of clinical course	Partial or complete resolution of the initial clinical signs of the previous VAP
Timing	From 5 days after the start of AAT for the previous VAP to 48-72 hours after its end	48-72 hours after the end of AAT for the previous VAP	From 5 days after the start of AAT for the previous VAP to 48-72 hours after its end	48-72 hours after the end of AAT for the previous VAP
Chest X-ray criterion	ARDS : not required No ARDS : no consensus			
Microbiological criterion	Same bacterium as the previous VAP episode		Different bacterium as the previous VAP episode	
Biological criterion	Increase or no change in bacterial load usefulness Absence of a decrease in procalcitonin concentration usefulness			

Microbiologie

- Antibiorésistance non consensuelle
  - Même espèce/même antibiogramme = même bactérie
  - Même espèce/antibiogramme différent = 50/50
- Polymicrobien ≈ superinfection/new pathogen-VAP (67% accord)

Conclusion

- Homogénéisation des critères de récurrence de VAP
- Homogénéisation des entités de récurrence de VAP
- Homogénéisation de la pratique clinique
- Outils pour de futures études

- <u>Limites:</u>
  - Européen
  - Genré
  - Résistance (=classification à la discrétion du clinicien)
  - PCR
  - Virus/champignon
  - TDM/Echographie