Peut-on relayer l'antibiothérapie par voie orale *(en MIR)* ?

Damien Roux, PUPH MIR

Médecine Intensive Réanimation

Hôpital Louis Mourier, AP-HP, Colombes

Conflits d’intérêt

- Financier :
  - Investigateur principal PHRC COTRIVAP (cotrimoxazole dans les PAVM)

- Académique :
  - Président du Conseil scientifique en médecine du CNCI (MESRI)
  - Coordonnateur Île-de-France de MIR

Plan

- Pourquoi se pose-t-on la question ?
  - Pour quelles raisons prescrit-on les antibiotiques par voie intraveineuse en réanimation ?
- Peut-on réellement le faire en réanimation ?
  - Principe de la désescalade
- Pourquoi FAUDAIT-IL relayer par voie orale quand on peut ?

Pour quelles raisons utilise-t-on la voie intraveineuse en réanimation ?

- **Parce qu'on veut mettre une céphalosporine de 3ème génération**, ou en tout cas un antibiotique disponible par voie IV…
  - Pneumonie aiguë communautaire
  - Pyélonéphrite aiguë
  - Péritonite aiguë

- **Parce qu'on veut optimiser le PK/PD**
  - Précocité d'une concentration sérique et donc tissulaire suffisante
  - Problème de volume de distribution notamment
  - Perfusion prolongée pour les antibiotiques temps-dépendant

"the right drug at the right time and the right dose for the right bug for the right duration"
(Ann Am Thorac Soc Vol 17, No 5, pp 531–540, May 2020)

Pour quelles raisons utilise-t-on la voie intraveineuse en réanimation ?

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

12. For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hr of recognition.

***Strong** , low quality of evidence (Septic shock)*

***Strong** , very low quality of evidence (Sepsis without shock)*

CHANGED from previous: "We recommend that administration of intravenous antimicrobials should be initiated as soon as possible after recognition and within one hour for both a) septic shock and b) sepsis without shock"

***strong recommendation** , moderate quality of evidence*

Recommendation
25. For adults with sepsis or septic shock, we **suggest** using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion. *Weak recommendation, moderate quality of evidence.*

Recommendation
26. For adults with sepsis or septic shock, we **recommend** optimizing dosing strategies of antimicrobials based on accepted pharmacokinetic/pharmacodynamic (PK/PD) principles and specific drug properties. *Best practice statement.*

…OK pour le tout début des soins

- Pneumonie à pneumocoque prouvée à H48 de réanimation
  - Antibiogramme : profil sauvage
  - Apyréxie, diminution de l’oxygénorequérance
  - Pas de catécholamine, pas de défaillance autre
  - Peut-on passer à l’amoxicilline par voie entérale ?

Pneumonie à pneumocoque prouvée à H48 de réanimation

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AMERICAN THORACIC SOCIETY DOCUMENTS

Antibiotic Stewardship in the Intensive Care Unit

An Official American Thoracic Society Workshop Report in Collaboration with the AACN, CHEST, CDC, and SCCM

Table 1. Major themes in antibiotic stewardship in the intensive care unit

- Critical care practitioners are important causes of and potential solutions to the crisis of antibiotic resistance.
- Antibiotic stewardship should be considered a core competency of critical care practitioners.
- Antibiotic stewardship must address the fear of inadequate empirical treatment in the critically ill to be effective.
- The adverse effect of excessive antibiotic treatment on the individual patient needs greater emphasis.
- Antibiotic stewardship programs must ensure that improving overall antibiotic use, not simply reducing antibiotic costs or increasing de-escalation, is the primary focus.
- The hope of rapid diagnostics is currently largely unfulfilled.
- A shift in emphasis to an individualized approach to antibiotic therapy is needed.

Ann Am Thorac Soc Vol 17, No 5, pp 531–540, May 2020

Pourquoi pourrait-on en théorie ?

Box Guidance for intravenous to oral switch

It is often appropriate to switch a patient's therapy from the intravenous to oral route when all of the following apply:*

- clinical improvement
- fever resolved or improving
- no unexplained haemodynamic instability
- tolerating oral intake with no concerns about malabsorption
- a suitable oral antimicrobial with the same or similar spectrum, or an oral formulation of the same drug, is available. For children, a suitable paediatric formulation is available.

désescalade

Aust Prescr 2020;43:45–8

Systematic review: the bioavailability of orally administered antibiotics during the initial phase of a systemic infection in non-ICU patients

Broek *et al. BMC Infectious Diseases* (2021) 21:285

Annemieke K. van den Broek[1*], Jan M. Prins[1], Caroline E. Visser[2] and Reinier M. van Hest[3]

Conclusion:

- There is a clear **knowledge gap** regarding the **bioavailability** of orally administered antibiotics in non-ICU patients during the initial phase of a systemic infection.
- **Well-designed studies on this topic are necessary** to elucidate whether patients can benefit from the advantages of an earlier IV-to-oral switch.

Biodisponibilité par voie orale (sujet sain)

Excellente **>90%**	**Suffisante** **50-90 %**
Cotrimoxazole Levofloxacine Linezolide Metronidazole Clindamycine Doxycycline	Amoxicilline (+/- ac. Clavulanique) Azithromycine Ciprofloxacine Céfalexine

Pharmacokinetics of Trimethoprim-Sulfamethoxazole in Critically Ill and Non-Critically Ill AIDS Patients

THOMAS W. F. CHIN,[1] ARTHUR VANDENBROUCKE,[2] AND IGNATIUS W. FONG[3]*

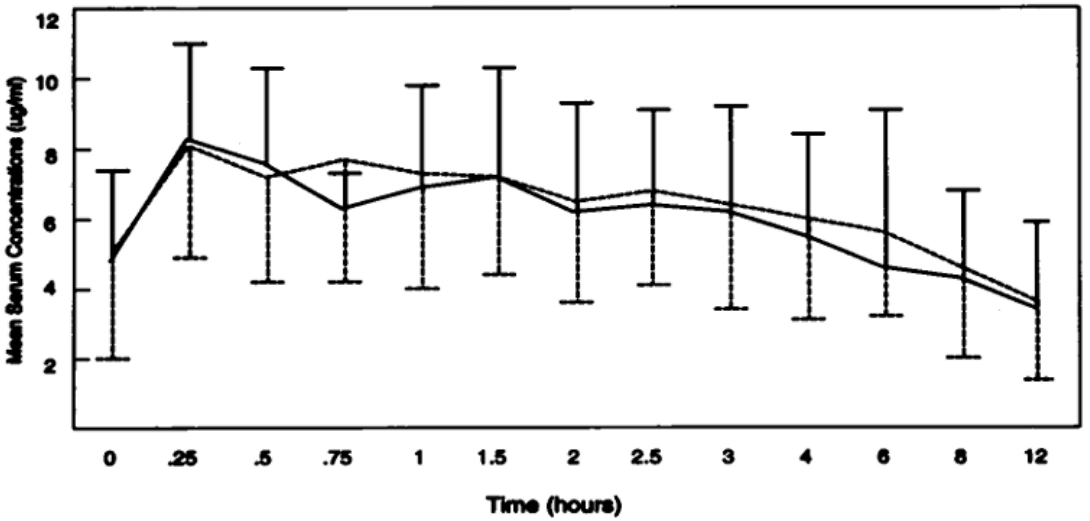

FIG. 1. Mean ± SD trimethoprim concentrations in serum after intravenous administration to critically ill patients (——) and non-critically ill patients (– – – –).

« It would also appear to be possible that when critically ill patients are initiated on trimethoprim-sulfamethoxazole intravenously, they **may be switched to the oral formulation** when they have been clinically **stabilized** and are **able to tolerate oral feeds**. »

TABLE 2. Pharmacokinetic parameters

Group	Dose-T (mg/kg/day)	Dose-S (mg/kg/day)	C_{max}-T (μg/ml)	C_{max}-S (μg/ml)	
Intravenous					
Critically ill (n = 8)	14.7 ± 2.1	73.4 ± 10.6	8.1 ± 2.6	163.6 ± 21.5	1
Non-critically ill (n = 9)	16.1 ± 4.0	80.5 ± 19.9	7.9 ± 3.2	186.4 ± 59.9	1
Oral					
Critically ill (n = 4)	15.1 ± 1.2	75.5 ± 6.0	6.6 ± 1.5	145.8 ± 42.0	
Non-critically ill (n = 8)	16.0 ± 4.2	80.1 ± 21.1	8.3 ± 3.3	181.8 ± 74.7	

[a] T, trimethoprim; S, sulfamethoxazole. Values are means ± SDs.

- Pas de choc septique
- Volume de distribution non altéré
- Mono-défaillance respiratoire
- N = 4

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 1995, p. 28–33

Effectiveness of early switch from intravenous to oral antibiotics in severe community acquired pneumonia: multicentre randomised trial

Jan Jelrik Oosterheert, Marc J M Bonten, Margriet M E Schneider, Erik Buskens, Jan-Willem J Lammers, Willem M N Hustinx, Mark H H Kramer, Jan M Prins, Peter H Th J Slee, Karin Kaasjager, Andy I M Hoepelman

- Pneumonie aiguë communautaire hospitalisée (hors ICU)
- 3j vs. 7j IV (7j au total)
- N=302

Characteristic	Treatment group	
	Intervention (n=150)	Control (n=152)
Men	102 (68)	97 (64)
Mean (SD) age (years)	69.9 (13.8)	69.0 (14.2)
Nursing home patients	7 (5)	5 (3)
Mean (SI) pneumonia severity score	111.6 (26.3)	113.7 (25.8)
Pneumonia severity class		
II	11 (7)	7 (5)
III	14 (9)	11 (7)
IV	93 (62)	111 (73)
V	32 (21)	23 (15)

Table 2 Micro-organisms identified in multicentre randomised trial of early switch from intravenous to oral antibiotics in severe community acquired pneumonia. Values are number of patients (percentage)

Micro-organism	Treatment group	
	Intervention (n=150)	Control (n=152)
Streptococcus pneumoniae	29 (19)	47 (31)
Isolated from sputum	6 (4)	16 (11)
Isolated from blood	9 (6)	16 (11)
Positive urinary antigen test	19 (13)	28 (19)
Staphylococcus aureus	7 (5)	5 (3)
Isolated from sputum	5 (3)	4 (3)
Isolated from blood	2 (1)	1 (1)
*Haemophilus influenzae**	6 (4)	3 (2)
*Mycoplasma catharralis**	5 (3)	0 (0)
Chlamydia pneumoniae†	8 (5)	7 (5)
Mycoplasma pneumoniae†	2 (1)	6 (4)
Legionella pneumophila	4 (3)	6 (4)
Serological evidence	4 (3)	6 (4)
Positive urinary antigen test	2 (1)	3 (2)
Other	17 (11)	24 (16)
Unknown cause	84 (56)	71 (47)

*Isolated from sputum.
†Based on serological evidence.

BMJ. 2006 Dec 9;333(7580):1193

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Table 3 Outcomes in multicentre randomised trial of early switch from intravenous to oral antibiotics in severe community acquired pneumonia. Intention to treat analysis. Values are number of patients (percentage) unless stated otherwise

Clinical outcome	Treatment group		Mean difference (95% CI)
	Intervention (n=132)	Control (n=133)	
Death after day 3	5 (4)	8 (6)	2% (–3% to 8%)
Clinical cure	110 (83)	113 (85)	2% (–7% to 10%)
Clinical failure:	22 (17)	20 (15)	–2% (–10% to 7%)
Clinical cure but still in hospital	9 (7)	6 (5)	–2% (–4% to 8%)
Clinical deterioration	8 (6)	6 (5)	–1% (–4% to 7%)
Death	5 (4)	8 (6)	2% (–3% to 8%)
Clinical deterioration and death	13 (10)	14 (11)	1% (–1% to 8%)
Mean (SD) length of hospital stay (days)	9.6 (5.0)	11.5 (4.9)	1.9 (0.6 to 3.2)
Mean (SD) duration of intravenous treatment (days)	3.6 (1.5)	7.0 (2.0)	3.4 (2.8 to 3.9)

BMJ. 2006 Dec 9;333(7580):1193

Et dans la vie réelle ?

Intravenous-to-oral antibiotic switch therapy: a cross-sectional study in critical care units

Juliano Gasparetto[1], Felipe Francisco Tuon[2*], Dayana dos Santos Oliveira[2], Tiago Zequinao[1], Gabriel Rammert Pipolo[1], Gabriel Velloso Ribeiro[1], Paola Delai Benincá[1], June Alisson Westarb Cruz[3] and Thyago Proenca Moraes[1]

Table 1 Characteristics of patients in the oral switch stewardship program

Data	All ($n = 349$)		No oral switch ($n = 238$)		Oral switch ($n = 111$)		*P*-value	Odds ratio	Multivariable analysis
	N	%		%		%			
Male	208	59.7%	132	56%	77	69%	0.010	1.79 (1.11–2.89)	NS
Female	140	40.3%	106	45%	34	31%			
Heart failure class IV	41	12%	25	11%	16	15%	0.181		
Immunosuppression	27	8%	17	7%	10	9%	0.324		
Cirrhosis	7	2%	5	2.1%	2	1.8%	0.662		
Respiratory		189		54.3%	122		51.3%	67	60.9%
Urinary		38		10.9%	32		13.4%	6	5.5%
Abdominal		45		12.9%	37		15.5%	8	7.3%
Skin and soft tissue	25	7.2%	11	4.6%	14	12.7%			

Table 2 Isolated bacteria by intervention group

	No oral switch ($n = 238$)		Oral switch ($n = 111$)		All ($n = 349$)		*P*-value
	N	%	N	%	N	%	
Negative	129	54%	76	69%	205	59%	0.024
Gram-positive	26	11%	15	14%			0.027
Stenotrophomonas maltophilia	1	0%	1	1%	2	1%	0.433
Listeria monocytogenes	1	0%	0	0%	1	0%	–
CN Staphylococcus	0	0%	1	1%	1	0%	0.433
Staphylococcus aureus	14	6%	6	5%	20	6%	0.372
MSSA	5	2%	3	3%	8	2%	
MRSA	9	4%	3	3%	12	3%	
Streptococcus pneumoniae	4	2%	4	4%	8	2%	0.097
Enterococcus spp.	4	2%	1	1%	4	1%	0.403

Total hospitalization (days)	13 (8–21)	13 (8–22)	13(8–20)	0.665
Days in the ICU	6 (4–9)	6 (4–10)	5 (3–7)	0.029

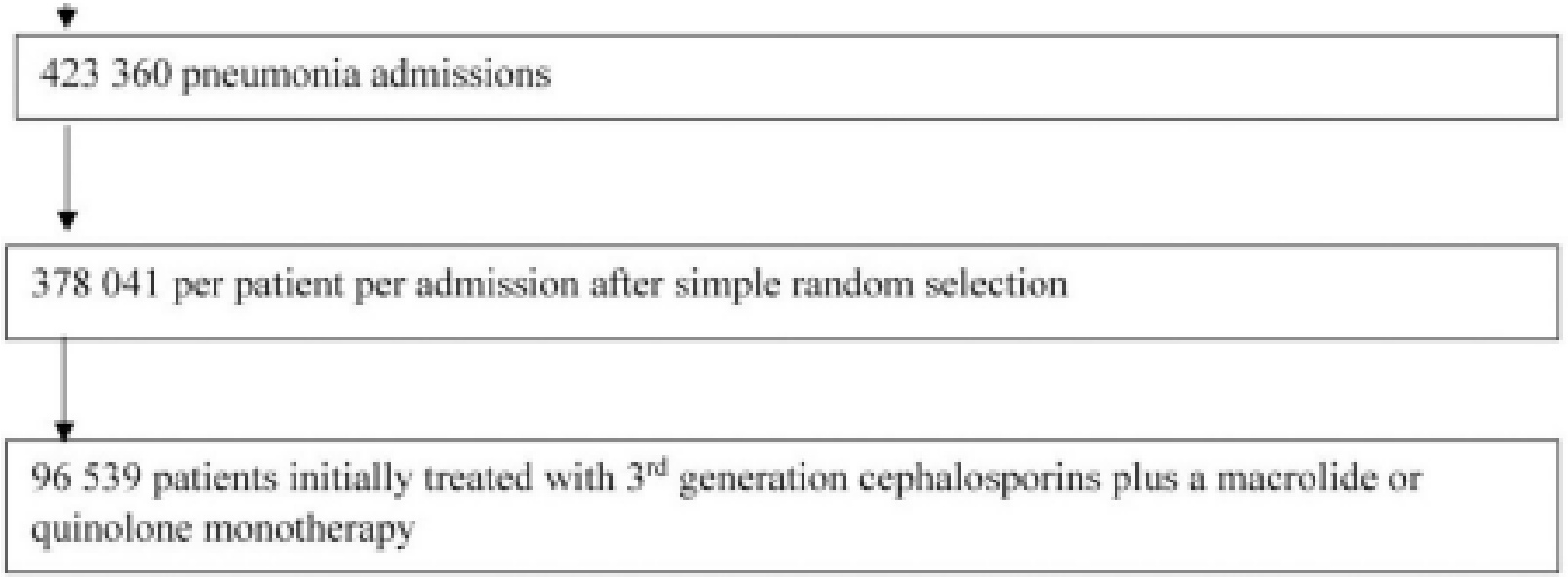
and chronic health evaluation

Intravenous to Oral Antibiotic Switch Therapy Among Patients Hospitalized With Community-Acquired Pneumonia

Abhishek Deshpande[1,2], Michael Klompas[3,4], Ning Guo[1,5], Peter B. Imrey[5,6], Andrea M. Pallotta[7], Thomas Higgins[8], Sarah Haessler[9], Marya D. Zilberberg[10], Peter K. Lindenauer[11], Michael B. Rothberg[1]

Clin Infect Dis. 2023 July 26; 77(2): 174–185

- 642 US hospitals from 2010 through 2015
- Adults admitted with CAP
- Initially treated with IV antibiotics
- Early switchers: switched to oral antibiotics by hospital day 3



30,7 % traitement oral avant sortie
(5,8% avant ou à J3)

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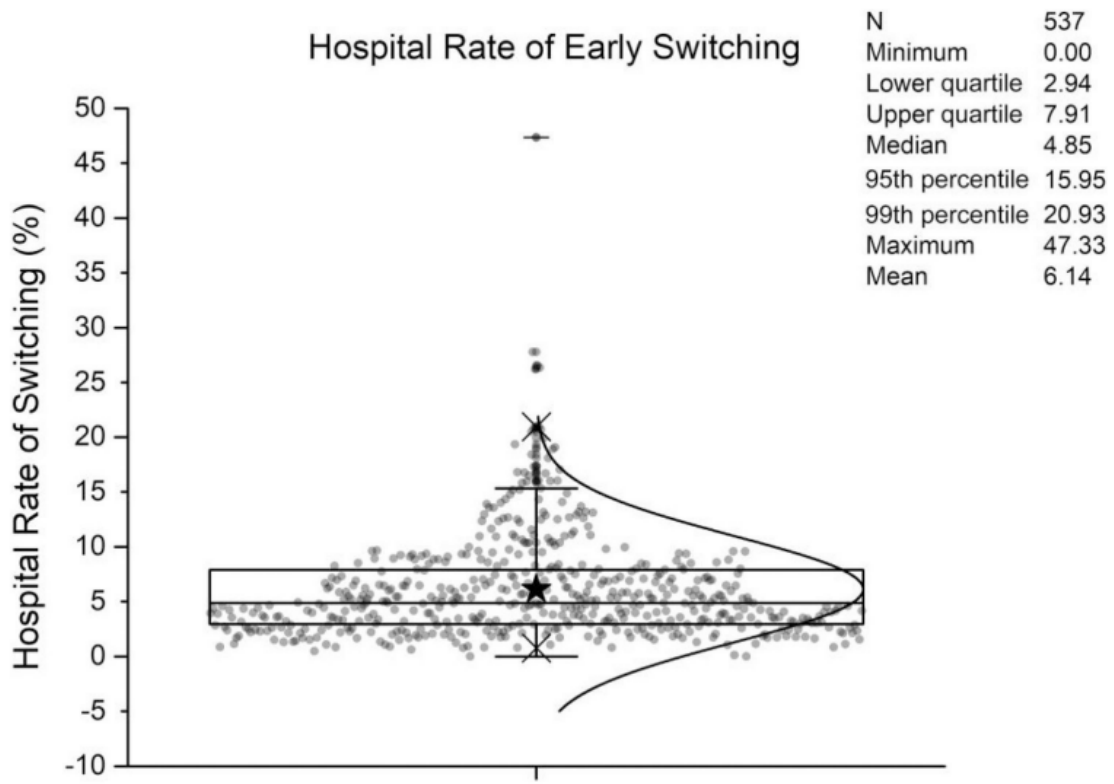


Figure 3.
Superimposed dot plot and box plot of hospital fractions of community-acquired pneumonia (CAP) patients who were receiving initial intravenous (IV) antibiotics and then switched to oral antibiotics within 3 days for N = 537 hospitals with at least 100 CAP patients initially receiving IV antibiotics. Black star represents mean.

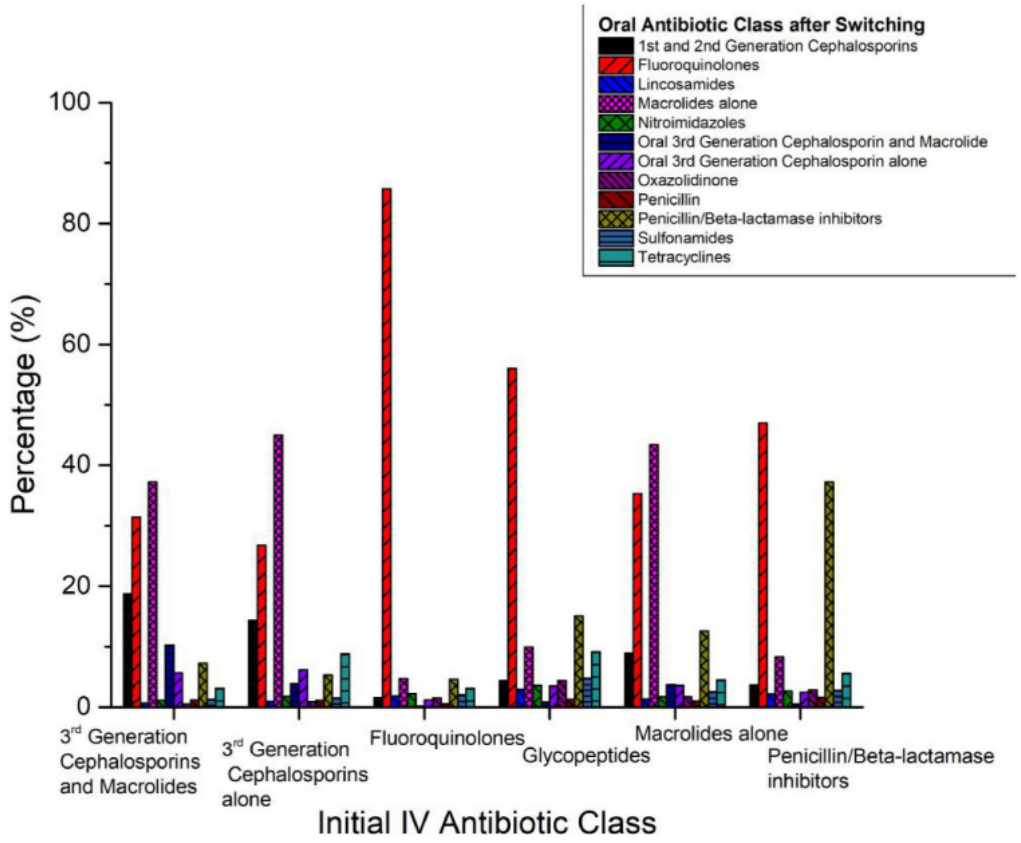


Figure 2.
Comparative distributions of oral antibiotic class after switching (colored bars, percentages of patients) by class of initial IV antibiotic (horizontal axis label). Abbreviation: IV, intravenous.

Intravenous to Oral Antibiotic Switch Therapy Among Patients Hospitalized With Community-Acquired Pneumonia

Abhishek Deshpande[1,2], Michael Klompas[3,4], Ning Guo[1,5], Peter B. Imrey[5,6], Andrea M. Pallotta[7], Thomas Higgins[8], Sarah Haessler[9], Marya D. Zilberberg[10], Peter K. Lindenauer[11], Michael B. Rothberg[1]

Clin Infect Dis. 2023 July 26; 77(2): 174–185

Population « passage par voie orale »

- En réanimation => 4,5%
- Sous ventilation invasive => 0,77%
- Sous amines => 0,37%

Adjusted Outcomes Comparing Odds of Events for Patients Who Were Switched Early vs Others on Hospital Day 3

	Entire Cohort		Subgroup of Patients (Ceftriaxone + Macrolide or Quinolone Monotherapy)	
Hospitalization Outcome	**Odds Ratio[a]**	***P* Value**	**Odds Ratio[a]**	***P* Value**
14-day in-hospital case fatality	0.65 (.55–.77)	<.0001	0.77 (.54–1.11)	.16
Late intensive care unit admission (hospital day 3+)	0.66 (.58–.75)	<.0001	0.75 (.57–.99)	.04
Late invasive mechanical ventilation initiation (hospital day 3+)	0.67 (.57–.79)	<.0001	0.84 (.60–1.17)	.31
Late vasopressor initiation (hospital day 3+)	0.70 (.60–.82)	<.0001	0.77 (.56–1.06)	.11
Clostridium difficile infection	0.58 (.28–1.23)	0.16	0.57 (.10–3.26)	.53
	Ratio of means		**Ratio of means**	
Total duration of intravenous antibiotic treatment	0.44 (.44–.44)	<.0001	0.41 (.41–.41)	<.0001
Total duration of antibiotic treatment	0.88 (.87–.88)	<.0001	0.92 (.92–.93)	<.0001
Length of stay	0.85 (.85–.86)	<.0001	0.90 (.89–.90)	<.0001
Cost[b]	0.84 (.84–.84)	<.0001	0.89 (.89–.90)	<.0001

Data are odds ratios (95% confidence intervals) except for cost and length of stay (mean multipliers).

Pourquoi est-ce pertinent ?

- Réévaluation et stratégie de désescalade (**ça oblige à une réflexion pertinente**) : ce sont des bonnes pratiques
- Retrait d'une voie veineuse
  - **Diminution du risque d'infection liée aux soins**
  - **Moindre travail infirmier**
- Moindre coût
- **MOINS de plastique**

Reducing plastic waste in intensive care from longer use of intravenous administration and invasive monitoring sets: A before-and-after study

Marc Schluep [a,*], Martijn Minheere [a], Michelle Baus [a,b], Stefan Machielse [c], Anita Donkers [d], Heleen Vroman [e]

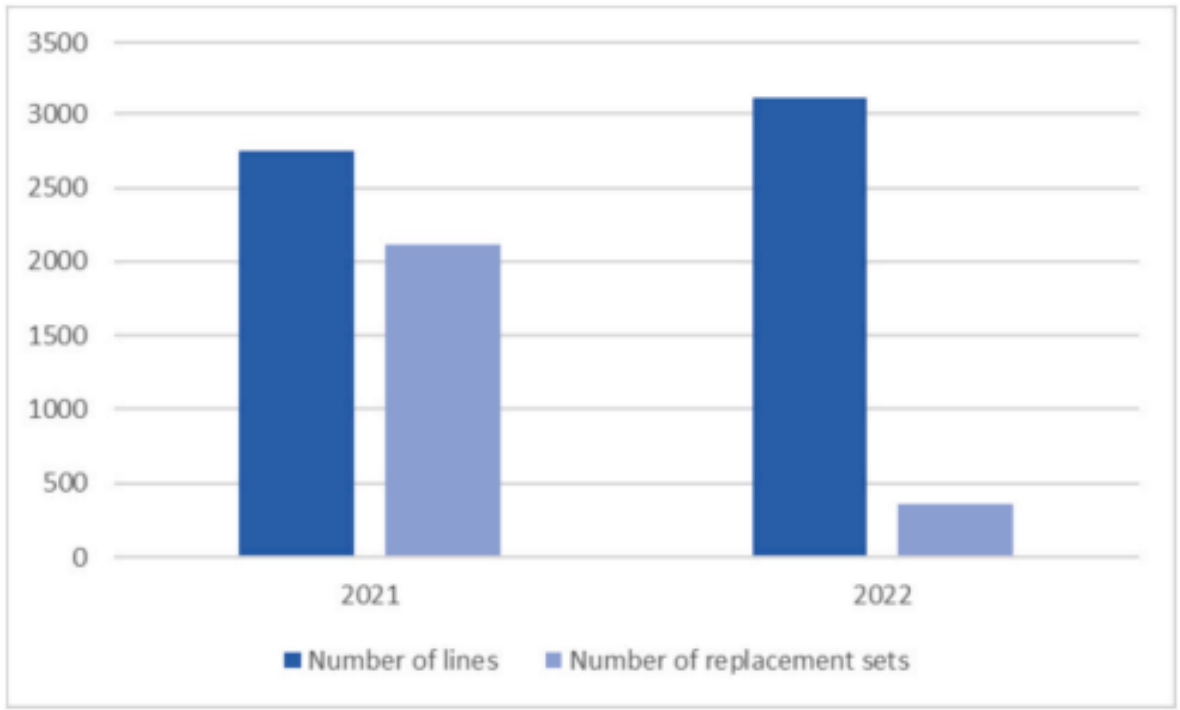


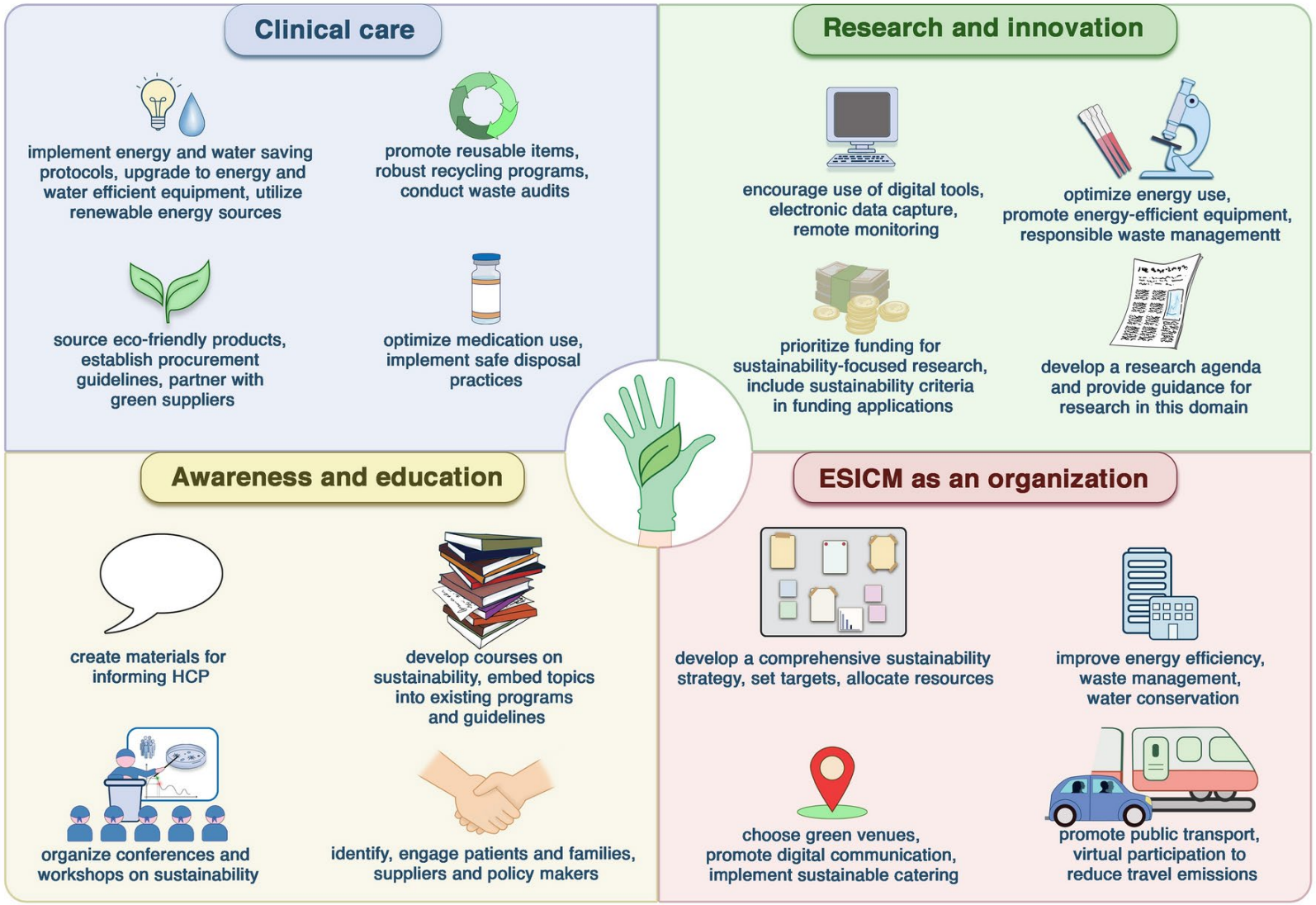
Fig. 1. The total number of lines used (n)in one year in the ICU and the number of line replacement sets needed. In 2022 we implemented the change to a 7-day replacement interval. Specified counts can be found in Table 2.

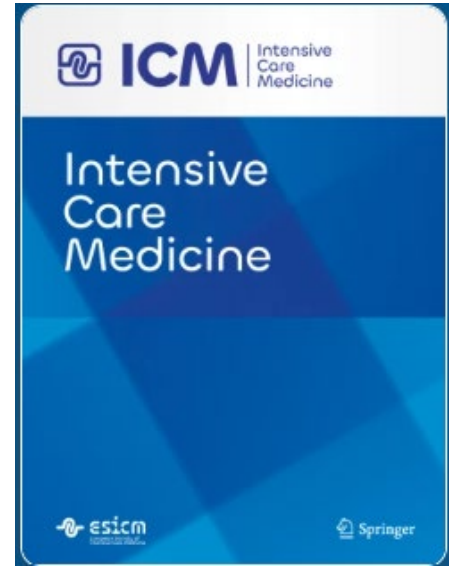
Table 3
Number of replacements saved in both years calculated by comparing a 7-day replacement interval as opposed to a 4-day interval. Further described are the impact on plastic waste reduction in kilograms and the subsequent reduction in nursing workload and cost reduction. *Materials and nursing staff salary.

	2022
Number of replacements saved	881
Time saved in total, hours	96
Cost reduction*, euro	33,288
Plastic waste reduction, kg	182

Journal of Critical Care 84 (2024) 154900

Environmental sustainability in intensive care: the path forward. An ESICM Green Paper



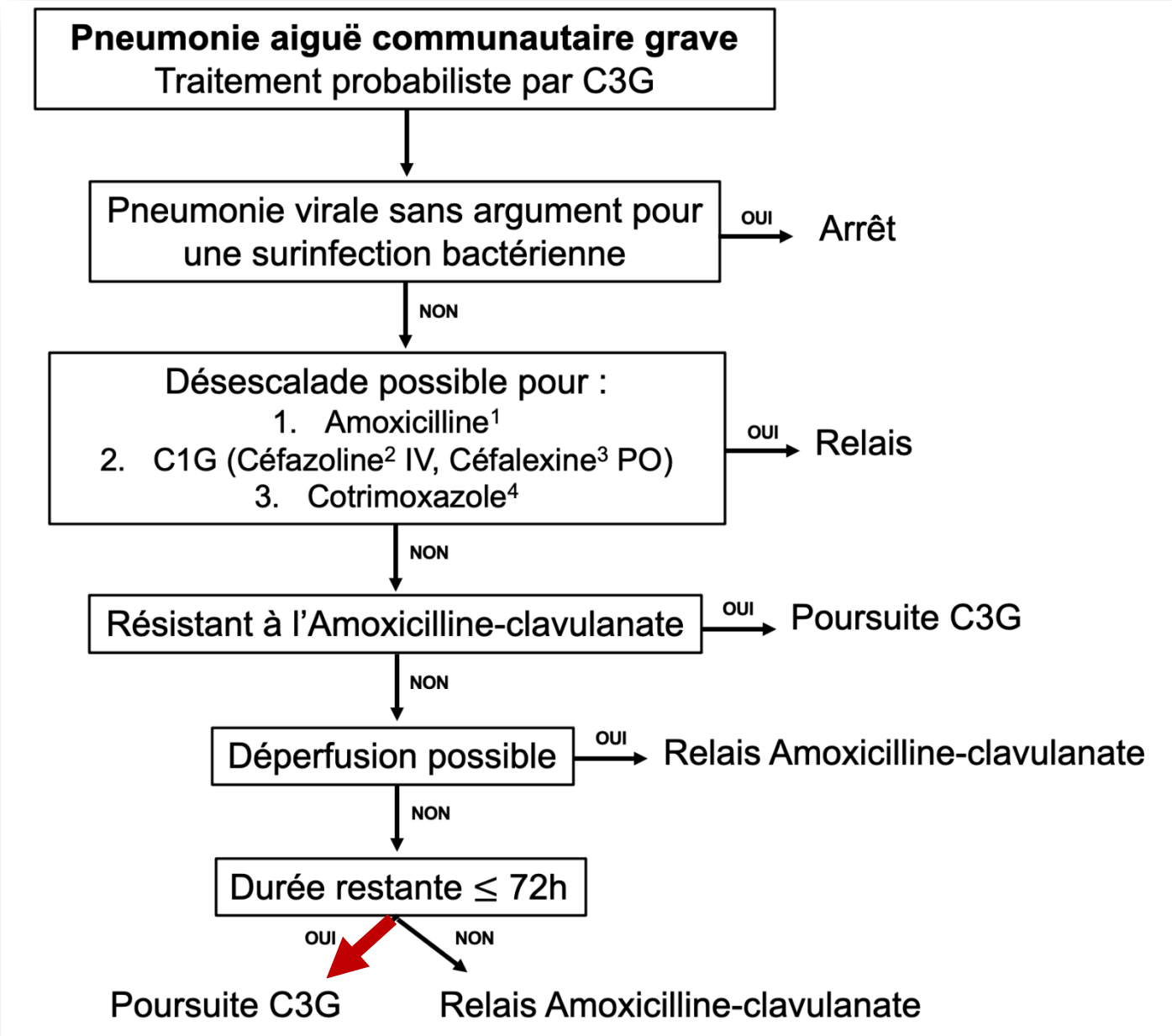


GROUPE SRLF RÉAGIR!

Exemple

Pneumonie aiguë communautaire

(Merci Simon Herbel)



Message clé

Antibiothérapie initiale toujours intraveineuse chez le patient grave de réanimation

<u>Passage per os pertinent :</u>

- Si on peut le déperfuser (donc patient stable)
- Sous réserve d'avoir une désescalade pertinente (spectre plus étroit avec une seule molécule)