

Quelles mesures de prévention efficaces en périodes endémiques pour lutter contre la diffusion des BMR ?

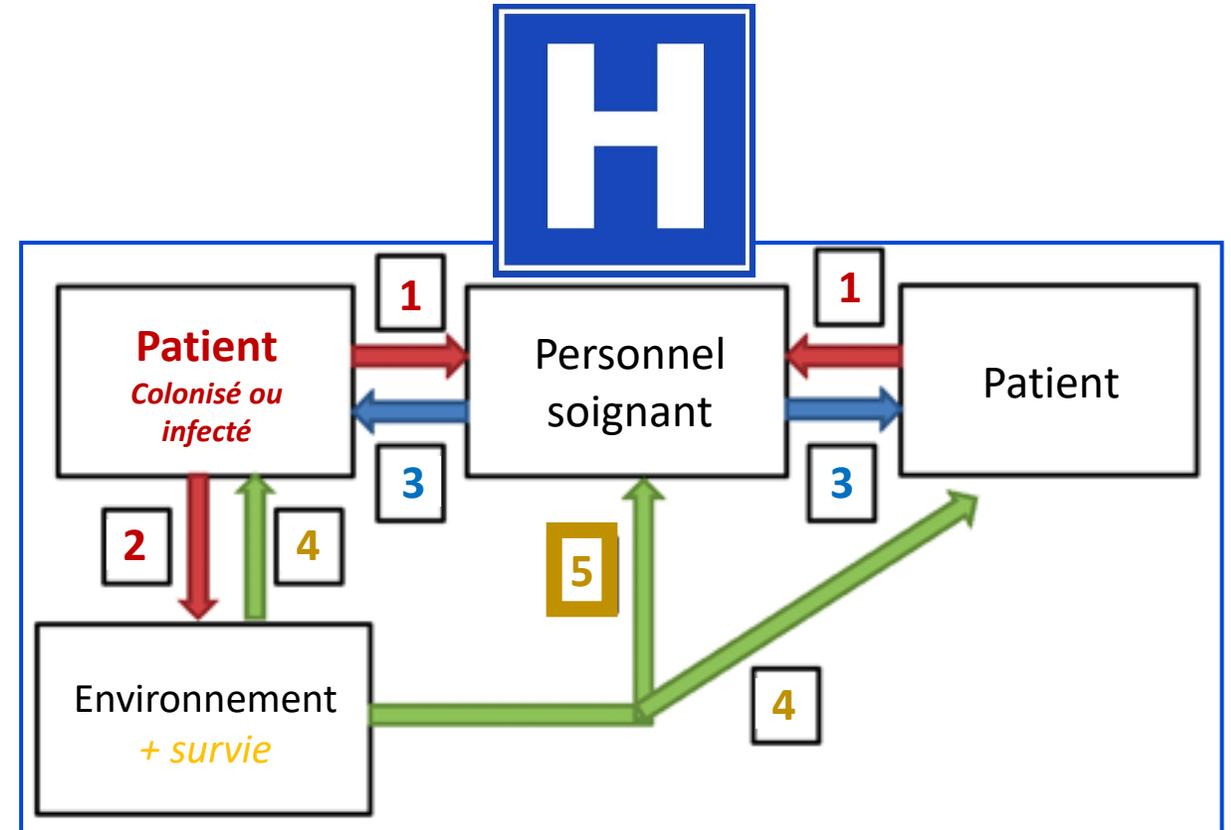
JR Zahar

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Facteurs associés à la diffusion des BMR

- Bactérienne
 - Espèce, « clones à succès »
 - Survie dans l'environnement
- Liée à l'hôte
 - Microbiote intestinal
 - Pression de sélection antibiotique
- Organisationnelle
 - Charge en soin
 - Bio-nettoyage
- Épidémiologique
 - Pression de colonisation



Les mesures possibles pour maîtriser le risque

- **Horizontales**

- Applicables chez tous les patients quel que soit leur statut
- Basée sur les précautions standard
- Peuvent y être associée une politique de décontamination
 - Cutanée (chlorhexidine)
 - Nasale (Mupirocine)
 - Digestive (DDS)

- **Verticales**

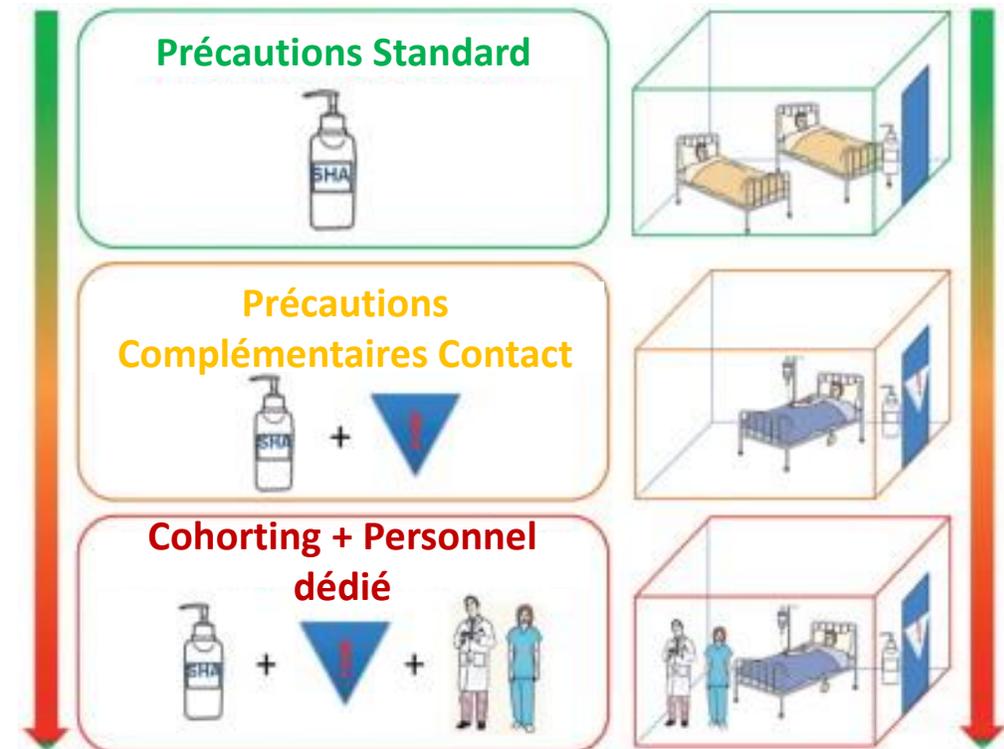
- Applicables autour de certains patients identifiés comme porteurs/infectés
- Basées sur les précautions complémentaires contact

Politiques appliquées et préconisées

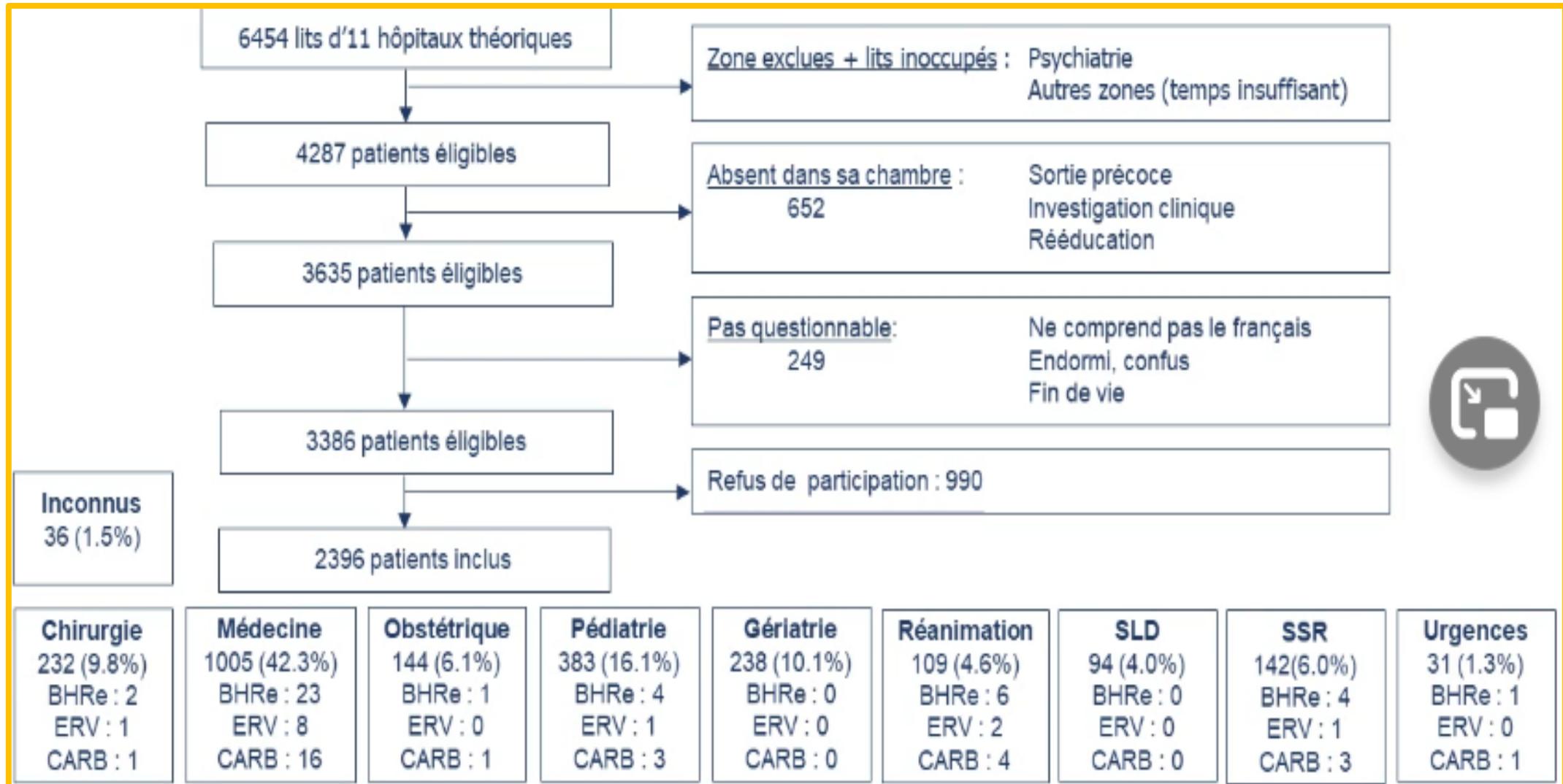
Une série de mesures de contrôle basée essentiellement sur une politique de « **dépistage et contrôle** » avec :

- Surveillance microbiologique
- Mesures barrières :
 - Chambres individuelles
 - Hygiène des mains
 - Précautions complémentaires contact
 - Cohorting

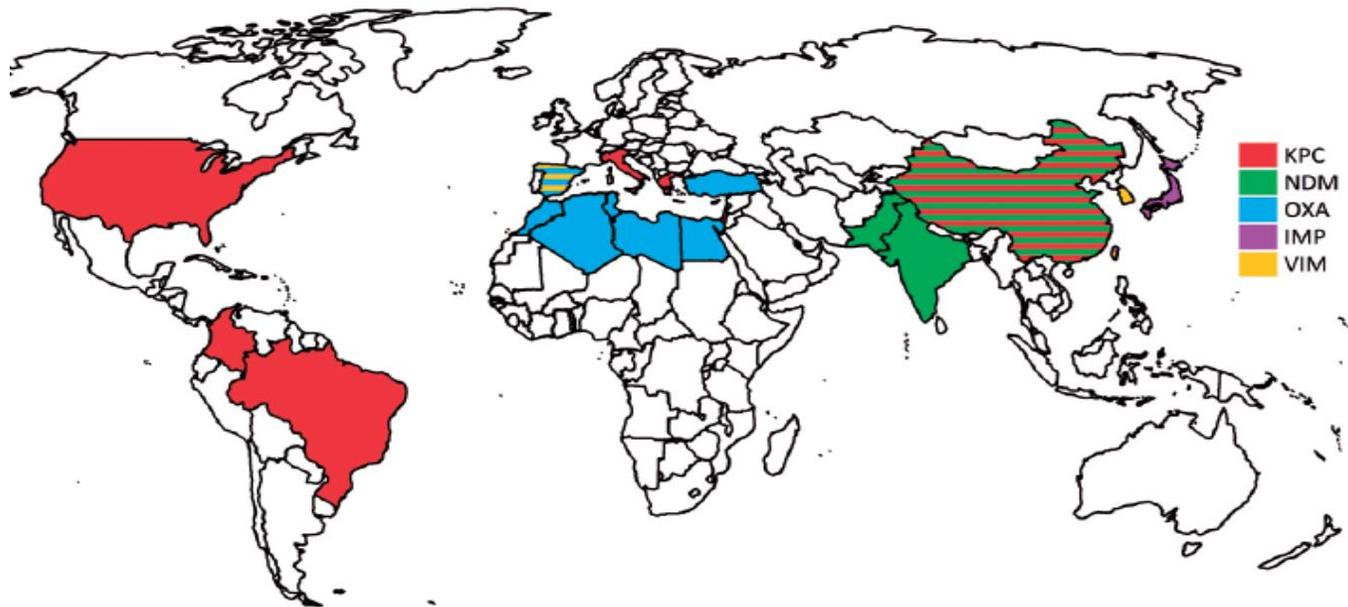
Maitrise de l'antibiothérapie



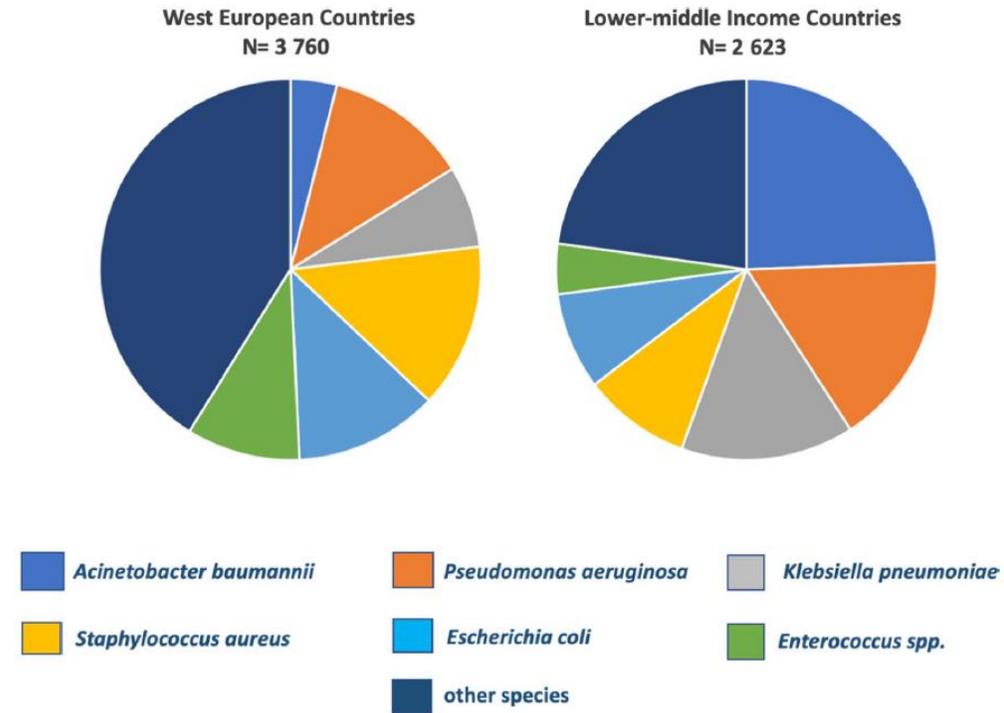
La prévalence un élément clé...



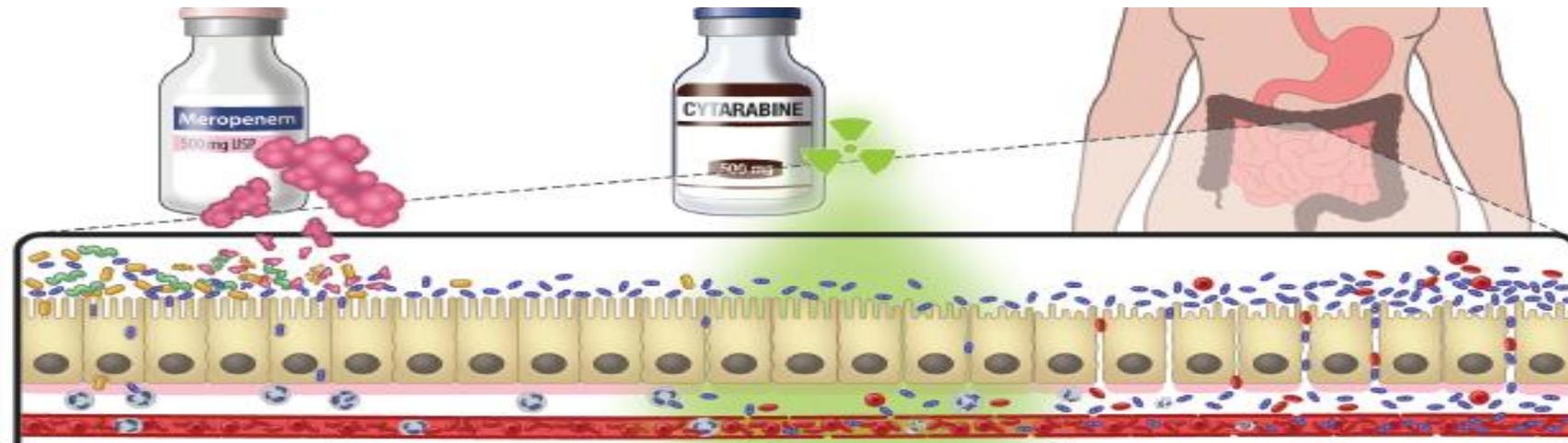
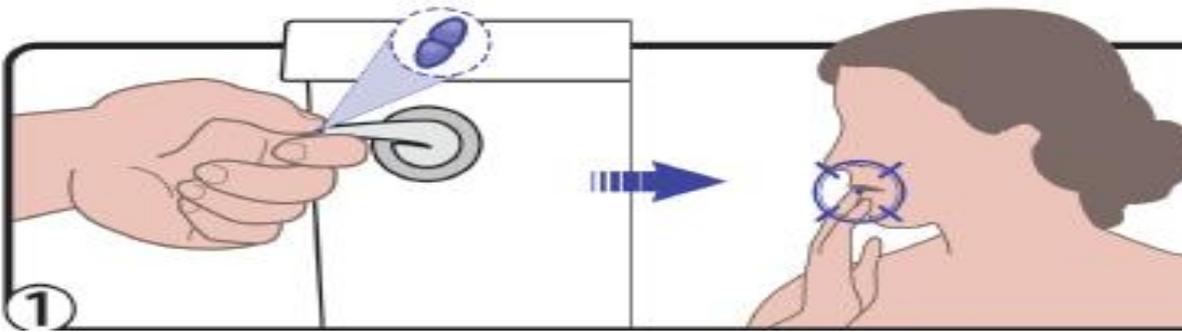
La prévalence un élément clé...



1. Global distribution of the most prominent carbapenemases in each country.



2 mesures à elles seules seraient suffisantes



Le Guern R, Grandjean T, Bauduin M, Figeac M, Millot G, Loquet A, Faure K, Kipnis E, Dessein R. Impact of the Timing of Antibiotic Administration on Digestive Colonization with Carbapenemase-Producing *Enterobacteriaceae* in a Murine Model. *Antimicrob Agents Chemother*. 2019 May 24;63(6):e00360-19.

Les mesures supplémentaires proposées et leurs limites

Politique de screening

- Définition des populations à risque, tenant compte du contexte épidémiologique et l'expansion en communautaire
- Sensibilité des méthodes de diagnostic microbiologique
- Disponibilité des techniques de dépistage et leurs couts

70%

Permet d'identifier le réservoir
Permet d'augmenter le niveau de vigilance

Chambre individuelle

- Disponibilité
- Nécessité débattue. Non-infériorité des chambres à plusieurs lits
- Risque augmenté d'effets indésirables physiques et psychologiques évitables

Permet de maitriser le risque environmental
Permet d'augmenter le niveau de vigilance

L'isolement contact est-il efficace pour les BLSE?

13 European ICUs between May, 2008, and April, 2011, in three phases

(phase 1) 6 month baseline period

(phase 2) Hand hygiene improvement programme at all ICUs in an interrupted time-series phase

Of 41 558 hand hygiene opportunities, mean compliance was 52% in phase 1, **69% in phase 2**

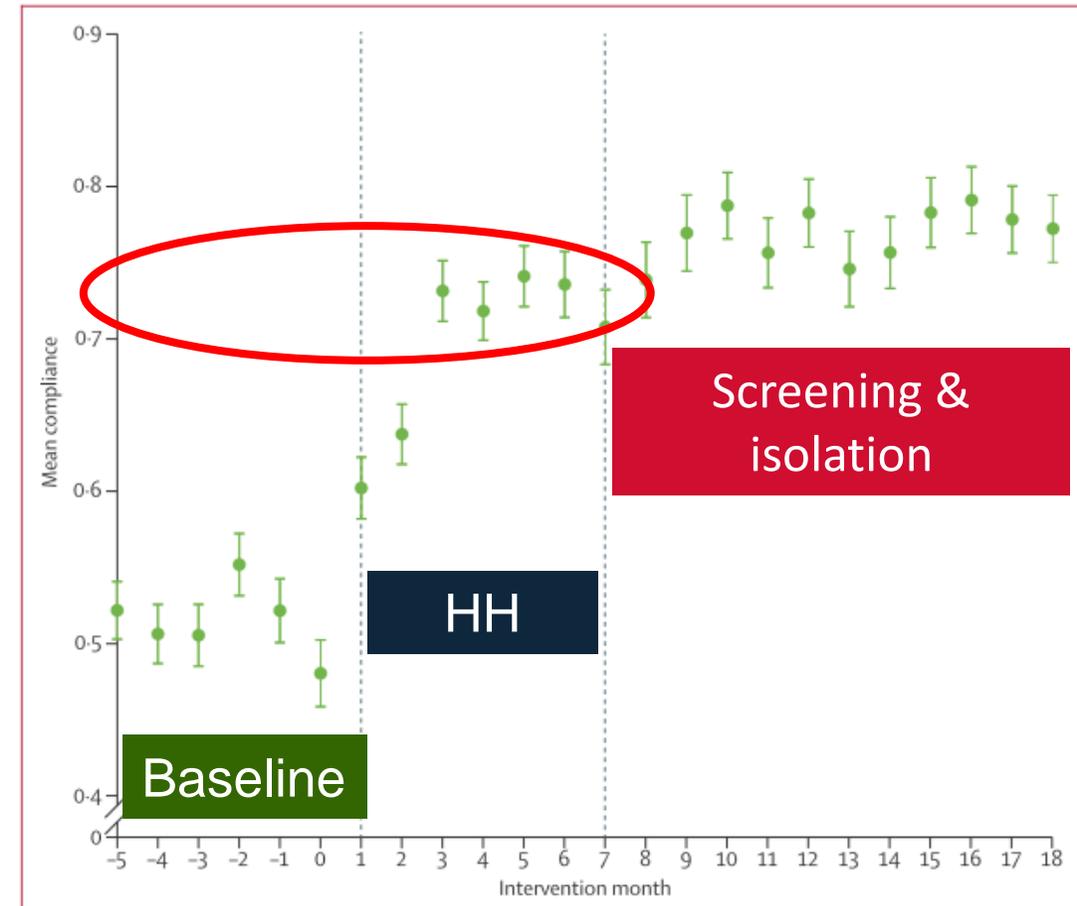


Figure 2: Mean hand hygiene compliance per month
Hand hygiene improvement intervention introduced at month 0. Error bars are 95% CIs.

Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial

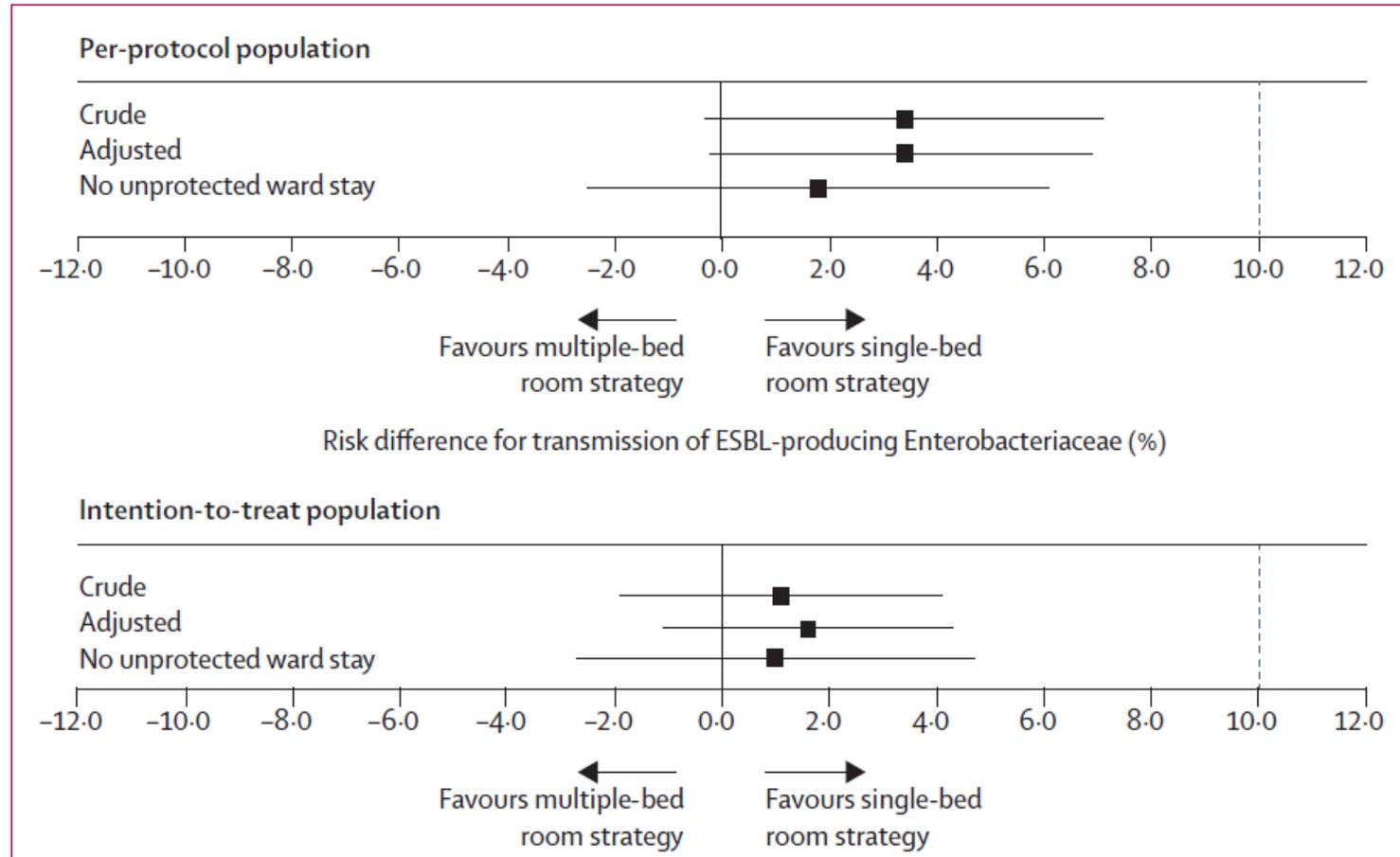
	Antimicrobial-resistant bacteria	MRSA	VRE	HRE
Phase 1 trend	1.014 (0.996–1.031; p=0.12)	1.042 (1.010–1.075; p=0.01)	1.000 (0.971–1.030; p=0.99)	1.012 (0.992–1.032; p=0.25)
Phase 2 step change	0.955 (0.676–1.348; p=0.79)	1.159 (0.654–2.053; p=0.61)	0.884 (0.481–1.626; p=0.69)	0.831 (0.559–1.235; p=0.36)
Phase 2 change in trend	→ 0.976 (0.954–0.999; p=0.04)	→ 0.925 (0.890–0.962; p<0.001)	0.982 (0.945–1.020; p=0.36)	0.994 (0.968–1.021; p=0.66)
Phase 3 step change	0.634 (0.349–1.153; p=0.14)	0.755 (0.252–2.257; p=0.62)	0.651 (0.209–2.031; p=0.46)	0.525 (0.263–1.048; p=0.07)
Phase 3 change in trend	1.015 (0.998–1.032; p=0.09)	1.057 (1.029–1.086; p<0.001)	1.015 (0.984–1.048; p=0.34)	0.991 (0.971–1.011; p=0.35)
Phase 3 step change (rapid vs conventional screening)	1.696 (1.090–2.638; p=0.02)	1.734 (0.768–3.916; p=0.19)	1.735 (0.711–4.234; p=0.23)	1.691 (1.012–2.828; p=0.05)
Phase 3 change in trend (rapid vs conventional screening)	0.996 (0.984–1.007; p=0.46)	0.985 (0.956–1.005; p=0.15)	0.993 (0.969–1.018; p=0.59)	1.000 (0.986–1.014; p=0.99)
Likelihood ratio test (rapid vs conventional screening)	p=0.06	p=0.34	p=0.47	p=0.10

MRSA

Data are IRR (95% CI) unless stated otherwise. IRR <1 represents a decrease in acquisition, whereas IRR >1 represents an increase. Cluster effects were accounted for in the analyses, and potential confounding factors (sex, age, month, invasive devices, nurse-to-patient staffing ratio, location before ICU admission, reason for admission, APACHE/SAPS, hospital, and number of days-at-risk for acquisition) were fitted as covariates. MRSA=meticillin-resistant *Staphylococcus aureus*. VRE=vancomycin-resistant enterococci. HRE=highly resistant Enterobacteriaceae. IRR=incidence rate ratio. APACHE=Acute Physiology and Chronic Health Evaluation. SAPS=Simplified Acute Physiology Score.

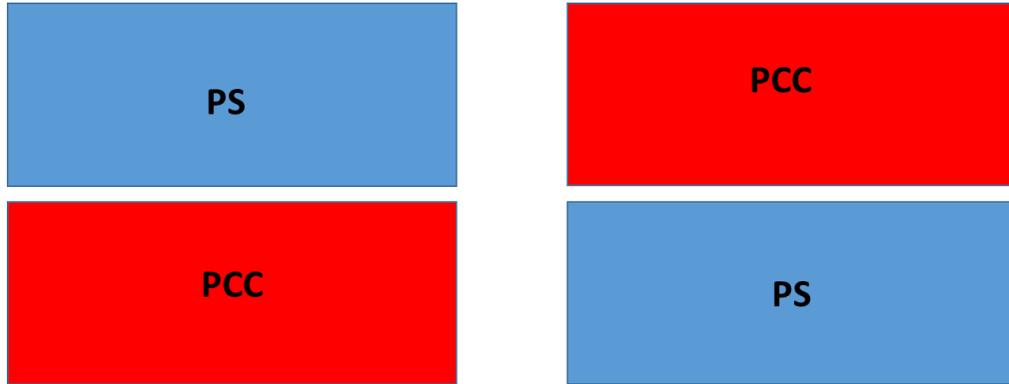
La politique de dépistage ne permet pas de réduire le risque de transmission des bactéries digestives résistantes aux antibiotiques VRE et HRE

L'intérêt de la chambre individuelle ?



La chambre double n'est pas inférieure à la chambre individuelle lorsque les Précautions complémentaires contact sont respectées

L'intérêt des Précautions complémentaires contact



	PS	PCC
Chambre individuelle	NON	Oui (si possible)
Gants	Au contact des fluides	Systématique
Protection tenue professionnelle	Soins salissants ou mouillants	systématique
HDM	oui	oui

Les PS si respectées à un haut niveau sont équivalentes aux PCC

Le dépistage est il utile ?

Outcomes	Relative effect (95% CI) – Patients/ studies	Effect	Certainty of evidence (GRADE)	Key messages
All-cause mortality	– Interrupted time series 2 studies 27,30	One study assessing surveillance alone reported that no differences were observed on mortality rate in the ICU (pre-intervention period: 8.8%; post-intervention period: 9.0%). ³⁰ One study assessing surveillance as part of a multimodal intervention reported that no difference was observed on mortality risk. ²⁷	⊕⊕○○ ^{*1,†} LOW	Screening strategy may result in little to no difference in the risk of all-cause mortality.
Length of hospital stay	– Interrupted time series 4 studies 26,27,28,30	One study assessing surveillance alone reported that no differences were observed in the length of ICU hospital stay (pre-intervention period: median 1 day (IQR= 1-6); post-intervention period: median 1 day (IQR=1-6)). ³⁰ Three studies assessing surveillance as part of a multimodal intervention reported that no differences were observed in the length of hospital stay. ^{26,27,28}	⊕⊕○○ ^{*1,†} LOW	Screening strategies may result in little to no difference in the length of hospital stay.
Carbapenem- resistant gram-negative bacteria infection	– Interrupted time series 8 studies 20,22,25,27,28,30,31,33	One study assessing surveillance alone reported an increase in infection by 13.04% every month (95% CI: 5.2- 21.5) during the pre-intervention period and a decrease in the infection rate during the intervention period (monthly percent change, –3.57%; 95% CI –6.9 to –0.1). ³⁰ On the other hand, from 7 studies assessing surveillance as part of a multimodal intervention, 6 reported a significant reduction in the infection rate after the implementation of surveillance cultures.	⊕⊕○○ ^{*1,†} LOW	Screening strategies may reduce the risk of carbapenem-resistant gram-negative bacteria infection.
Carbapenem- resistant gram-negative bacteria colonization	– Interrupted time series 9 studies. ^{21,23,24, 25, 27,30,32,33,34}	Two studies assessed surveillance alone. One study reported a decrease in the colonization rate during the intervention period (monthly percent change –3.02% (95% CI: –4.7 to –1.3)). ³⁰ Another study reported an increase in the CRE colonization rate from 1.0 per 1,000 admissions when the intervention was implemented to 2.7, but the proportion of positive screens remained at approximately 0.4% (range 0.2%-0.6%) throughout the study period. ³² All the 7 studies assessing surveillance as part of a multimodal intervention reported a significant reduction in colonization rate after the implementation of surveillance cultures.	⊕⊕○○ ^{*1,†} LOW	Screening strategies may reduce the risk of carbapenem-resistant gram-negative bacteria colonization

Le dépistage et le risque de faux négatifs

R. Saliba, A. Lomont, J.-L. Eudesson et al.

International Journal of Antimicrobial Agents 59 (2022) 106479

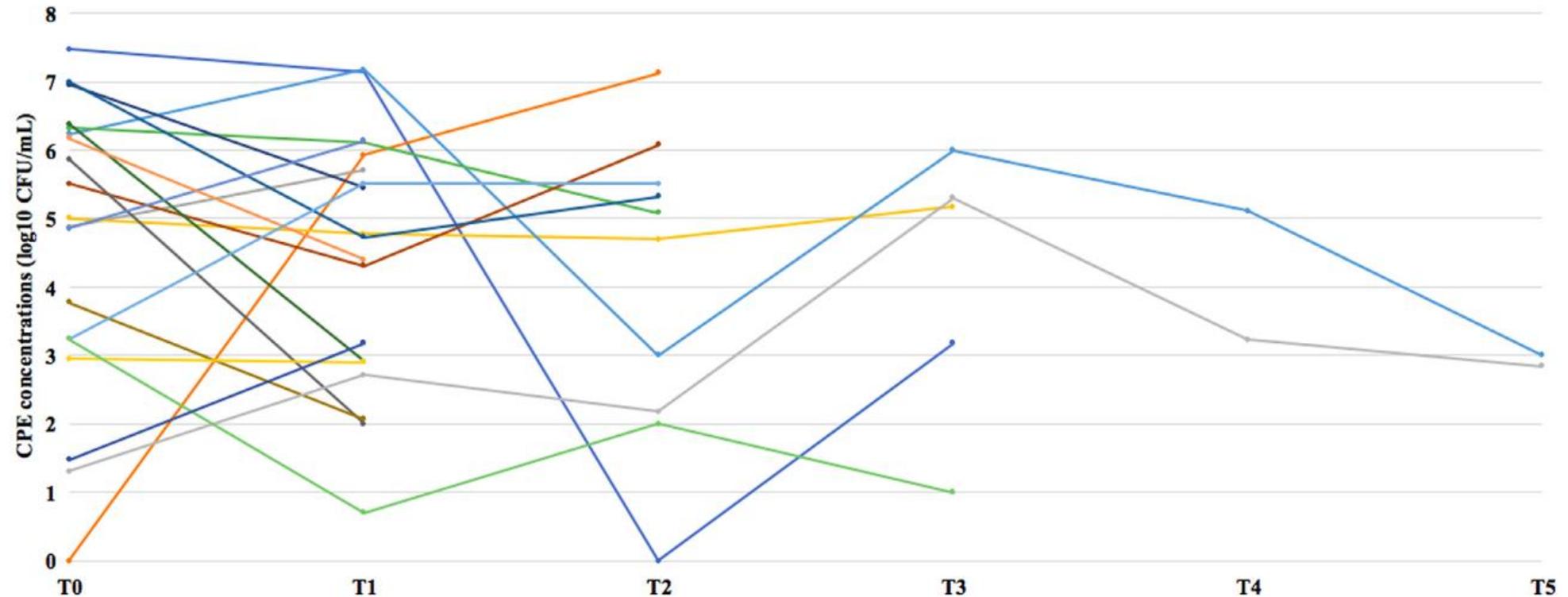
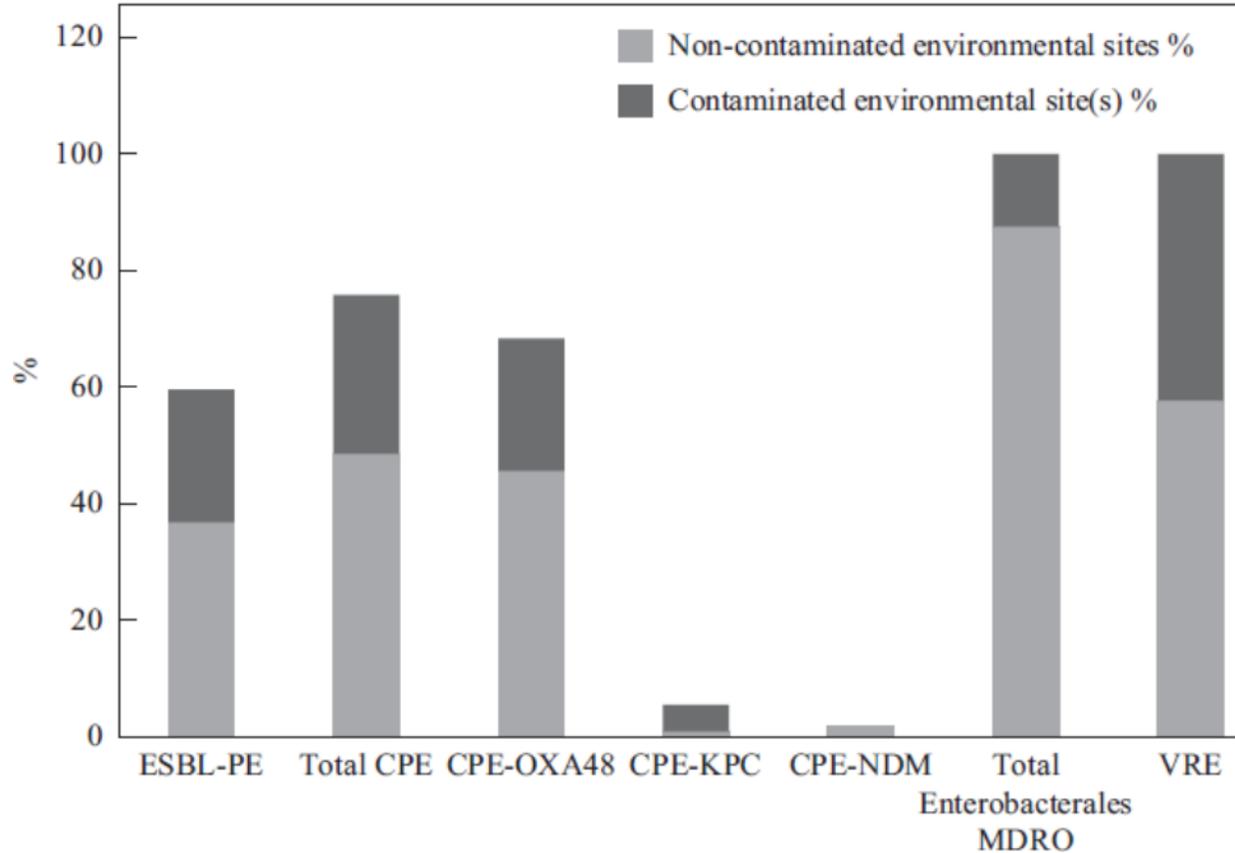
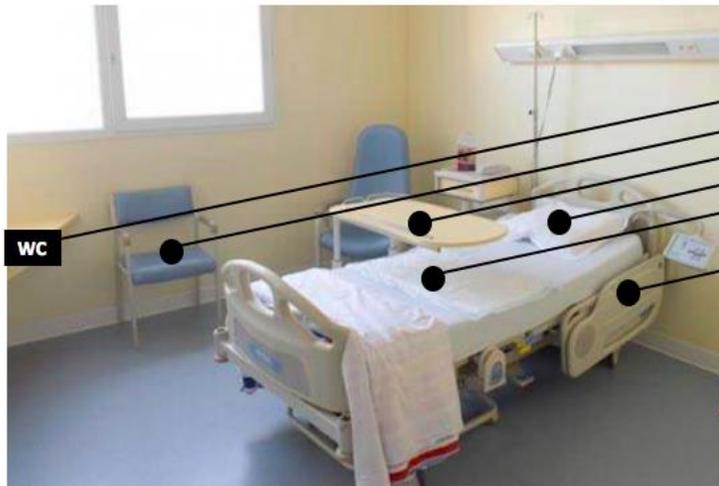


Fig. 1. Variations in carbapenemase-producing Enterobacteriaceae (CPE) concentrations (log₁₀ CFU/mL) between two rectal screening samples for each hospitalisation.

La contamination environnementale



	Site(s) contaminé(s) (n=22)	Site(s) non contaminé(s) (n=103)	P-value
Homme, n (%)	10 (43.7)	62 (60.2)	0.23
Âge (an), médiane [IQR]	63 [53 – 69]	62 [54 – 70]	0.81
Score de comorbidité de Charlson, médiane [IQR]	5 [3.5 – 5.5]	5 [3 – 6.25]	0.72
Admission aux soins intensifs, n (%)	4 (18.2)	24 (23.3)	0.78
Antibiothérapie en cours, n (%)	12 (52.2)	47 (45.6)	0.48
Voyage récent à l'étranger, n (%)	10 (45.4)	44 (43.1)	0.81
Espèce bactérienne, <i>E. coli</i> n (%)	5 (22.7)	58 (56.3)	0.0048
Espèce bactérienne, <i>K. pneumoniae</i> n (%)	5 (22.7)	33 (32)	0.45
Mécanisme de résistance, n (%)			
BLSE	5 (22.7)	38 (36.9)	0.22
EPC	6 (27.2)	54 (52.4)	0.03
OXA-48	5 (22.7)	47 (45.6)	0.03
KPC	1 (4.5)	3 (2.9)	0.56
NDM	0 (0)	4 (3.8)	1
VanA	11 (50)	15 (14.5)	0.0004
Abondance fécale relative (%), médiane [IQR]	10.8 [0.4 – 52]	6 [0.2 – 43]	0.54
Abondance fécale absolue, médiane [IQR]	2.8x10 ⁵ [6.6 x 10 ³ – 1.8 x 10 ⁷]	10 ⁵ [1.6 x 10 ³ – 1 x 10 ⁷]	0.27
Score de dépendance de Katz, médiane [IQR]	3.5 [2.1 – 6]	5 [1.5 – 6]	0.33
Diarrhée, n (%)	5 (22.7)	11 (10.7)	0.17
Incontinence, n (%)	10 (45.4)	42 (40.8)	0.81
Sonde urinaire, n (%)	6 (27.3)	54 (52.4)	0.03
Cathéter veineux central, n (%)	7 (31.8)	31 (30.1)	1
Cathéter veineux périphérique, n (%)	6 (27.3)	41 (39.8)	0.33
Inhibiteur de la pompe à proton, n (%)	11 (50)	49 (47.6)	1
Antidépresseurs, n (%)	2 (9.1)	2 (1.9)	0.14
Antécédent d'hospitalisation < 12 mois, n (%)	16 (72.7)	78 (75.7)	1
Antécédent d'antibiothérapie < 12 mois, n (%)	15 (68.2)	67 (65)	1

Saliba R, Ghelfenstein-Ferreira T, Lomont A, Pilmis B, Carbonnelle E, Seytre D, Nasser-Ayoub E, Zahar JR, Karam-Sarkis D. Risk factors for the environmental spread of different multidrug-resistant organisms: a prospective cohort study. J Hosp Infect. 2021 May;111:155-161

Risque liés aux points d'eau



73 réanimations

3 mois de suivis

51% des siphons contaminés

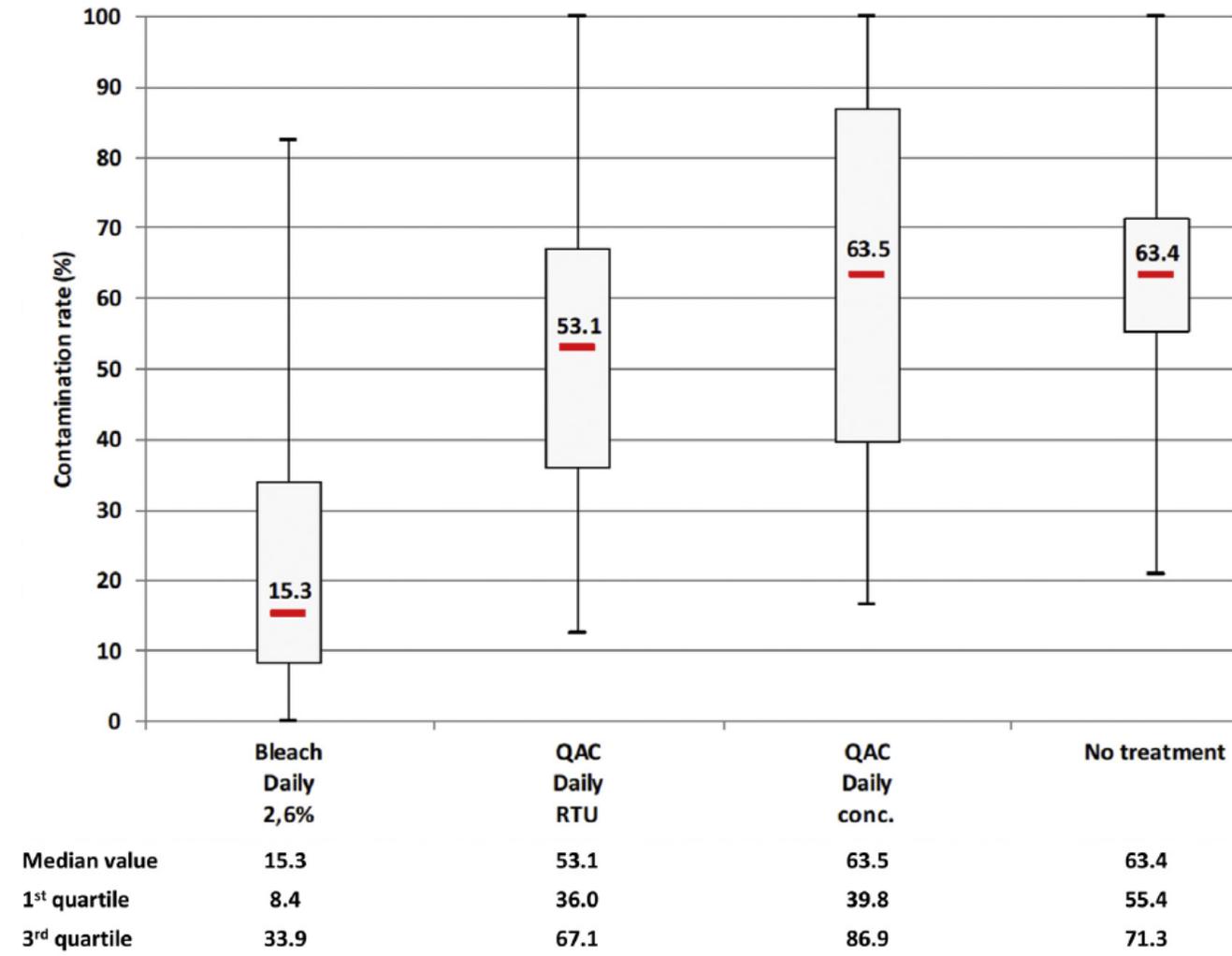
Risques associés à :

Prévalence des contaminations

Proximité du patient

Fréquence de l'entretien

Fréquence des « splachs »



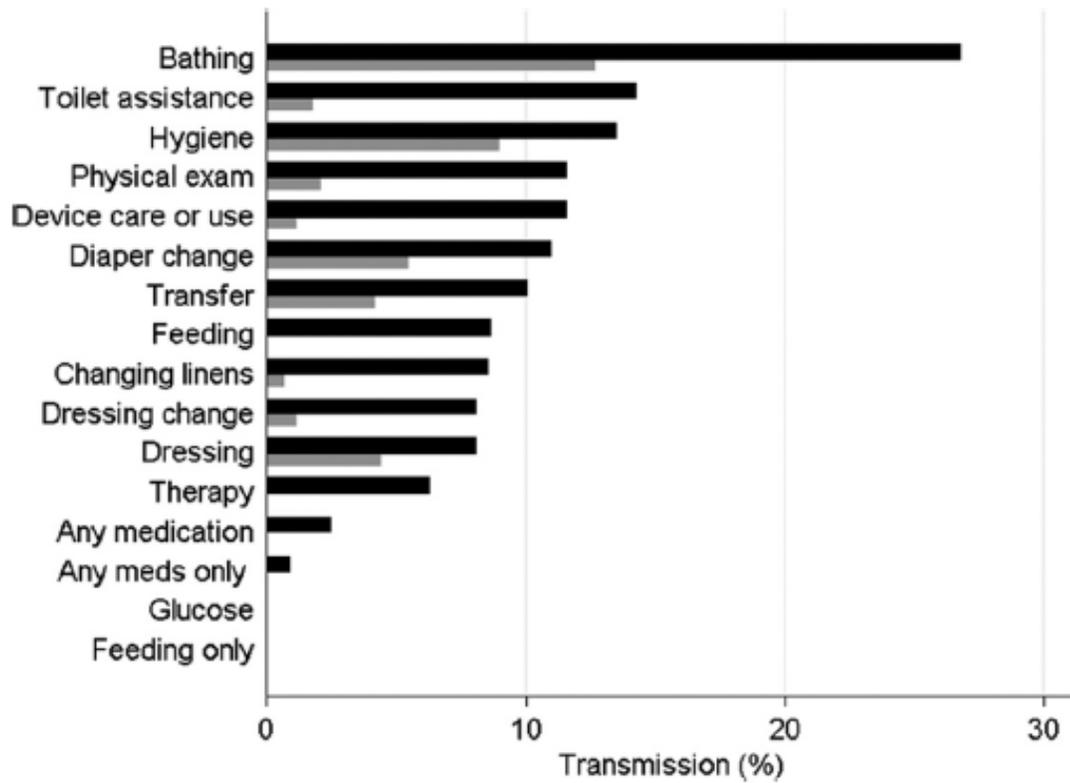
La transmission et ces inégalités ...

- Tous les soins n'ont pas le même risque (acquisition/transmission) (1)
- Tous les patients n'ont pas le même risque d'acquisition (2)
- Tous les services n'exposent pas au même risque (3)
 - Charge en soin
 - Pression de sélection antibiotique
 - Pression de colonisation

1-Blanco N. Transmission of resistant Gram-negative bacteria to healthcare personnel gowns and gloves during care of residents in community-based nursing facilities. *Infect Control Hosp Epidemiol.* 2018 Dec;39(12):1425-1430. 2-Hilliquin D, *et al.* Risk factors for acquisition of OXA-48-producing *Klebsiella pneumoniae* among contact patients: a multicentre study. *J Hosp Infect.* 2018 ;98(3):253-259. 3- Legeay C, Thépot-Seegers V, Pailhoriès H, Hilliquin D, Zahar JR. Is cohorting the only solution to control carbapenemase-producing *Enterobacteriaceae* outbreaks? A single-centre experience. *J Hosp Infect.* 2018 Aug;99(4):390-395.

Transmission of Resistant Gram-Negative Bacteria to Health Care Worker Gowns and Gloves during Care of Nursing Home Residents in Veterans Affairs Community Living Centers

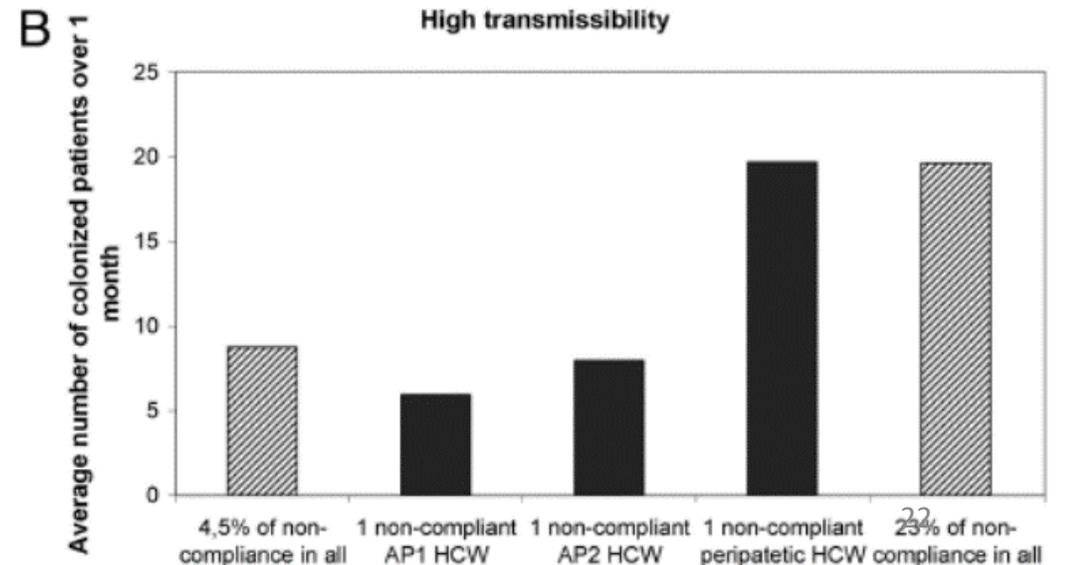
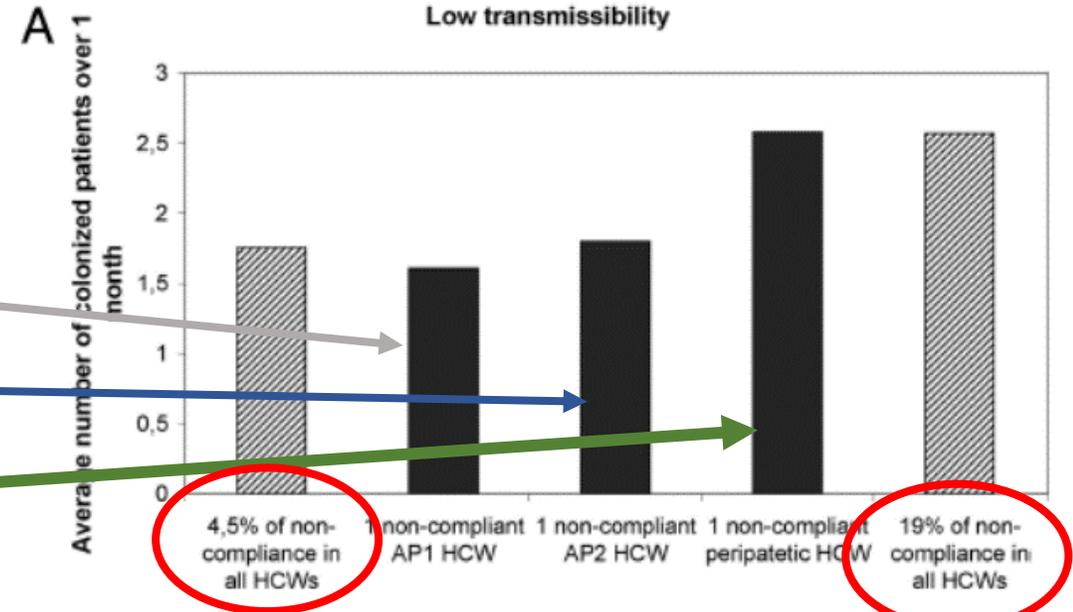
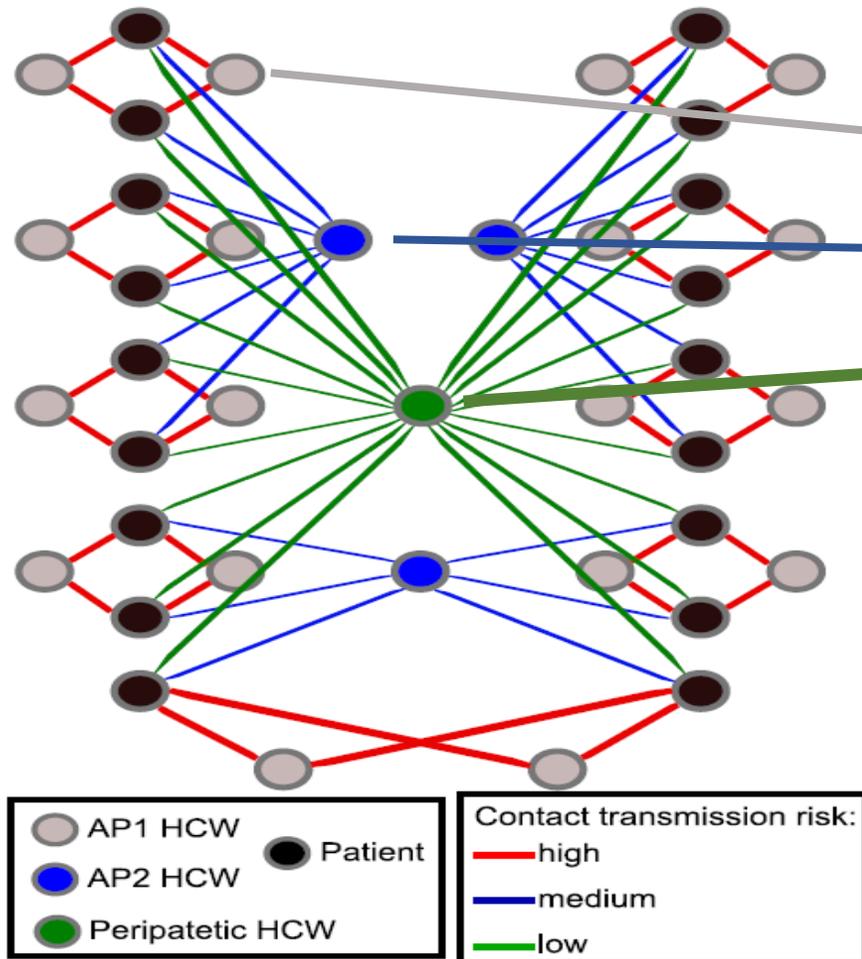
Certains soins sont plus à risque que d'autres



Type of care	No. of interactions	Care given with other care (%)	Transmission to ^a :			
			Gloves		Gowns	
			OR	P value	OR	P value
Bathing	71	83	5.60	<0.01	10.05	<0.01
Toilet assistance	56	80	2.46	0.01	0.76	0.83
Hygiene	111	87	2.22	0.02	7.17	<0.01
Any device care or use	86	56	1.87	0.04	0.45	0.60
Physical exam	95	32	1.75	0.05	1.10	0.89
Transfer of resident	168	72	1.55	0.19	2.35	0.14
Diaper change	145	82	1.48	0.20	0.76	0.03
Dressing change	86	42	1.46	0.25	0.49	0.50
Dressing resident	137	91	1.37	0.37	2.27	0.25
Changing linens	139	42	1.26	0.41	0.25	0.23
Feeding	23	26	0.65	0.74	No transmission	
Any therapy	16	6	0.51	0.73	No transmission	
Any medications	279	19	0.29	<0.01	No transmission	
Any medication alone	227	0	0.12	<0.01	No transmission	
Feeding alone	17	0	No transmission		No transmission	
Glucose monitoring	36	78	No transmission		No transmission	

Blanco N. Transmission of resistant Gram-negative bacteria to healthcare personnel gowns and gloves during care of residents in community-based nursing facilities. Infect Control Hosp Epidemiol. 2018 Dec;39(12):1425-1430.

Il existe des soignants à haut risque

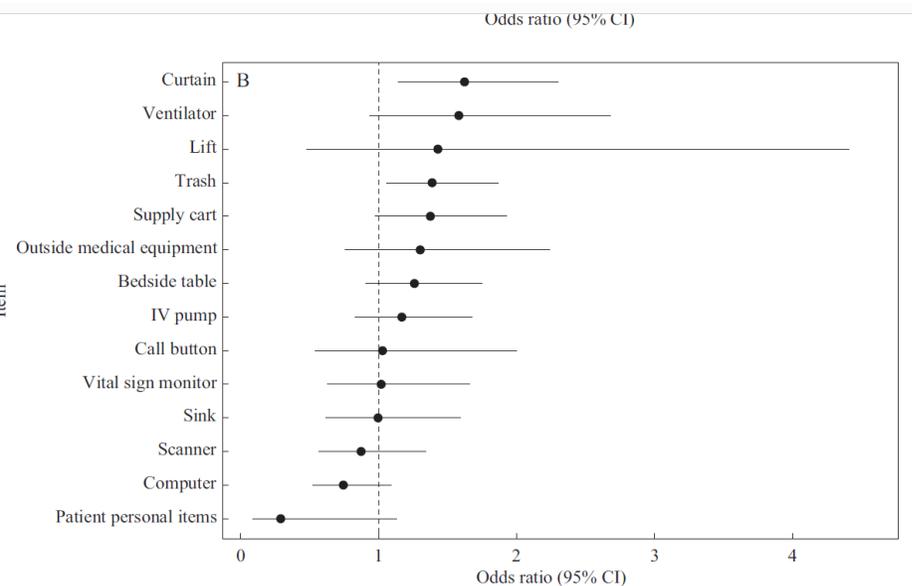


Risk factors for transmission of carbapenem-resistant Enterobacterales to healthcare personnel gloves and gowns in the USA

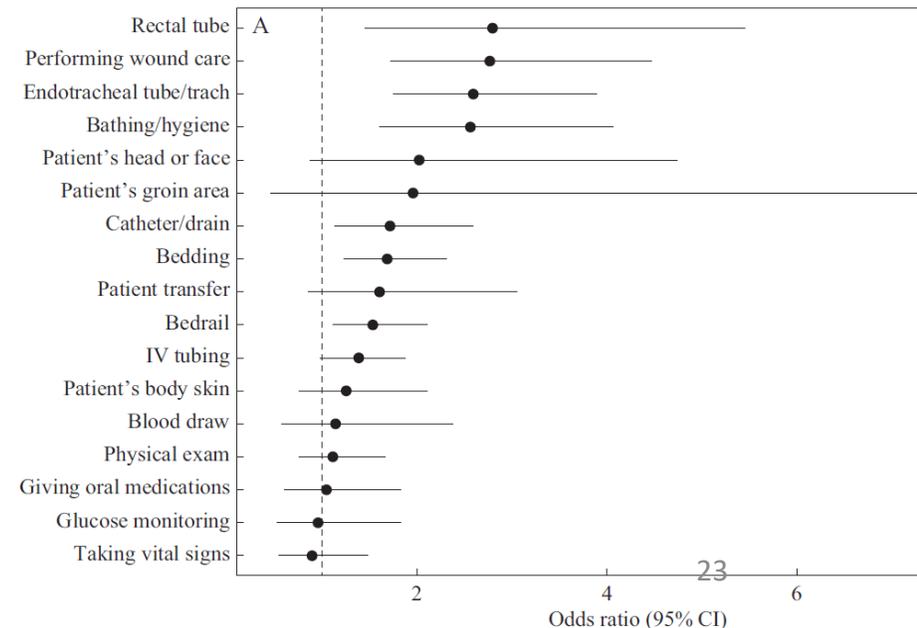
Services à risque

Association between healthcare personnel type and contamination of gloves or gown with carbapenem-resistant Enterobacterales

Type of healthcare personnel (N = 3070)	Observations	Interactions resulting in contamination	aOR (95% CI)	P-value
Respiratory therapist	157 (5.1%)	15.3%	3.79 (1.61–8.94)	0.002
Occupational/physical therapist	97 (3.2%)	9.3%	2.82 (0.96–9.32)	0.06
Environmental services	174 (5.7%)	10.3%	2.68 (1.13–6.37)	0.03
Nurse	1605 (52.3%)	11.6%	2.50 (1.28–4.86)	0.007
Patient care technician	329 (10.7%)	7.9%	1.56 (0.70–3.46)	0.28
Medical doctor/nurse practitioner	462 (15.0%)	6.5%	1.09 (0.50–2.37)	0.83
Other ^a	246 (8.0%)	5.7%	Ref.	Ref.

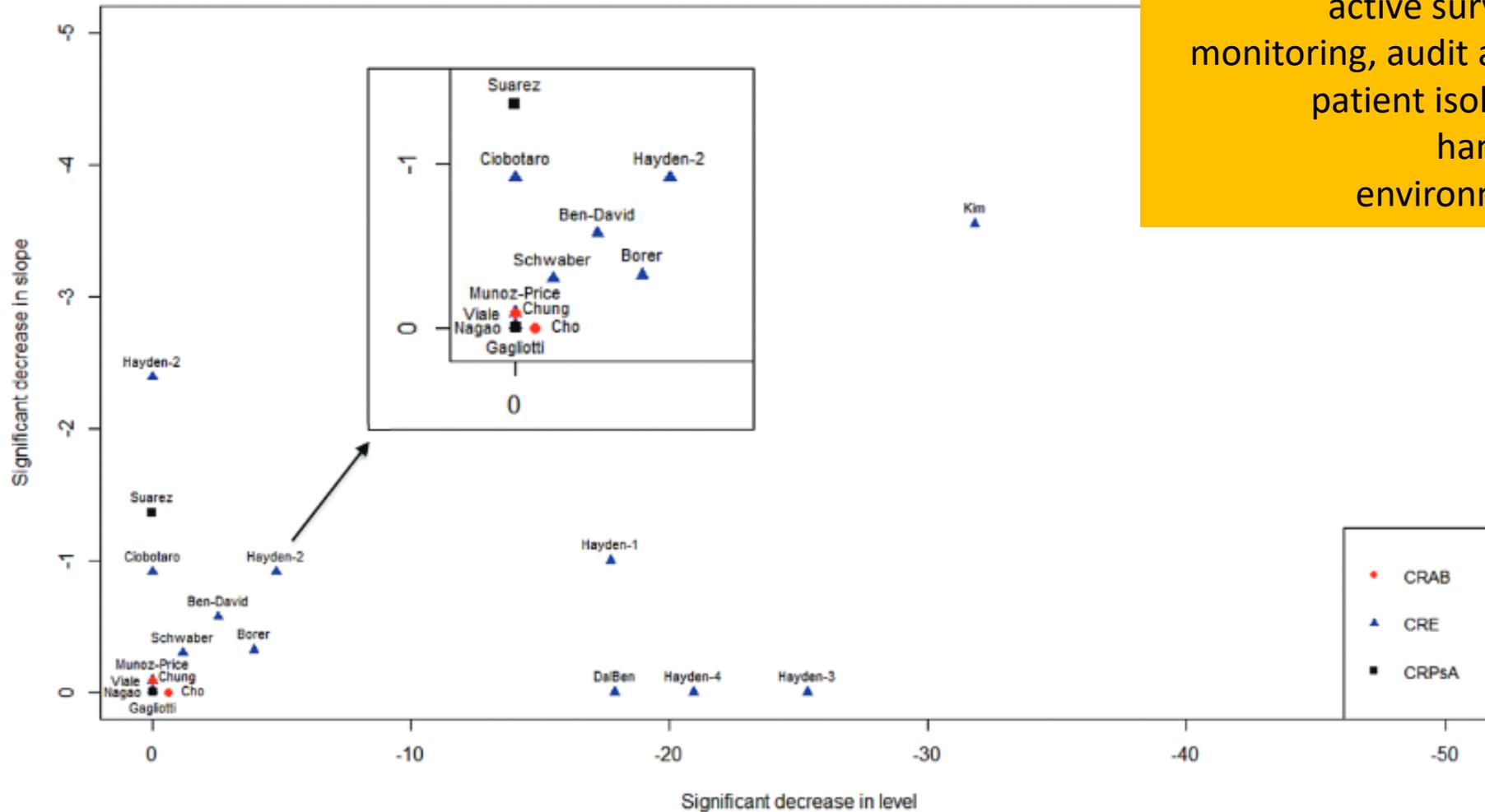


10% de transmission
Reanimation
Prélèvement clinique (+)
Charge bactérienne



Les mesures proposées sont elles efficaces ?

contact precautions (90%),
active surveillance cultures (80%),
monitoring, audit and feedback of measures (80%),
patient isolation or cohorting (70%),
hand hygiene (50%),
environmental cleaning (40%);

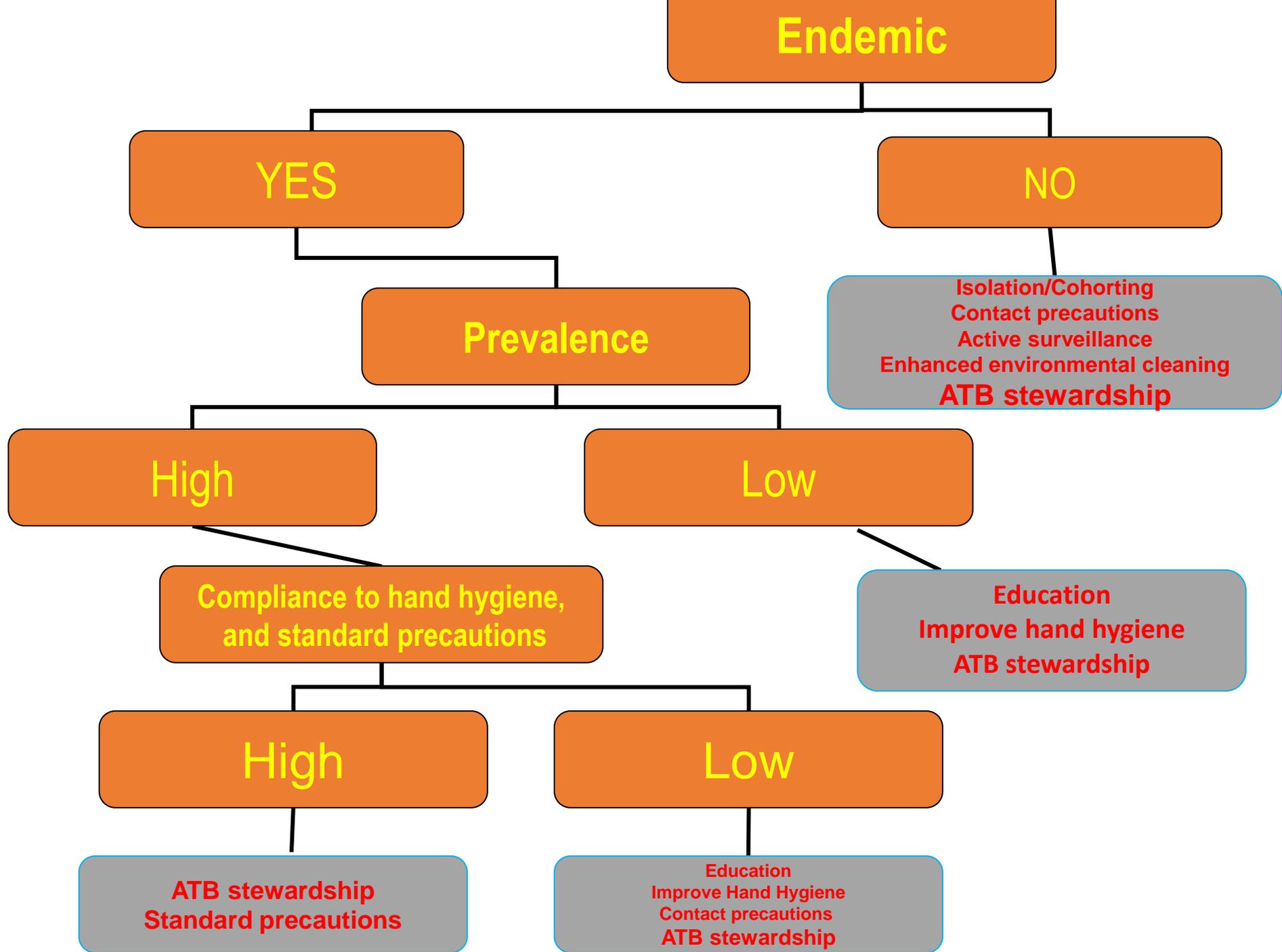


Comment choisir les mesures : la grille de lecture

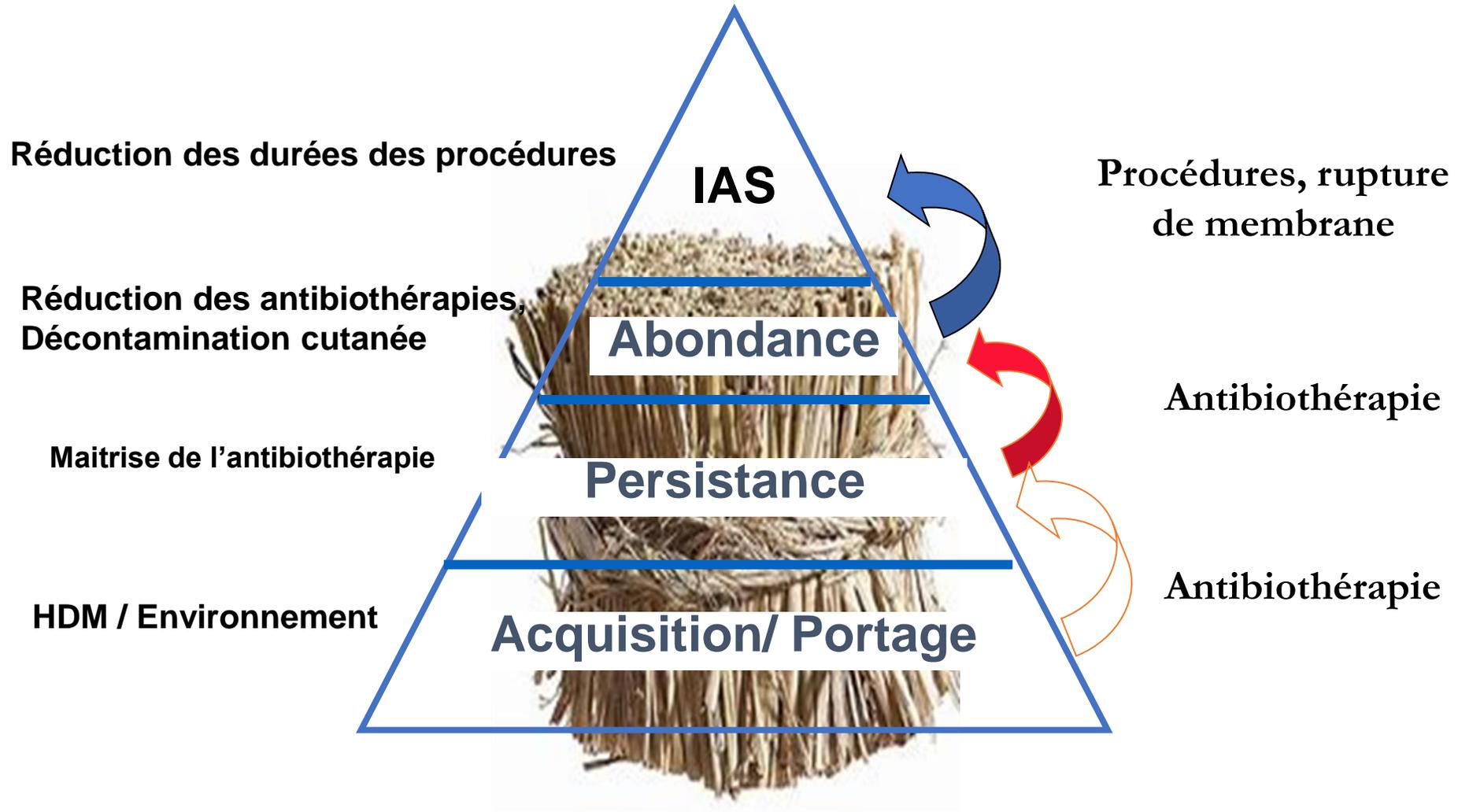
- Bactéries saprophytes ou commensales
- Situation endémiques ou épidémiques
- Prévalence élevée ou faible (ie endémique ou sporadique)
- Type de service : charge en soins faible ou élevée (ex : Réa, Ehpad)
- Niveau d'observance des précautions standard (élevée vs faible)

Espèces et risques : ...

	Commensalisme	Environnement contamination	Environnement survie	Pouvoir Epidemiogène
ABRI	-	++	++	++
ERV	+	+++	+++	++
EPC				
<i>Kp</i>	+	+	+	++
<i>E.Cloacae</i>	+	+	+	++
<i>E.coli</i>	+	-	-	-:+
EBLSE				
<i>Non-coli</i>	+	+/-	+/-	+
<i>E. coli</i>	+	-	-	-
MRSA	+	+/-	+/-	+/-
<i>Pseudomonas aeruginosa</i>	-	+	+	-



En cas d'échec : réduire l'exposition aux risques



Messages clés

Stratégie adaptée à la problématique locale

→ Connaître l'épidémiologie locale, la charge en soins dans les services, leur niveau de respect des précautions

Mesures réalisables et comprises par les équipes

→ Adapter les recommandations selon les situations et expliquer leur finalité

Risques plurifactoriels

→ « Bundle » de mesures à mettre en place

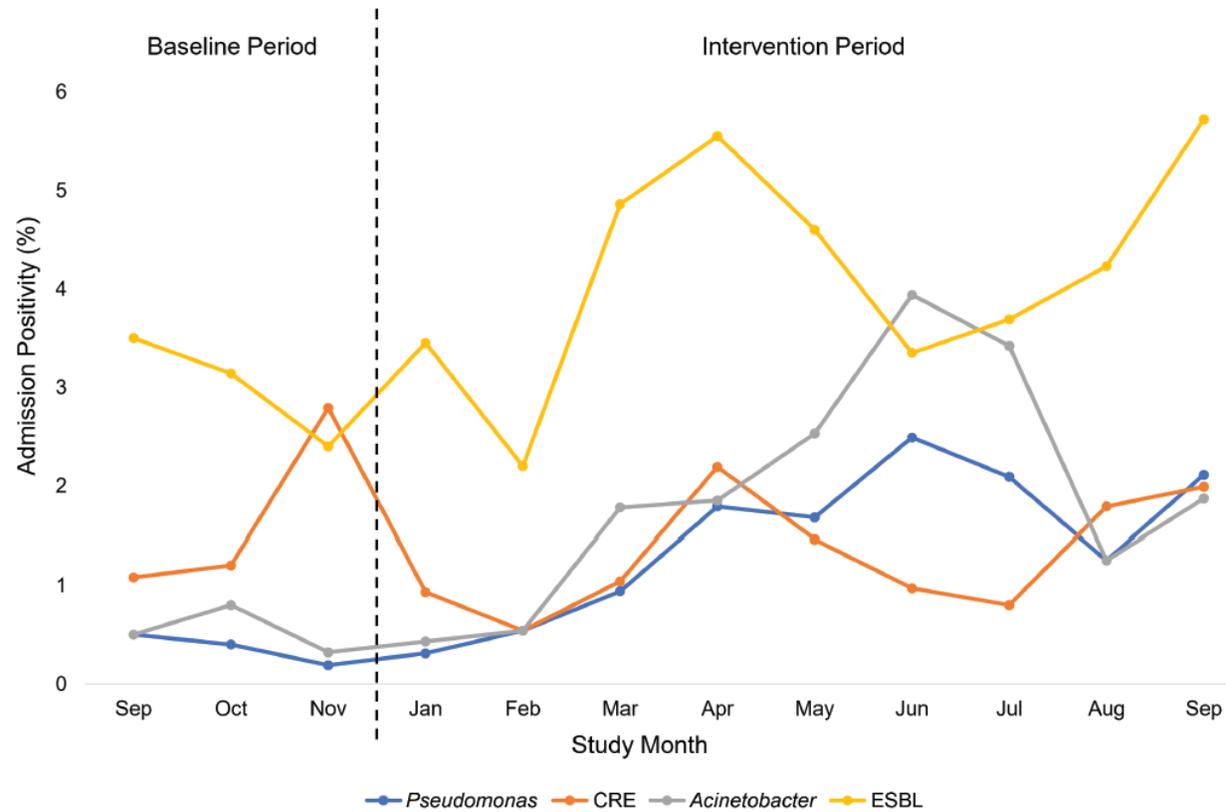
Situation évolutive (nb de cas, respect des mesures, charge en soins)

→ Réévaluer régulièrement la stratégie



Merci de votre attention

Acquisition of Antibiotic-Resistant Gram-negative Bacteria in the Benefits of Universal Glove and Gown (BUGG) Cluster Randomized Trial



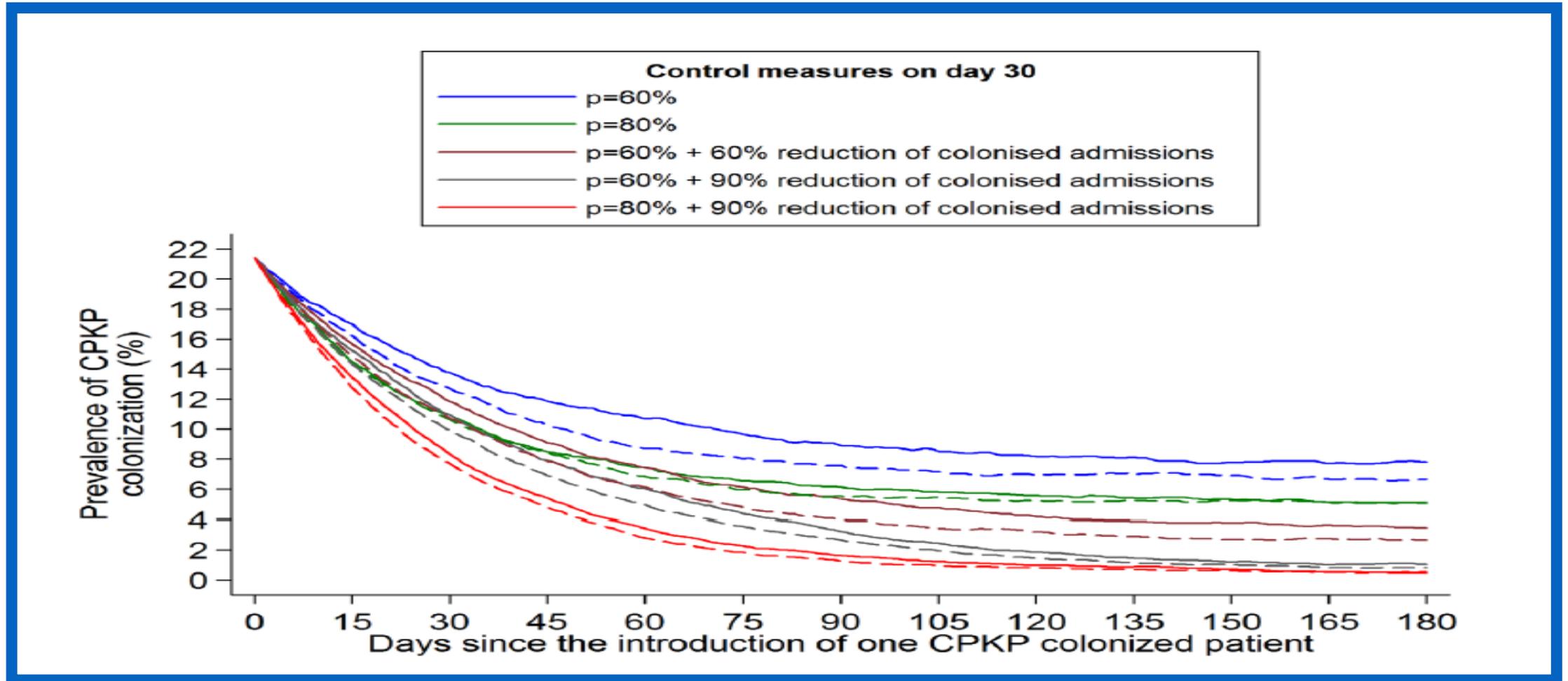
Organism	RR for Impact of the Intervention Adjusted for Site-specific Admission Prevalence (95% CI)	PValue
<i>Pseudomonas</i> , carbapenem-resistant <i>Pseudomonas aeruginosa</i>	0.78 (.51–1.19)	.25
Carbapenemase-resistant Enterobacteriaceae	0.88 (.62–1.23)	.45
<i>Acinetobacter</i>	0.75 (.50–1.13)	.17
ESBL-producing bacteria	0.95 (.74–1.21)	.67
Any	0.90 (.73–1.10)	.31

Les recommandations nationales



- Cohorting patients et soignants
- Arrêt des transferts dans les unités d'aval
- Recherche de cas secondaires par dépistage hebdomadaire (3 semaines consécutives)
- Maitrise de l'antibiothérapie (ie, des carbapénèmes)

Transmission Dynamics of Carbapenemase-Producing *Klebsiella Pneumoniae* and Anticipated Impact of Infection Control Strategies in a Surgical Unit



En pratique comment je gère ?

- Une découverte fortuite

- Un patient fléché
 - Sans transmission secondaire
 - Une transmission secondaire



	Patient repéré à l'admission	Patient connu sans transmission	Découverte Fortuite	Patient connu avec transmission
Evaluation du réservoir (index)	X	X	X	X
Evaluation de la charge en soin	X	X	X	X
Evaluation du respect des mesures	X	X	X	X
Dépistage				
	Quand hebdomadaire	hebdomadaire	J0 + hebdomadaire	J0 + hebdomadaire
	Comment Culture classique	Culture classique	PCR + Culture classique	PCR + Enrichissement
Qui Contacts sélectionnés	Contacts sélectionnés	Tout le service	Tout le service	
Diminution de la charge de travail			X	X
Intensification du bio nettoyage	ERV	ERV	ERV	ERV
Maitrise de l'antibiothérapie			X	X
Bloquer les admissions			X (Attente résultats)	X
Bloquer les transferts			X	X

Grille de lecture pour arrêter ma politique d'isolement

Variables	objectifs	
Incidence des BLSE	< Incidence médiane nationale	
Espèce prédominante	<i>E coli</i>	
Observance HDM	> 70 %	
Prévalence régionale	Faible	
Maitrise de la prescription ATB	?	

Maitriser les antibiotiques

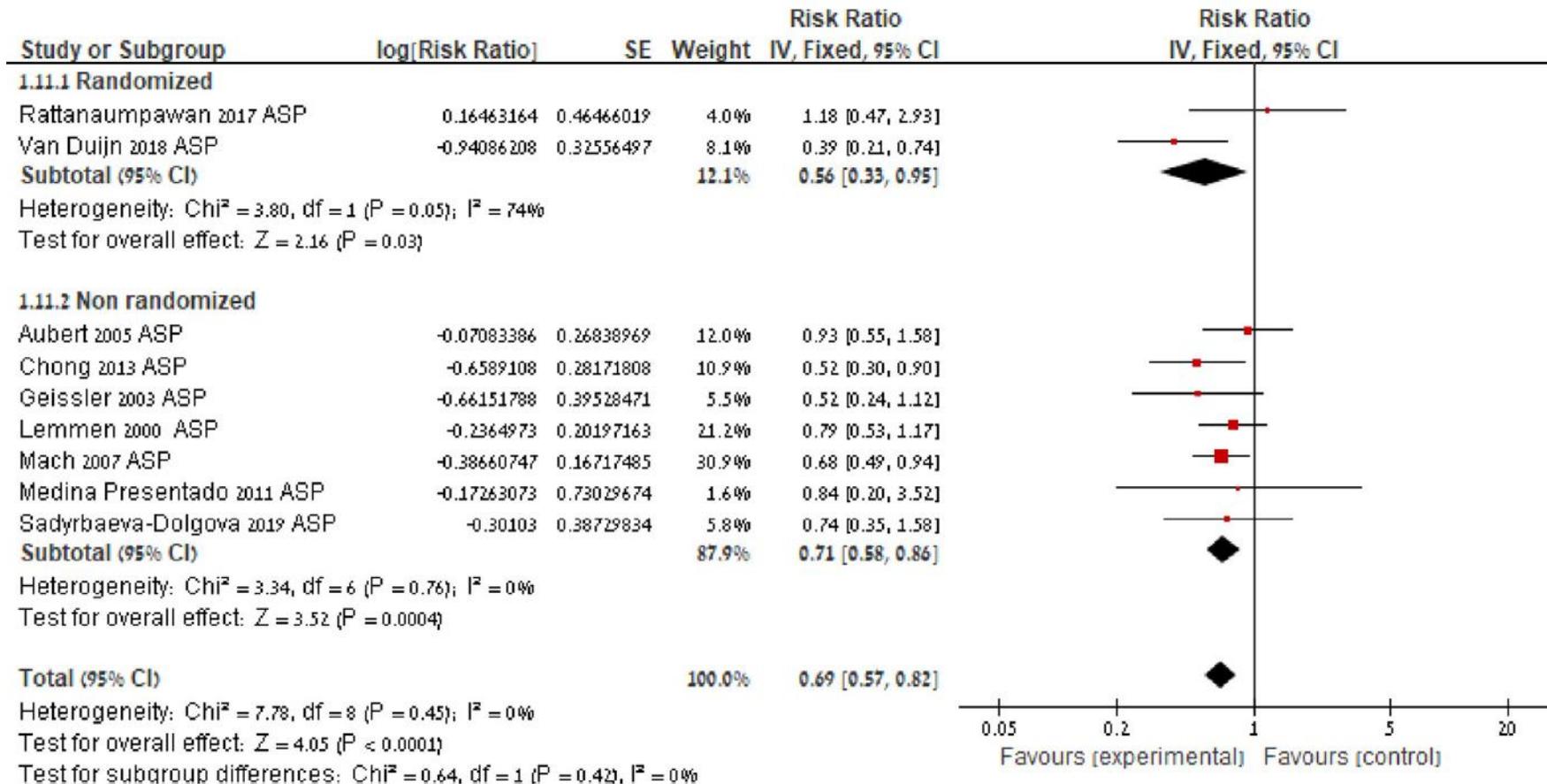


Fig. 5. Antimicrobial stewardship program (ASP) – colonization caused by MDR-E.

Prevention and Control of Multidrug-Resistant Gram-Negative Bacteria in Adult Intensive Care Units: A Systematic Review and Network Meta-analysis

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STD+ASP+ ENV+SCT							
0.05 (.01, 0.38)	STD+ENV +SCT						
0.04 (.01, 0.16)	0.76 (.19, 3.13)	STD+ASP+ ENV					
0.04 (.01, 0.27)	0.75 (.12, 4.87)	0.99 (.27, 3.66)	STD+ASP+ DCL				
0.02 (.00, 0.13)	0.48 (.17, 1.41)	0.63 (.25, 1.58)	0.64 (.14, 2.96)	STD+ENV			
0.02 (.00, 0.11)	0.38 (.07, 1.93)	0.50 (.18, 1.37)	0.50 (.13, 2.02)	0.79 (.23, 2.68)	STD+DCL		
0.02 (.00, 0.08)	0.31 (.07, 1.45)	0.40 (.18, 0.90)	0.41 (.15, 1.15)	0.64 (.21, 1.95)	0.81 (.32, 2.04)	STD+ASP	
0.01 (.00, 0.04)	0.17 (.04, 0.72)	0.22 (.10, 0.46)	0.22 (.07, 0.74)	0.34 (.13, 0.94)	0.44 (.22, 0.88)	0.54 (.29, 1.00)	STD

Pour résumer : Le risque est variable

Table 1. Locally variable factors that may influence the likelihood of benefit of contact isolation.

Local factor	Lower likelihood of benefit	Higher likelihood of benefit
Hand-hygiene compliance by health care workers	High	Low
Epidemiology of health care–associated infections	Low endemic rates	Epidemic or uncontrolled rates
Organism of concern	All or easily treatable	Selected or difficult to treat
Prevalence of organism	Common	Rare
Clinical features of source patient	Asymptomatic	Open wound, diarrhea, or uncontained secretions
Clinical features of patients at risk of infection	Healthy	Vulnerable to infection because of age, immune status, or other risks
Physical environment	Clean, spacious, single rooms	Crowded, dirty wards
Available resources	Limited	Plentiful