JNI 23es Journées Nationales d'Infectiologie
Bordeaux et la région Aquitaine
Palais des Congrès
du mercredi 15 juin 2022
au vendredi 17 juin 2022

Quoi de neuf sur l'antibioprophylaxie?

Solen Kernéis
Equipe de Prévention du Risque Infectieux
APHP-Bichat et Université Paris Cité

Déclaration d'intérêts de 2014 à 2021

- **Intérêts financiers : 0**
- **Liens durables ou permanents : membre d'un board bioMérieux jusqu'en 2019**
- **Interventions ponctuelles : bioMérieux, Accelerate Diagnostics, MSD jusqu'en 2019**
- **Intérêts indirects : 0**

- **Gestion de l'allergie aux antibiotiques**

- **Quelle antibioprophylaxie pour les porteurs de bactéries multirésistantes? Actualisation ESCMID 2022**

Allergie aux antibiotiques

Investigating the impact of a β-lactam allergy label on preoperative antibiotic prophylaxis administration

Nguyen
Infect Control Hosp Epidemiol 2021

Etude monocentrique rétrospective
130 patients allergiques aux BL et 130 non-allergiques
PTG (n=98), hystérectomie (n=66), chirurgie colorectale (n=48), PAC (n=48).

Variable	No β-lactam Allergy Label (N=130), No. (%)	β-lactam Allergy Label (N=130), No. (%)	*P* Value
Appropriate preoperative antibiotic prophylaxis	99 (76)	48 (37)	<.001
Knee replacement (KPRO)	38 (77) (n=49)	14 (29) (n=49)	<.001
Hysterectomy (HYST)	32 (97) (n=33)	19 (58) (n=33)	<.001
Colorectal (COLO)	19 (79) (n=24)	8 (33) (n=24)	.003
Coronary artery bypass (CBGB)	10 (42) (n=24)	7 (29) (n=24)	.547
Appropriate intraoperative redosing[b]	120 (92)	124 (95)	.302
Duration of postoperative antibiotics, median days (IQR)	1 (0–1)	1 (0–1)	.706

→ **Les patients dits allergiques reçoivent plus souvent une ABP inappropriée**

Diapo P Montravers

DOI: 10.1093/cid/cix794

- 8385 patients, 9004 interventions
- Allergie pénicilline n=922 (11%)
- ISO n=241 (2,7%)
- Allergie pénicilline augmente de 51% le risque d'ISO

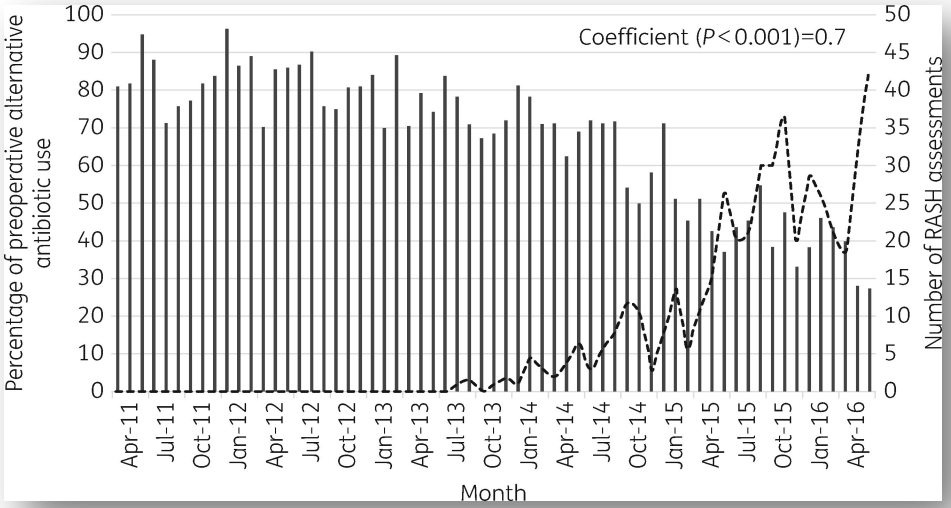
→ Les patients dits allergiques sont plus à risque d'ISO

J Antimicrob Chemother 2017; **72**: 2657–2660
doi:10.1093/jac/dkx171 Advance Access publication 10 June 2017

Journal of Antimicrobial Chemotherapy

Optimizing preoperative prophylaxis in patients with reported β-lactam allergy: a novel extension of antimicrobial stewardship

Alon Vaisman[1]*, Janine McCready[2], Sandy Hicks[3] and Jeff Powis[2]



- **Réévaluation allergie par un binôme pharmacien / infectiologue**
- **Août 2013 - Juin 2016 : 485 patients**

Pourcentage (par mois) d'utilisation d'une molécule alternative en cas d'allergie supposée:
Avant : 82%
Après : 56%

Pas d'impact négatif en termes de morbi/mortalité

→ **Il est possible de faire mieux!**

pharmacy

MDPI

Article

Effectiveness and Feasibility of Pharmacist-Driven Penicillin Allergy De-Labeling Pilot Program without Skin Testing or Oral Challenges

You-Chan Song *, Zachary J. Nelson, Michael A. Wankum and Krista D. Gens

Pharmacy 2021

	Time Spent (min)
Mean	5.2
Median	5
Range	12
Minimum	3
Maximum	15

"De-labeling":
Checklist simple remplie par un interne de pharmacie

66 patients allergiques
De-labeling chez 16 et reintroduction Blactamines chez 9

Prescribed Antibiotics after De-Labeling/or Re-Labeling as Intolerance	Tolerated a Beta-Lactam Agent after De-Labeling	Agents Tolerated	
De-labeled 7/12 (58.3%)	7/7 (100%)	Amoxicillin/Clavulanate	1
		Piperacillin/Tazobactam	2
		Cephalexin	5
		Cefazolin	3
		Cefuroxime Axetil	1
		Ceftriaxone	3
		Cefepime	2
Intolerance 2/4 (50%)	2/2 (100%)	Ampicillin/Sulbactam	1
		Cefuroxime Axetil	2
		Cefdinir	1
Total 9/16 (56.3%)	9/9 (100%)		

→ **Faire mieux n'est ni plus long, ni délétère pour le patient**

Antibioprophylaxie et portage de bactéries multirésistantes

Actualisation ESCMID

E. Tacconelli ECCMID 2022

Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study

Aude Teillant, Sumanth Gandra, Devra Barter, Daniel J Morgan, Ramanan Laxminarayan

Lancet Infect Dis 2015; 15: 1429–37

Published Online October 16, 2015 http://dx.doi.org/10.1016/S1473-3099(15)00270-4

Estimation du nombre d'infections supplémentaires liées à une baisse d'efficacité de l'ABP :

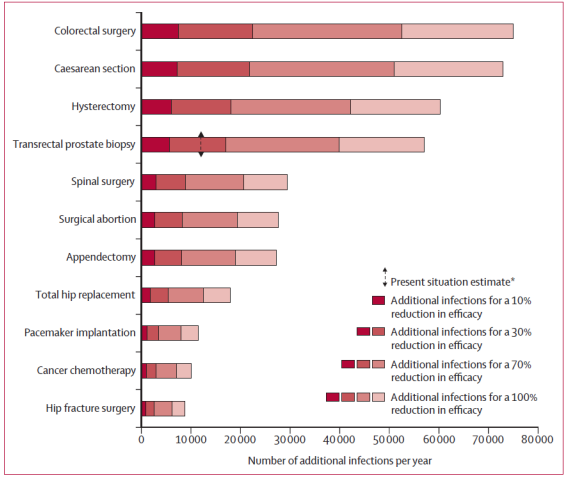


Figure 2: **Number of additional infections per year in the USA under four scenarios of decreased efficacy of antibiotic prophylaxis**

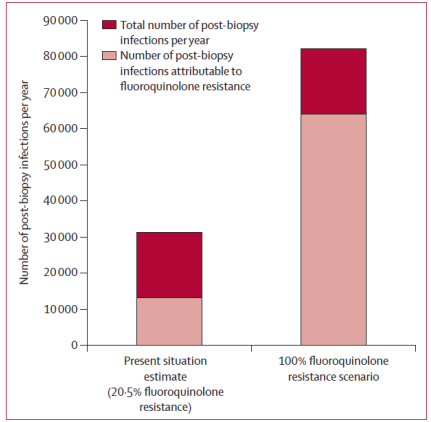


Figure 4: **Number of post-biopsy infections per year attributable to fluoroquinolone resistance in the USA**
Fluoroquinolone resistance refers to resistant rectal cultures.

Une baisse de 30% de l'efficacité de l'ABP entraînerait 120 000 infections et 6 300 décès supplémentaires /an aux USA

Prévalence du portage de bmr au moment de la chir

Procedure	Resistance type	Setting	Years	*N*	Carriage prevalence
Colorectal surgery[6]	ESBL	Israel	2011–12	150	18.0%
Colorectal surgery[7]	ESBL	Israel	2012–17	740	28.8%
Colorectal surgery[7]	ESBL	Switzerland	2012–17	582	12.0%
Colorectal surgery[7]	ESBL	Serbia	2012–17	227	9.4%
Gastrointestinal and gynaecological surgeries in cancer patients[8]	ESBL	Mexico	2014–15	171	17.5%
Pancreatico-duodenectomy[9]	ESBL	Italy	2015–16	338	11.8%
Abdominal surgery[10]	ESBL	Thailand	2017–19	360	35.8%
TRUS-PB[11]	FQ	Colombia	2009–13	548	45.6%
TRUS-PB[12]	FQ	Virginia, USA	2010–15	244	17.6%
TRUS-PB[13]	FQ	Hong Kong	2011–12	371	40.4%
TRUS-PB[14]	FQ	Egypt	2011–15	262	29.0%
TRUS-PB[15]	FQ	Chicago, USA	2012–15	510	15.7%
TRUS-PB[16]	FQ	Rhode Island, USA	2013–14	314	12.1%
TRUS-PB[17]	FQ	California, USA	2013–14	1802	24.5%
TRUS-PB[18]	FQ	Japan	2013–15	694	31.3%
TRUS-PB[19]	FQ	Texas, USA	2016–17	503	19.5%
TRUS-PB[13]	ESBL	Hong Kong	2011–12	371	41.0%
TRUS-PB[16]	ESBL	Rhode Island, USA	2013–14	314	0.6%
TRUS-PB[18]	ESBL	Japan	2013–15	640	13.3%

Temkin JAC 2021

France, E. coli en communauté:

FQ-R : 10 à 20%

BLSE : 5 à 10%

Source : medqualville

- ***La résistance des entérobactéries aux molécules utilisées en ABP est en augmentation***
- ***Grande hétérogénéité géographique***
- ***Importance de connaître son épidémiologie locale+++***

Questions pratiques

1. Les porteurs de BGN-MR ont-ils un risque plus élevé d'ISO?

2. Faut-il faire un dépistage de BGN-MR avant chirurgie? Chez quels patients? Quand?

3. Faut-il modifier l'antibioprophylaxie en fonction des résultats du dépistage? Molécule? Posologie? Durée?

Recommandations

- ECDC 2013
- WHO 2016
- CDC 2017
- SFAR 2018 (mise à jour prévue en 2023)
- ESCMID 2019
- Spanish SEIMC & AEC 2020
- EAU 2022
- ESCMID 2022

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Systematic review and evidence based guidance on perioperative antibiotic prophylaxis, 2013

Table 19. PAP modalities as outlined at the first expert meeting

10 modalities of perioperative antibiotic prophylaxis	
1	A multidisciplinary AM team (including surgeons, anaesthesiologists, nurses, pharmacists, infection control specialists, and clinical microbiologists) should develop and implement a protocol of appropriate PAP.
2	A multidisciplinary AM team should regularly update the PAP protocol according to standard, approved guidelines.
3	To control the appropriate selection of antibiotics, as well as timing and duration of prophylaxis, a multidisciplinary AM team should perform an audit of surgeons, anaesthesiologists and OR nursing staff and provide, if necessary, structured feedback and education to healthcare staff and decision-makers.
4	In order to encourage appropriate duration and dosage of PAP, a computer-assisted decision support system and automatic reminder system should be implemented.
5	PAP should be the responsibility of the anaesthesiologist.
6	PAP should be administered within 30–60 minutes before incision (except for vancomycin and fluoroquinolones), ideally at the time of anaesthetic induction.
7	Although a single dose of PAP is preferred, subsequent doses should be given depending on the duration of the procedure and the half-life of the antibiotic, and if significant blood loss occurs during surgery.
8	Prolonging prophylaxis after the end of surgery is not recommended.
9	The PAP protocol should take into account individual patient factors like BMI, underlying diseases, or colonisation with resistant pathogens.
10	In surgical departments, patterns of MDROs and incidence of *Clostridium difficile* infections should be monitored proactively so PAP can be appropriately adjusted.

Summary of evidence for Objective 5: Does the use of PAP have an effect on the incidence of *Clostridium difficile*-associated diarrhoea (CDAD) or the development of antimicrobial resistance?

The following measures could prevent an increase in the development of multidrug-resistant bacteria or an increase of incidence of *C. difficile* infections due to PAP:

- In order to adapt the antibiotic prophylaxis to a patient's individual colonisation with MDROs, a screening should be performed pre-operatively [57].
- Surveillance data of MDROs should be analysed periodically by an AM team to adjust selection of antibiotic prophylaxis [63,65,121,122].
- Active surveillance of MDROs (e.g. MRSA, ESBL-positive *Enterobacteriacae* and toxin-producing *Clostridium difficile*) should be performed regularly on surgical wards by trained personnel (infection control personnel or clinical microbiologists) [123].

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GLOBAL GUIDELINES FOR THE PREVENTION OF SURGICAL SITE INFECTION

4.3 Screening for extended-spectrum beta-lactamase colonization and the impact on surgical antibiotic prophylaxis

Recommendation

The panel decided not to formulate a recommendation due to the lack of evidence.

Rationale for the recommendation

The literature search did not identify any relevant studies comparing the tailored modification of SAP for the prevention of SSI in areas with a high prevalence of extended spectrum beta-lactamase (ESBL)-producing Enterobacteriacae (including patients with rectal colonization of ESBL) to no modification of standard antibiotic prophylaxis. Furthermore, no studies comparing routine screening for ESBL (irrespective of ESBL prevalence prior to surgery) with no screening that could inform a recommendation for this question were identified.

Remarks

- The prevalence of ESBL-producing Enterobacteriacae was considered to be high when demonstrating a prevalence of >10% on the total number of all samples submitted to the laboratory for investigation, including both infection and/or colonization.
- The GDG believes that routine screening for ESBL prior to surgery might increase the widespread use of broad-spectrum antibiotics (particularly carbapenems) pre-surgery in ESBL-colonized patients. This practice may be harmful as it is likely to further increase the emergence of resistance in gram-negative bacteria, especially carbapenem-resistant Enterobacteriacae. The WHO global surveillance report on AMR has already highlighted concerns about the emergence of antibiotic-resistant bacteria due to the inappropriate use of antimicrobial agents. Importantly, the options for the treatment of infections are now extremely limited due to the lack of development of a new class of antimicrobial agents over the past decades *(1)*.

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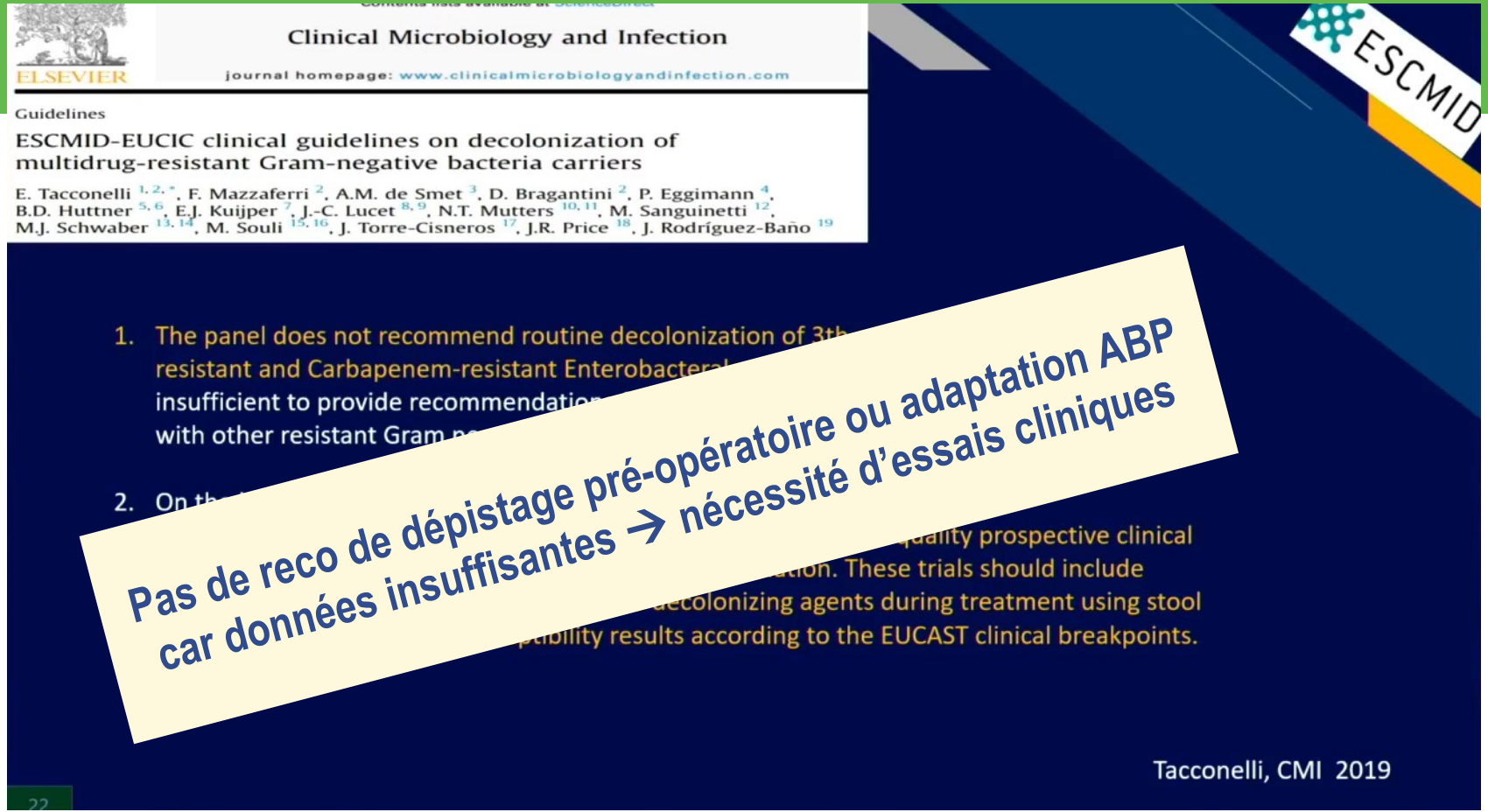
ESCMID

Table 1. **Summary of core topics, research questions and recommendations for the prevention of surgical site infection**

Topic	Research questions	Recommendations	Strength	Quality of evidence
Screening of ESBL colonization and the impact on antibiotic prophylaxis	1. Should SAP be modified in high (>10%) ESBL prevalence areas? 2. Should SAP be modified in patients who are colonized with or a carrier of ESBL? 3. Should patients be screened for ESBL prior to surgery?	The panel decided not to formulate a recommendation due to the lack of evidence.	NA	NA

CDC recommendations 2017: no mention pre surgery colonisation with MDR Gram negatives

World Health Organization, 2016


Clinical Microbiology and Infection
journal homepage: www.clinicalmicrobiologyandinfection.com
Guidelines
ESCMID-EUCIC clinical guidelines on decolonization of multidrug-resistant Gram-negative bacteria carriers
E. Tacconelli [1,2,*], F. Mazzaferri [2], A.M. de Smet [3], D. Bragantini [2], P. Eggimann [4], B.D. Huttner [5,6], E.J. Kuijper [7], J.-C. Lucet [8,9], N.T. Mutters [10,11], M. Sanguinetti [12], M.J. Schwaber [13,14], M. Souli [15,16], J. Torre-Cisneros [17], J.R. Price [18], J. Rodríguez-Baño [19]
ESCMID
1. The panel does not recommend routine decolonization of 3th
resistant and Carbapenem-resistant Enterobacter
insufficient to provide recommendatio
with other resistant Gram n
2. On th
uality prospective clinical
tion. These trials should include
decolonizing agents during treatment using stool
tibility results according to the EUCAST clinical breakpoints.
Pas de reco de dépistage pré-opératoire ou adaptation ABP
car données insuffisantes → nécessité d'essais cliniques
Tacconelli, CMI 2019
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Executive summary of the Consensus Document of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and of the Spanish Association of Surgeons (AEC) in antibiotic prophylaxis in surgery

Should prophylaxis be changed in patients colonized with multidrug-resistant organisms?

- In high-risk surgery (cardiac, orthopedic) in patients with MRSA colonization, a glycopeptide plus a beta-lactam can be given as prophylaxis, accompanied by other measures for decolonization (**A-II**).
- For patients with extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae colonization, prophylactic coverage should only be considered in high-risk patients (**B-III**).

del Toro López, Enferm Infec Microbiol Clin 2020

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Recommendations	Strength rating
Do not use fluoroquinolones for prostate biopsy in line with the European Commission final decision on EMEA/H/A-31/1452.	Strong
Use either target prophylaxis based on rectal swab or stool culture; augmented prophylaxis (two or more different classes of antibiotics); or alternative antibiotics (e.g. fosfomycin trometamol, cephalosporin, aminoglycoside) for antibiotic prophylaxis for transrectal biopsy.	Weak

Transrectal prostate biopsy	Yes	1.Targeted prophylaxis - based on rectal swab or stool culture. 2.Augmented prophylaxis - two or more different classes of antibiotics*. 2.Alternative antibiotics • fosfomycin trometamol (e.g. 3 g before and 3 g 24-48 hrs after biopsy) • cephalosporin (e.g. ceftriaxone 1 g i.m.; cefixime 400 mg p.o. for 3 days starting 24 hrs before biopsy) • aminoglycoside (e.g. gentamicin 3mg/kg i.v.; amikacin 15mg/kg i.m.)

EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam, the Netherlands 2022

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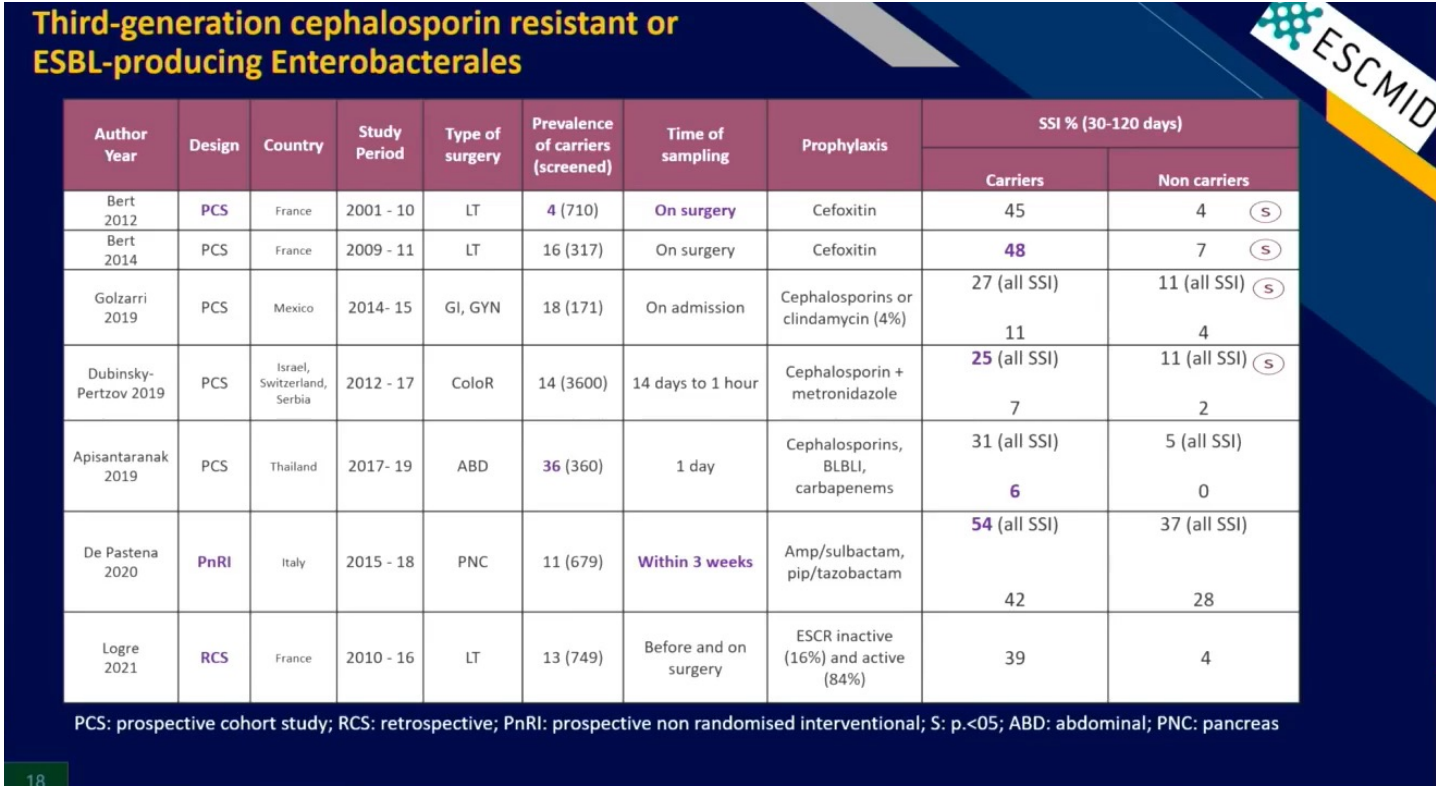
Les porteurs de BLSE ont-ils un risque plus élevé d'ISO?



Third-generation cephalosporin resistant or ESBL-producing Enterobacterales

ESCMID

Author Year	Design	Country	Study Period	Type of surgery	Prevalence of carriers (screened)	Time of sampling	Prophylaxis	SSI % (30-120 days)	
								Carriers	Non carriers
Bert 2012	PCS	France	2001 - 10	LT	4 (710)	On surgery	Cefoxitin	45	4 (S)
Bert 2014	PCS	France	2009 - 11	LT	16 (317)	On surgery	Cefoxitin	48	7 (S)
Golzarri 2019	PCS	Mexico	2014- 15	GI, GYN	18 (171)	On admission	Cephalosporins or clindamycin (4%)	27 (all SSI) 11	11 (all SSI) (S) 4
Dubinsky-Pertzov 2019	PCS	Israel, Switzerland, Serbia	2012 - 17	ColoR	14 (3600)	14 days to 1 hour	Cephalosporin + metronidazole	25 (all SSI) 7	11 (all SSI) (S) 2
Apisantaranak 2019	PCS	Thailand	2017- 19	ABD	36 (360)	1 day	Cephalosporins, BLBLI, carbapenems	31 (all SSI) 6	5 (all SSI) 0
De Pastena 2020	PnRI	Italy	2015 - 18	PNC	11 (679)	Within 3 weeks	Amp/sulbactam, pip/tazobactam	54 (all SSI) 42	37 (all SSI) 28
Logre 2021	RCS	France	2010 - 16	LT	13 (749)	Before and on surgery	ESCR inactive (16%) and active (84%)	39	4

PCS: prospective cohort study; RCS: retrospective; PnRI: prospective non randomised interventional; S: p.<05; ABD: abdominal; PNC: pancreas

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Clinical Infectious Diseases
MAJOR ARTICLE

Carriage of Extended-spectrum Beta-lactamase–producing Enterobacteriaceae and the Risk of Surgical Site Infection After Colorectal Surgery: A Prospective Cohort Study

Biana Dubinsky-Pertzov,[1,2] Elizabeth Temkin,[1] Stephan Harbarth,[3] Carolina Fankhauser-Rodriguez,[3] Biljana Carevic,[4] Ivana Radovanovic,[4] Frederic Ris,[5] Yehuda Kariv,[6] Nicolas C. Buchs,[5] Eduardo Schiffer,[7] Shimrit Cohen Percia,[1] Amir Nutman,[1,2] Noga Fallach,[1] Joseph Klausner,[2,6] and Yehuda Carmeli[1,2]; for the R-GNOSIS WP4 Study Group

- Etude de cohorte prospective
- Israël, Suisse, Serbie
- 3600 patients
- Dépistage BLSE avant chirurgie colorectale
- ABP: CTX+Métro

Risque d'ISO chez les porteurs de BLSE:
OR = 2.36 [1.50–3.71]

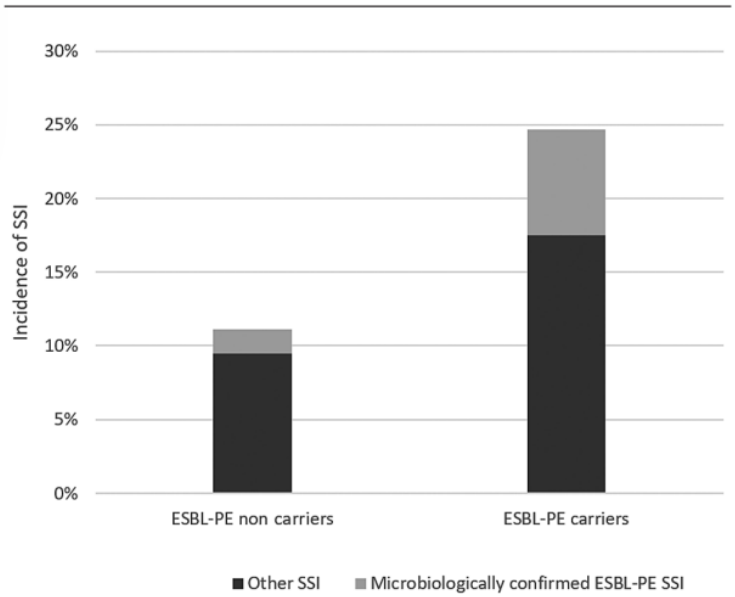
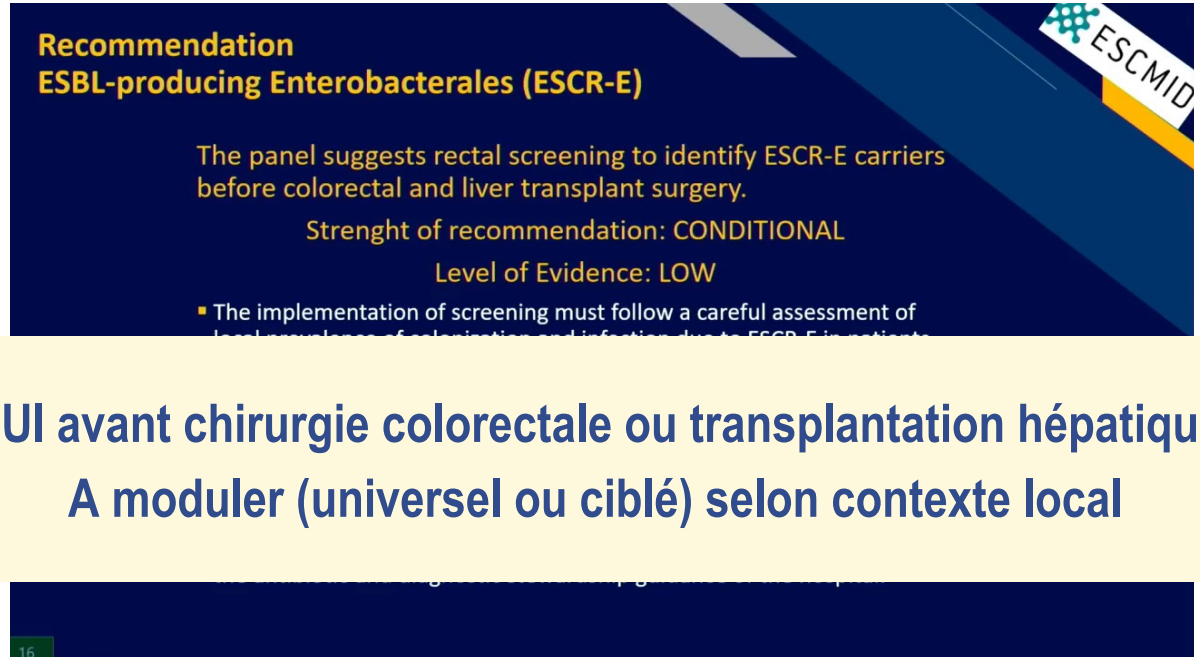


Figure 1. Incidence of surgical site infection in extended-spectrum beta-lactamase–producing Enterobacteriaceae carriers and noncarriers after colorectal surgery. Abbreviations: ESBL-PE, extended-spectrum beta-lactamase–producing Enterobacteriaceae; SSI, surgical site infection.

BLSE: dépistage avant chirurgie?



OUI avant chirurgie colorectale ou transplantation hépatique

A moduler (universel ou ciblé) selon contexte local

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Clinical Infectious Diseases

MAJOR ARTICLE

Personalized Ertapenem Prophylaxis for Carriers of Extended-spectrum β-Lactamase–producing Enterobacteriaceae Undergoing Colorectal Surgery

Amir Nutman,[1,2] Elizabeth Temkin,[1] Stephan Harbarth,[3] Biljana Carevic,[4] Frederic Ris,[5] Carolina Fankhauser-Rodriguez,[3] Ivana Radovanovic,[4] Biana Dubinsky-Pertzov,[1] Shimrit Cohen-Percia,[1] Yehuda Kariv,[6] Nicolas Buchs,[5] Eduardo Schiffer,[7] Noga Fallach,[1] Joseph Klausner,[6] and Yehuda Carmeli[1,2]; for the Resistance in Gram-negative Organisms: Studying Intervention Strategies (R-GNOSIS) WP4 Study Group

- **Etude interventionnelle prospective avant/après**
- **Israël, Suisse, Serbie**
- **Dépistage BLSE avant chirurgie colorectale**
- **Intervention : ABP chez les porteurs BLSE**
  - **AVANT : CTX+Métro (n=209)**
  - **APRES : ERTA (n=269)**

Taux d'ISO : 23% vs 16% (-33%)
ARD : -7,7% [-14,6% à -8%]

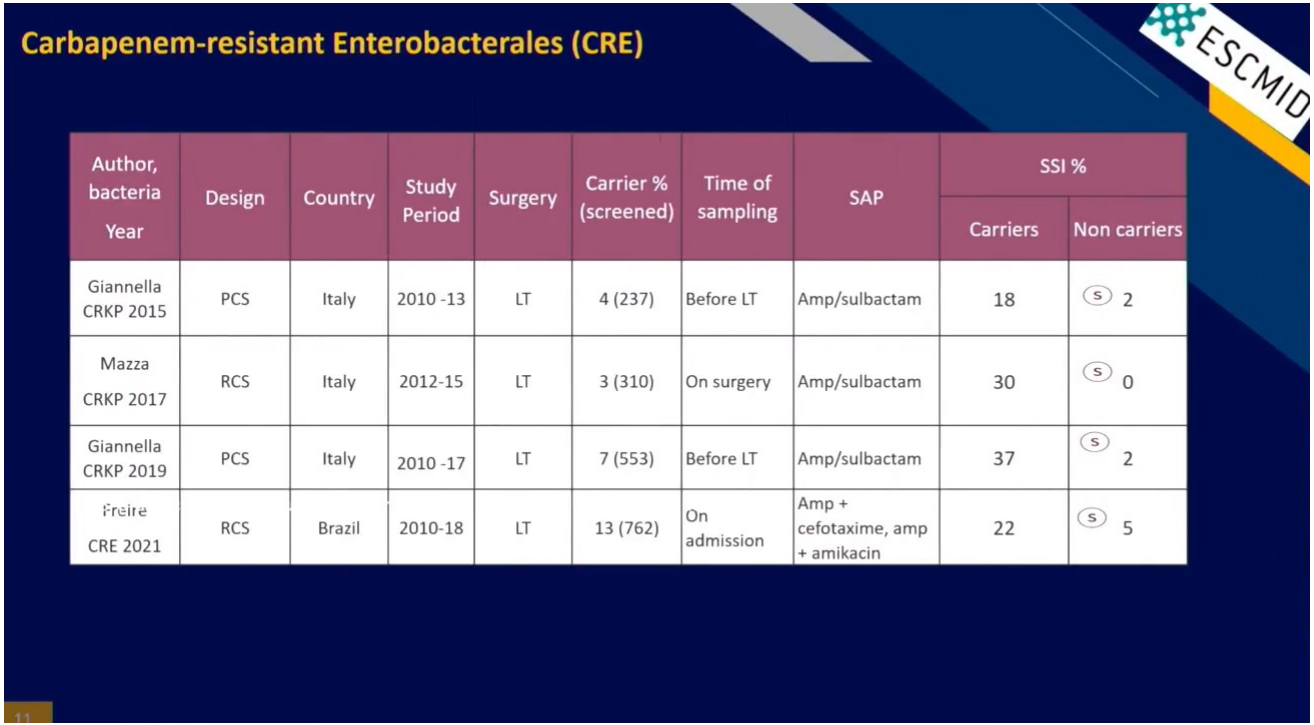
Taux d'ISO à BLSE : 6,5% vs 0,9% (-86%)
ARD : -5,6% [-8,9% à -2,3%]

BLSE : modification de l'ABP en fonction du dépistage?

OUI pour chirurgie colorectale ou transplantation hépatique

Choisir les molécules à impact écologique le plus faible

Les porteurs d'EPC ont-ils un risque plus élevé d'ISO?



Author, bacteria Year	Design	Country	Study Period	Surgery	Carrier % (screened)	Time of sampling	SAP	SSI %	
								Carriers	Non carriers
Giannella CRKP 2015	PCS	Italy	2010 -13	LT	4 (237)	Before LT	Amp/sulbactam	18	S 2
Mazza CRKP 2017	RCS	Italy	2012-15	LT	3 (310)	On surgery	Amp/sulbactam	30	S 0
Giannella CRKP 2019	PCS	Italy	2010 -17	LT	7 (553)	Before LT	Amp/sulbactam	37	S 2
Freire CRE 2021	RCS	Brazil	2010-18	LT	13 (762)	On admission	Amp + cefotaxime, amp + amikacin	22	S 5

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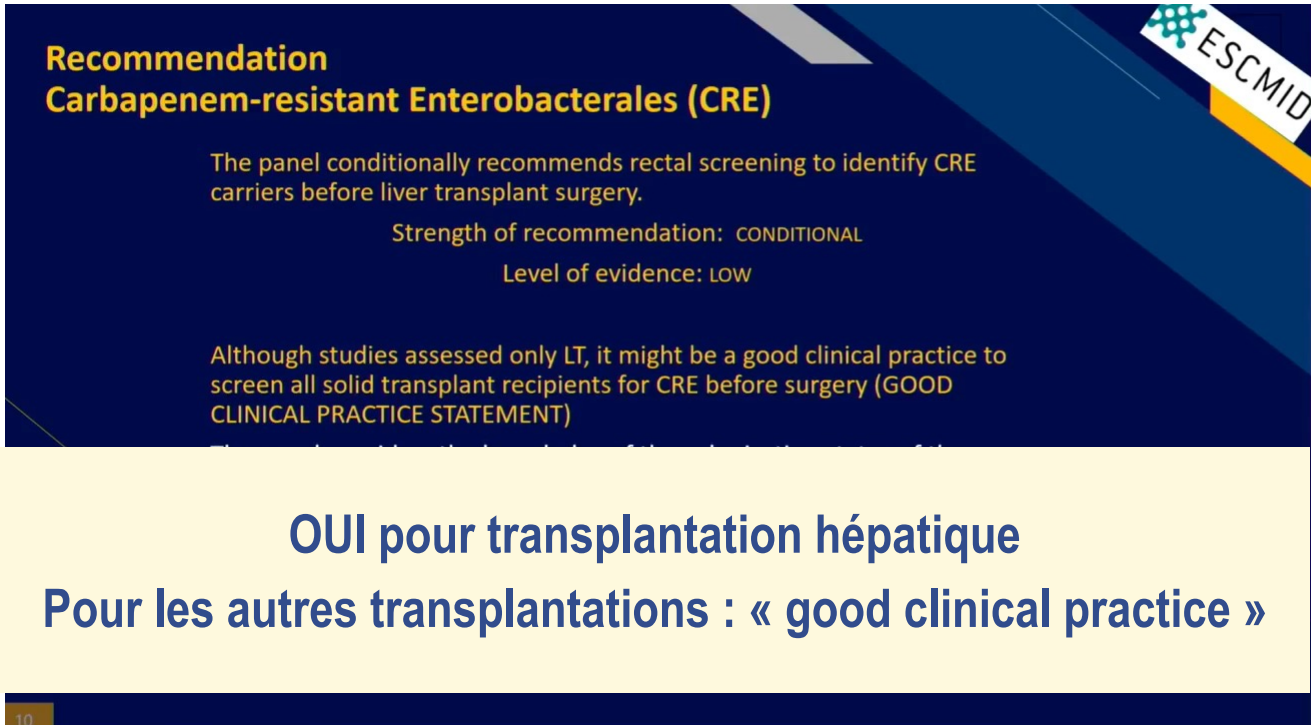
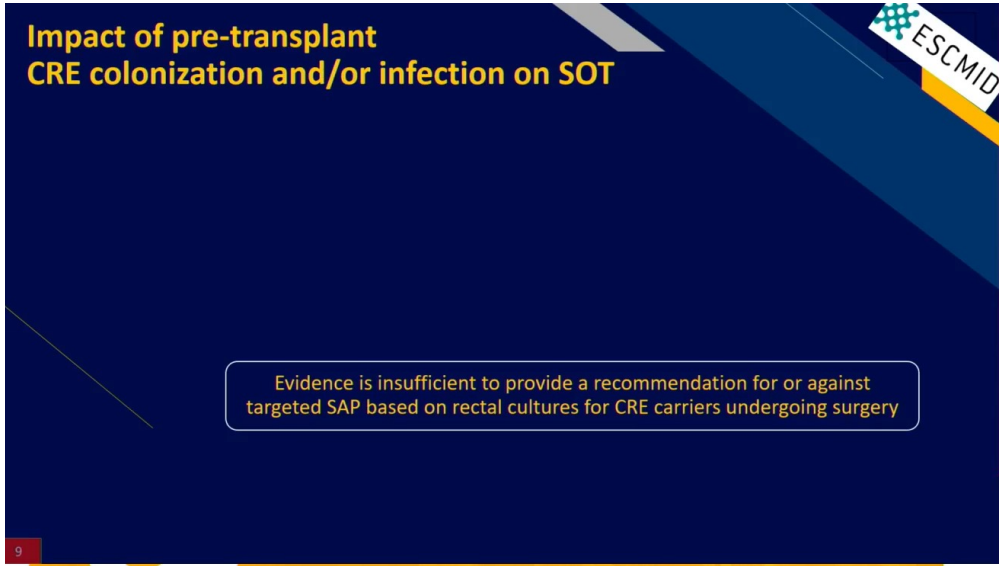
EPC: dépistage avant chirurgie?



OUI pour transplantation hépatique

Pour les autres transplantations : « good clinical practice »

EPC : modification de l'ABP en fonction du dépistage?



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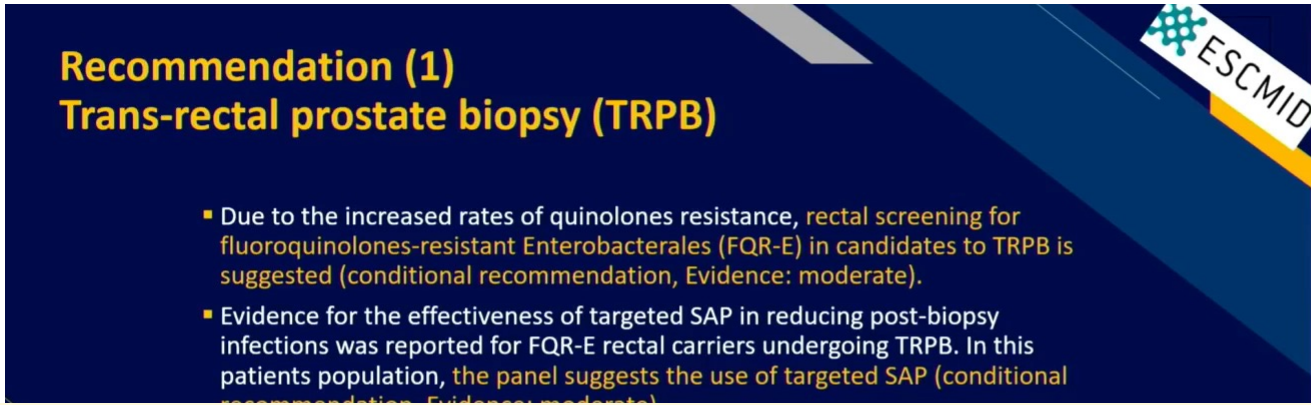
Alors pourquoi le faire?

- **Choix antibiothérapie probabiliste si sepsis post-opératoire**
- **Mise en place précoces des PCC**
- **Eviter de « relarguer » des patients colonisés dans la communauté**

?..

Biopsie transrectale de prostate



Dépister avant le geste par écouvillonnage rectal

En cas de résistance aux FQ, adapter l'ABP

Molécule? Aminosides ou fosfo?

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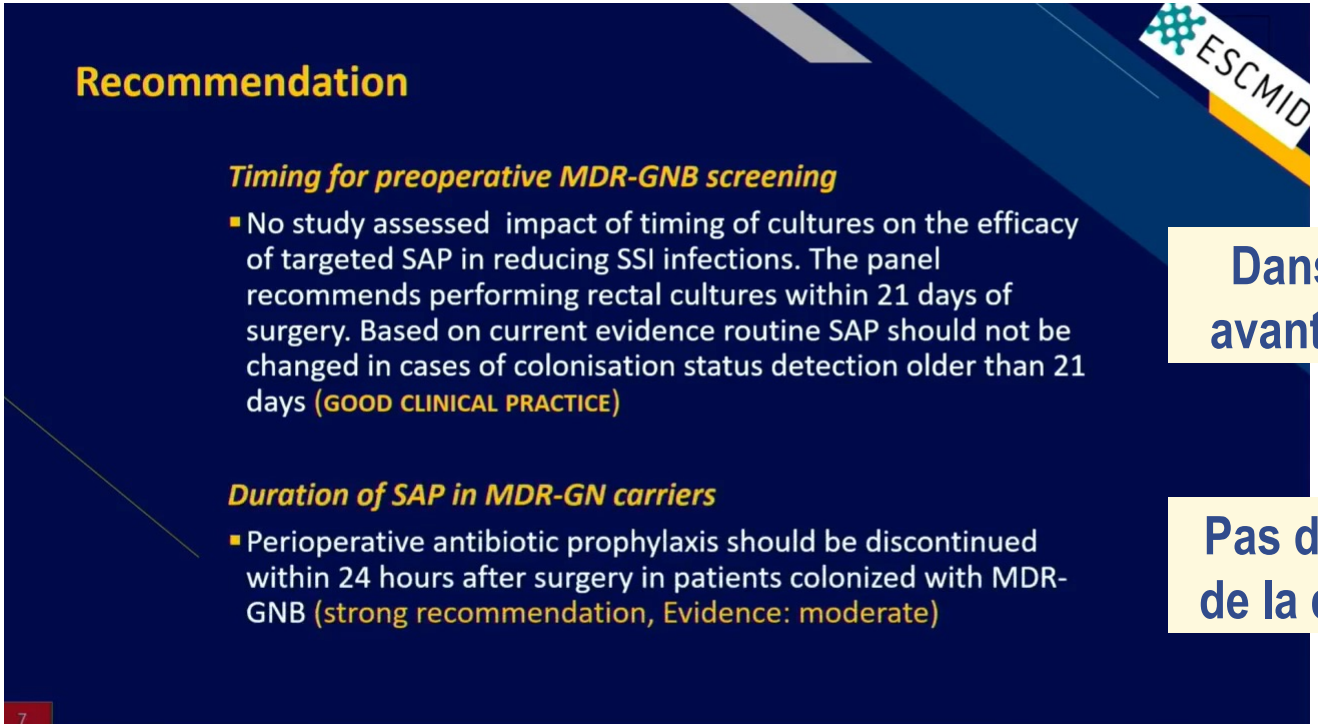
Quand dépister? Faut-il prolonger l'ABP?



Dans les 21 jours avant l'intervention

Pas de modification de la durée de l'ABP

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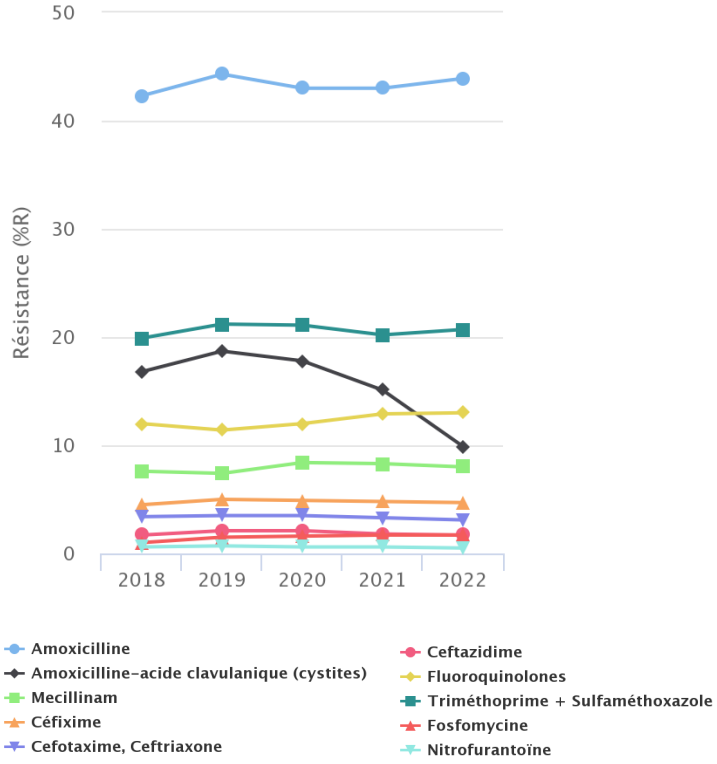
Recommandations ESCMID : pour résumer

- **Avant chirurgie colorectale et transplantation hépatique**
  - Dépister E-BLSE et EPC
  - Modifier l'ABP chez les porteurs
- **Avant biopsie transrectale de prostate**
  - Dépister le portage d'Entérobactérie résistante aux FQ
  - Modifier l'ABP chez les porteurs (fosfo, aminosides)
- **Dépistage dans les 21 jours précédant l'intervention**
- **Pas de modification de la durée de l'ABP**

Questionnements pour la suite

E. coli – Evolution de la résistance (%R) aux antibiotiques



- Contexte français : portage communautaire d'E-BLSE relativement faible et d'EPC très faible
- Dépend sûrement de l'épidémiologie locale
- Quel seuil pour décider du dépistage?
- Comment on dépiste les Enterobactéries FQ-R?
- Et si ciblé, quels patients? Idem BHRe? Plus large?
- Quelle molécule choisir pour l'adaptation de l'ABP?
  - Activité antibactérienne
  - Impact microbiote
- Peut-on s'en sortir avec la cefoxitine?
- Quel impact de cette modification de pratiques? Sur la résistance, les coûts, les effets indésirables?
- Adhésion des équipes à ce changement?

→ To be continued…