Antimicrobial Stewardship : état des lieux

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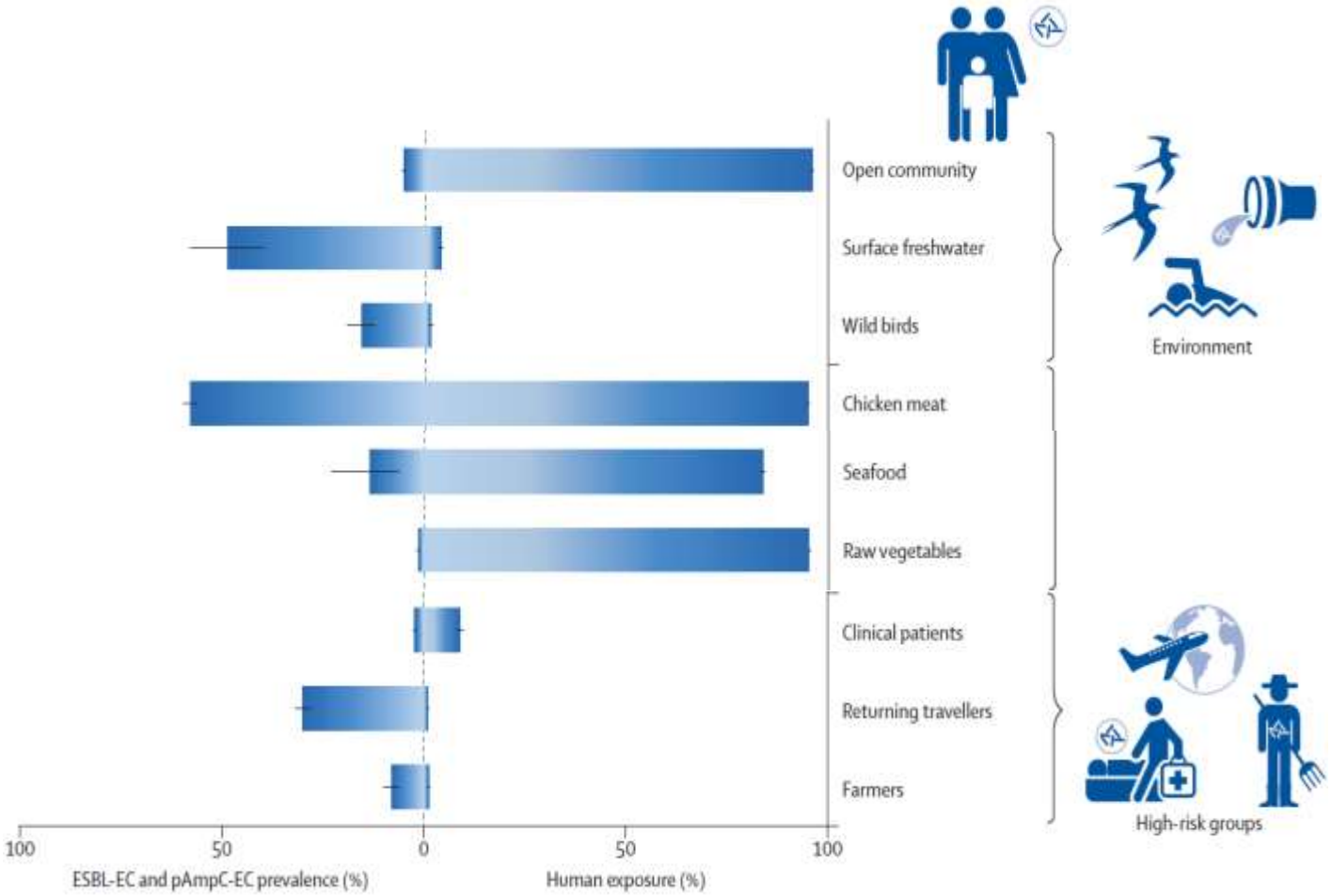
Liens d'intérêts

- Activités d'intérêt général

- Investigateur pour la recherche académique
  - CAMOMY (PHRC national), CLOCEBA (PHRC national), ADDAMAP (PHRC national), TEP STAR (PHRC national), SHASAR (PHRC national), RODEO (PHRC national), TEPvENDO (PHRC national), DISCOVERY (PHRC national), CORIMUNO (PHRC national), French COVID (ANR), DEEP covid (APHP), MicroCOVID (ANR), Aphroclic (ANRS)
- Investigateur pour la recherche industrielle
  - Posy TEICO (SANOFI), CONDUCT (MSD), OZAVIE (Pfizer), EFC16844 (SANOFI)
- Invitation à des Congrès
  - JANSSEN-CILAG, GILEAD SCIENCES, SANOFI AVENTIS France, ViiV HEALTHCARE SAS, MSD France, bioMérieux, CORREVIO
- Collaboration avec rémunération reversée sur une RAF hospitalière
  - bioMérieux, SANOFI AVENTIS France, GUERBET, MSD France
- Collaboration avec rémunération
  - GILEAD SCIENCES (1206 euros), MSD France (438 euros)

Attributable sources of community-acquired carriage of *Escherichia coli* containing β-lactam antibiotic resistance genes: a population-based modelling study



- Population-based modelling study
- Quantify the overall and gene-specific attributable sources of community-acquired ESBL-EC and pAmpC-EC intestinal carriage.
- Netherlands population for 2005–17
- Model based on ESBL-EC and pAmpC-EC **prevalence** and gene data for humans, farm and companion animals, food, surface freshwater, and wild birds, and human **exposure data**

Mughini-Gras L et al. Lancet PH 2019

Attributable sources of community-acquired carriage of *Escherichia coli* containing β-lactam antibiotic resistance genes: a population-based modelling study

	Mean (95% CrI)
Human sources	
Human-to-human transmission in the open community	60·1% (40·0–73·5)
Secondary transmission from high-risk groups	6·9% (4·1–9·2)
Returning travellers	3·9% (2·3–5·5)
Clinical patients	2·0% (1·2–2·6)
Poultry and pig farmers	1·0% (0·5–1·6)
Food consumption and preparation	18·9% (7·0–38·3)
Animals	
Contact with companion animals	7·9% (1·4–19·9)
Non-occupational contact with farm animals	3·6% (0·6–9·9)
Environment	2·6% (0·2–8·7)
Swimming in surface freshwater	2·3% (0·1–8·4)
Contact with wild birds	0·3% (0–1·1)

- 1220 occurrences genes in humans
  - patients, asymptomatic carriers, travelers, etc.
- 6275 occurrences in non-human sources
  - companion animals, farm animals, food products, freshwater, etc.)

Mughini-Gras L et al. Lancet PH 2019

Les interventions des équipes mobiles hospitalières

	Definitions
Empirical therapy according to the guidelines	Empirical systemic antibiotic therapy prescribed according to local guide or national guidelines*
Blood cultures	Take at least two sets of blood cultures before starting systemic antibiotic therapy
Cultures from the site of infection	Take cultures from suspected sites of infection, preferably before starting systemic antibiotic therapy
De-escalation of therapy	Change to narrow-spectrum antibiotic or stop antibiotics as soon as culture results are available[10–13]
Adjustment of therapy to renal function	Adjustment of dose and dosing interval of systemic antibiotics
Switch from intravenous to oral therapy	Switch after 48–72 h, when the clinical condition of the patient is stable, oral intake and gastrointestinal absorption are adequate, and when sufficiently high concentrations in blood with a suitable oral antibiotic can be achieved[10,14,15]
Documented antibiotic plan	Documented antibiotic plan should include indication, drug name and dose, and administration route and interval, and should be included in the case notes at the start of systemic antibiotic treatment
Therapeutic drug monitoring	NA
Discontinuation of antibiotic therapy if infection is not confirmed	Discontinuation of empirical treatment based on lack of clinical or microbiological evidence of infection†
Presence of a local antibiotic guide	Local antibiotic guide present in the hospital and assessed for update every 3 years
Local antibiotic guide in agreement with national antibiotic guidelines	Corresponds for all features but can deviate on the basis of local resistance patterns
List of restricted antibiotics	Removal of specific antibiotics from the formulary or restriction of use by requiring preauthorisation by a specialist (infectious diseases or medical microbiology) or allowing use for only 72 h with mandatory approval for further use; studies in outbreak settings excluded
Bedside consultation	Formal consultation by an infectious disease specialist leading to written comments and advice on treatment based on physical examination and review of medical records (informal consultation, for example by telephone, does not count as bedside consultation)
Assessment of patients' adherence	NA

Schuts et al. LID 2016

Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis

	Years	Country	Study design	Setting	Infection or colonisation	Intervention	Infection control measures	Main objective	Results
Borde et al[16]	2013–14	Germany	ITS	Hospital	Infection	Audit, guideline implementation	No change	Reduction of antibiotic use	Reduced RDD per 1000 patient-days; no effect on incidence of *Clostridium difficile* infection
Cruz-Rodriguez et al[17]	2012–13	Mexico	Before–after	Orthopaedics	Infection	Antibiotic restriction, audit	Hand hygiene	Reduction of clindamycin use and incidence of *C difficile* infection	Reduced DDD per 1000 patient-days and incidence of *C difficile* infection
Apisarnthanarak et al[18]	2010–12	Thailand	Before–after	Medical ICU	Infection and colonisation	Audit, feedback	Isolation, environmental cleaning, hand hygiene, chlorhexidine bathing	Reduction of incidence of XDR *Acinetobacter baumannii*	Reduced incidence of XDR *A baumannii*
Lübbert et al[19]	2010–12	Germany	Before–after	Hospital	Infection and colonisation	Guideline implementation	No change	Reduction of antibiotic use and incidence of antibiotic resistance and *C difficile* infection	Reduced DDD per 1000 patient-days, VRE rates, and incidence of *C difficile* infection
Zou et al[20]	2009–13	China	ITS	Hospital	Infection and colonisation	Audit	No change	Reduction of antibiotic use and incidence of antibiotic resistance	Reduced DDD per 100 patient-days; decreased or stable incidence of antibiotic resistance

…….. 3 pages

Baur et al. LID 2017

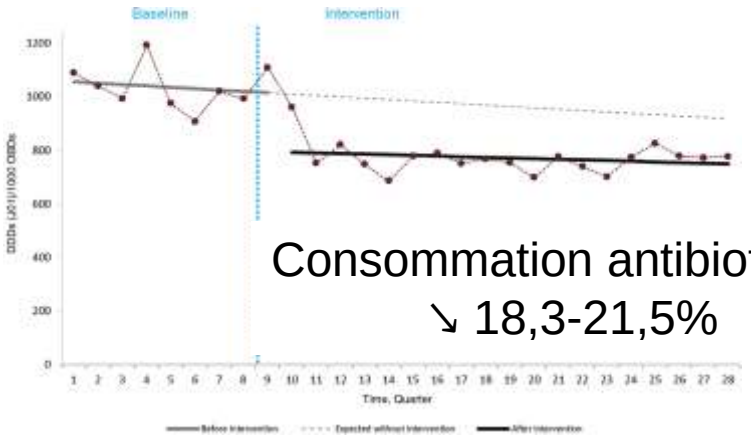
Impact positif des programmes de référence antibiotique dans les études

- Respect des recommandations
- Volumes de consommation antibiotique
- Résistance bactérienne
- Coût de la prise en charge
  - coût des anti-infectieux
  - Durée moyenne de séjour
  - Taux de réadmission
- Mortalité

Baur et al. LID 2017, Schuts et al. LID 2016, Karanika et al. AAC 2016, Feazel et al. JAC 2014, Davey et al. Cochrane 2017

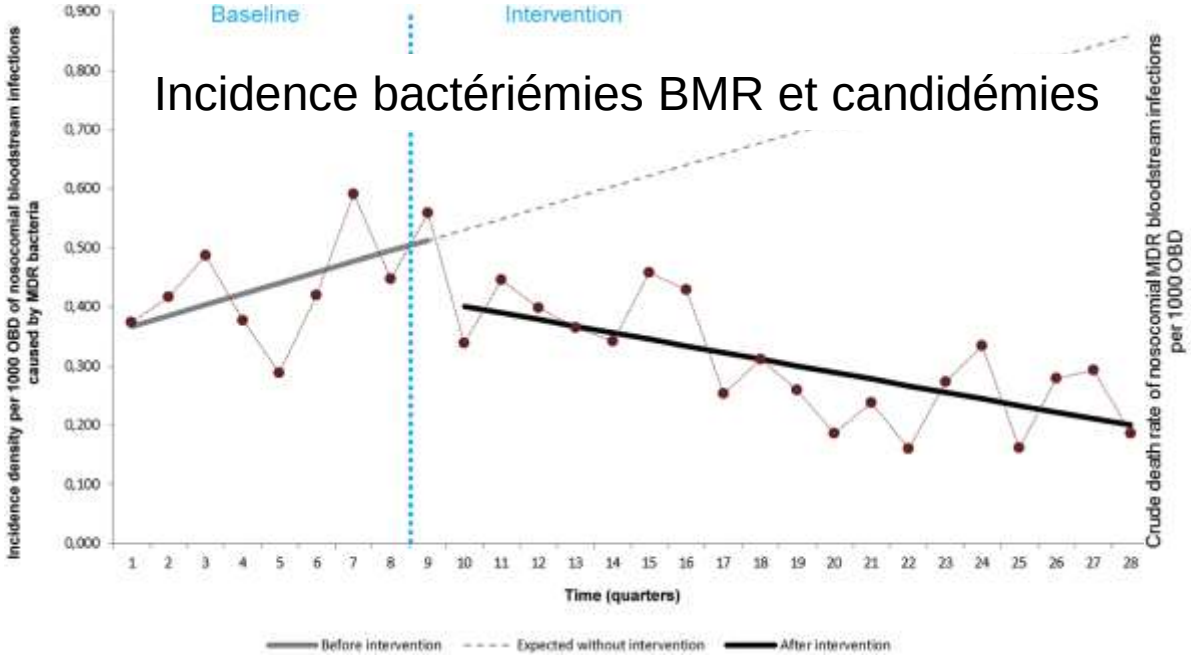
Effet de l'AMS sur la mortalité // résistance

10 counselors !

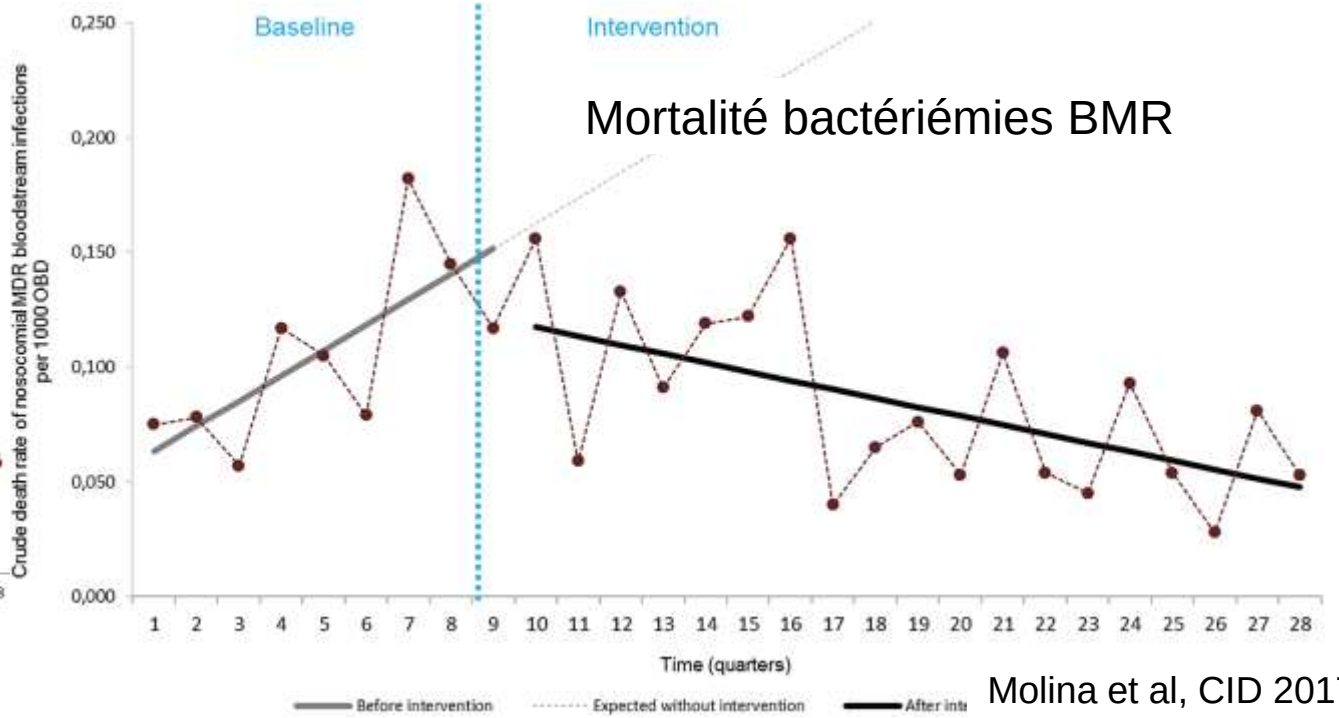


Consommation antibiotiques
↘ 18,3-21,5%

Quasi-experimental intervention study
Interrupted time-series analysis
Multifaceted educational intervention
Over a 5-year period in a 1177-bed teaching hospital



Incidence bactériémies BMR et candidémies



Mortalité bactériémies BMR

Molina et al, CID 2017

AMS aux urgences

13 ED ID physicians 24/7 !

	Pre	Post	p
N	195	187	
Avis	15 (7,7%)	187 (100%)	
Compliance*	9 (4,6%)	59 (32%)	<0.001
ATB appropriée	58 (30%)	148 (79%)	<0.001
Modification antibiothérapie	86 (44%)	110 (59%)	0.004
Mortalité J14	77 (39%)	53 (29%)	0,02

Mortalité J14 en analyse multivariée :
post-phase Ora = 0,64 [0,43-0,94]

Quasi experimental pre–post study
General ED Bologna
1420-bed teaching hospital
Intervention: « sepsis team » in ED
June 2013–July 2014
382 adult patients
Median age 82 years (IQR, 70–88)
Source of infection
lung (43%)
urinary tract (17%)

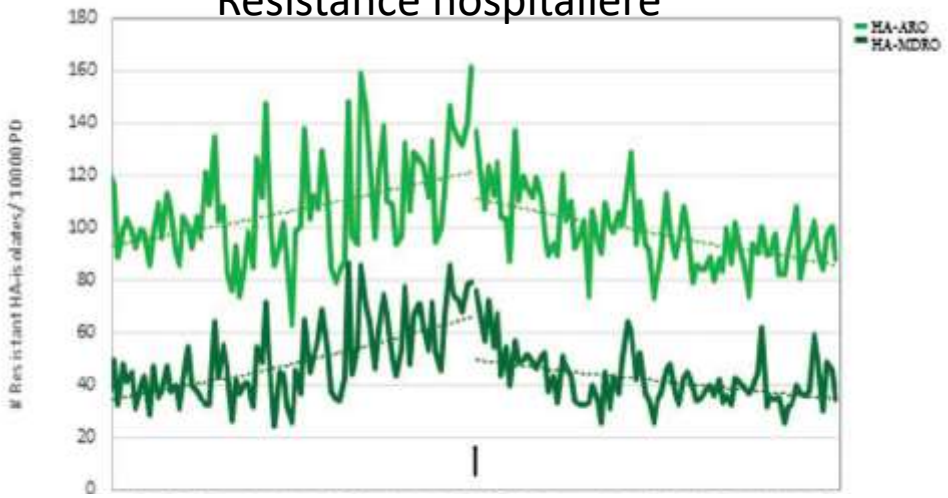
* Survival Sepsis Campaign bundle
lactate measurement, fluid resuscitation, drawing of blood cultures, and administration of antibiotics within 3 hours of ED admission

Viale et al. CID 2017

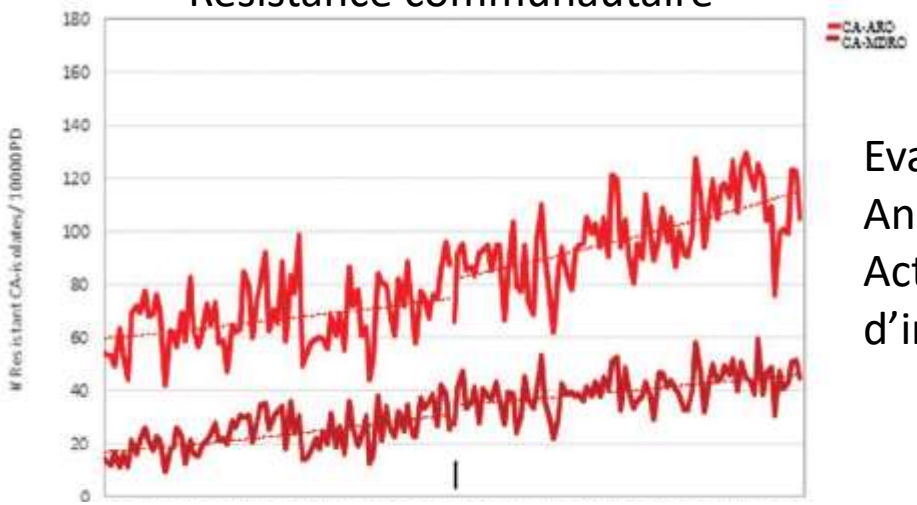
AMS à l'hôpital et impact long terme

Outcome	Mean Monthly IR for Baseline[a]	Mean Monthly IR for the Intervention Period[a]	Trend for Baseline[b] (95% CI)	Trend for Intervention[b] (95% CI)	IRR[c] (95% CI)
HA-ARO	108	98	1.005 (1.004–1.005)	0.998 (.997–.999)	0.91 (.83– .99)
HA-MDRO	50	43	1.010 (1.008–1.011)	0.997 (.996–.998)	0.87 (.73–1.04)
CA-ARO	68	99	1.004 (1.003–1.005)	1.005 (1.004–1.006)	1.40 (1.28–1.54)
CA-MDRO	24	41	1.009 (1.007–1.010)	1.005 (1.003–1.006)	1.68 (1.57–1.82)
Targeted antibiotic use	3424	2692	1.007 (1.006–1.007)	0.998 (.998–.998)	0.98 (.87–1.10)
Nontargeted antibiotic use	3186	2516	1.002 (1.002–1.002)	0.998 (.998–.998)	0.93 (.83–1.04)
Total antibiotic therapy	6611	5207	1.004 (1.004–1.004)	0.998 (.998–.998)	0.94 (.85–1.04)

Résistance hospitalière



Résistance communautaire

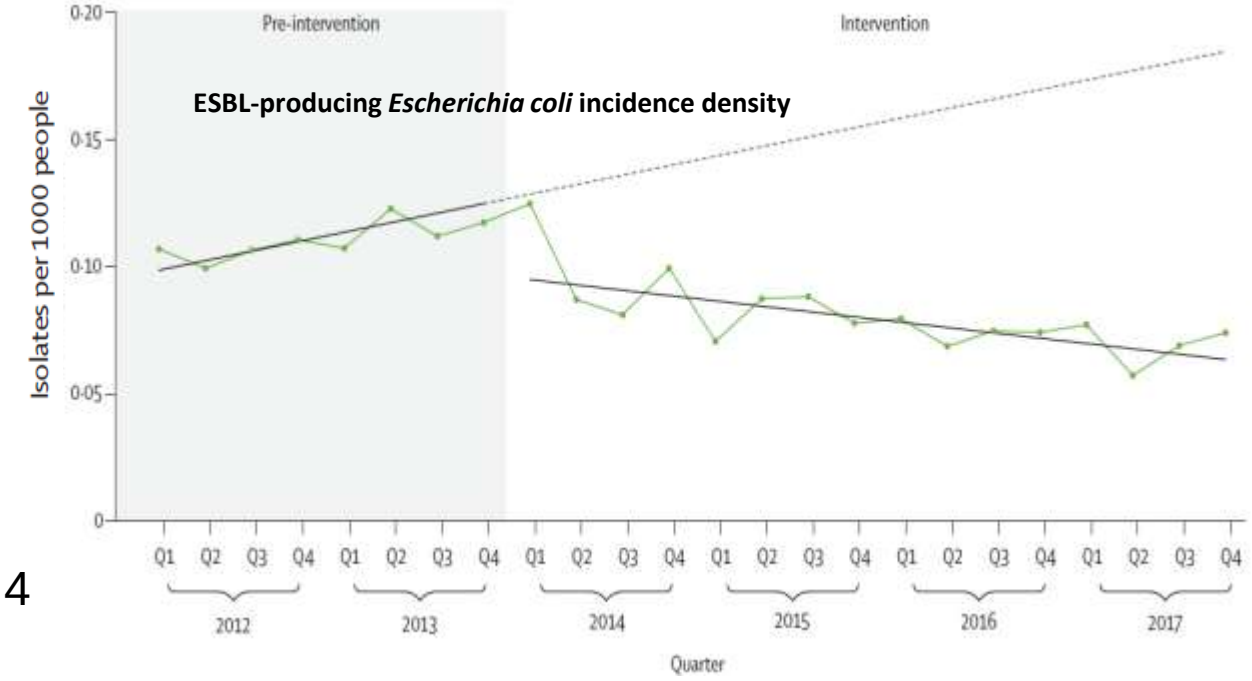


Evaluation sur 2 périodes de 7 ans
Analyse en régression segmentée
Activité d'une équipe dédiée d'infectiologues et de pharmaciens

Peragine et al. CID 2019

AMS en ville et impact long terme

Quasi-experimental intervention study
Interrupted time-series analysis
214 primary health centres in Spain
2012 - 2017
Multimodal, education-based ASP
5 educational interviews /prescriber & /study year
1387 physicians (1116 GP and 271 pediatricians)
1 937 512 people
24 150 educational interviews were done over the 4 years



Inappropriate antibiotic prescribing: 26·9% in 2017 vs 36·5% in 2014 (p<0·0001).

↘ of ciprofloxacin use: –15·9%, [–23·9 to –8·0] and cephalosporins: –22·6% [–35·9 to –9·2]

↗ of amoxicillin use: 22·2% [6·4 to 38·0] and fosfomycin trometamol: 6·1% [2·6 to 9·6]

↘ of incidence density of ESBL-P*E coli* by –0·028 cases per 1000 inhabitants [0·034 to –0·021) // –65·6% /4Y

Penalva et al. PIRASOA-FIS team. Lancet ID 2019

Typologie des interventions

Persuasive interventions:

- Educational materials
- Educational meetings
- Local consensus processes
- Educational outreach visits
- Local opinion leaders
- Reminders provi
on paper or on com
- Audit and feedback

Restrictive interventi

- Selective report
laboratory s
- Forr
ation
substitutions
atic stop orders
- Antibiotic policy changes; cycling, rotation, recycling

tural ntions:

anging from paper to computerized records

- Computerized decision support systems
- Rapid laboratory testing

Persuasive PUIS restrictive
Audit et feedback
Synergie avec l'hygiène hospitalière

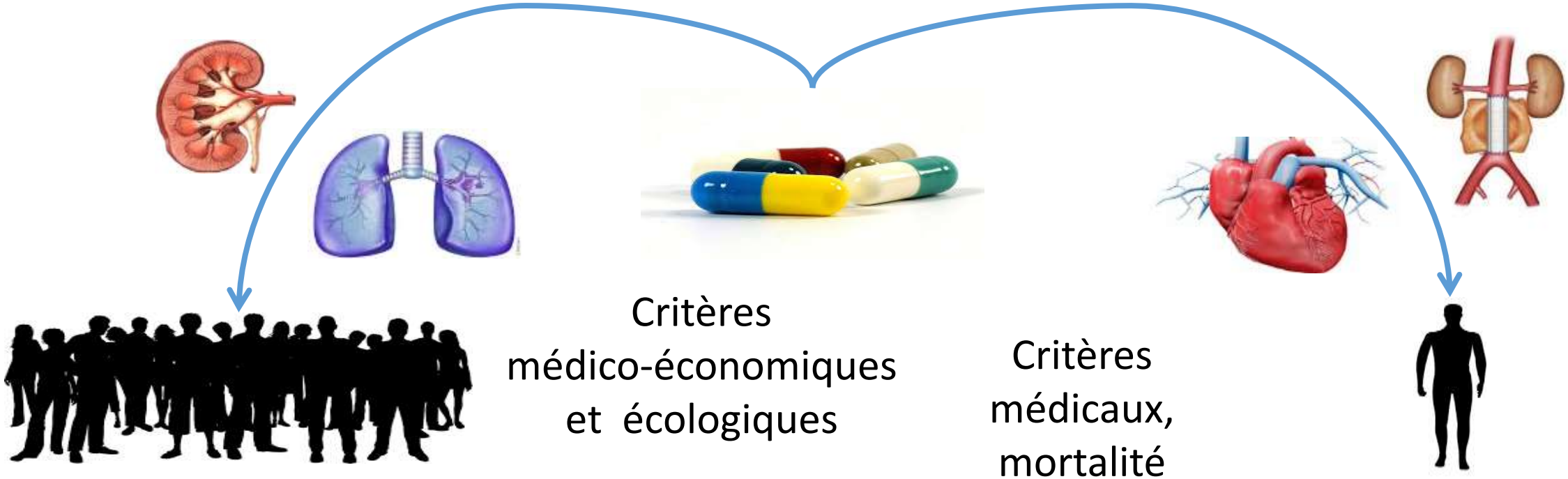
Baur et al. LID 2017

Davey et al . Cochrane 2011

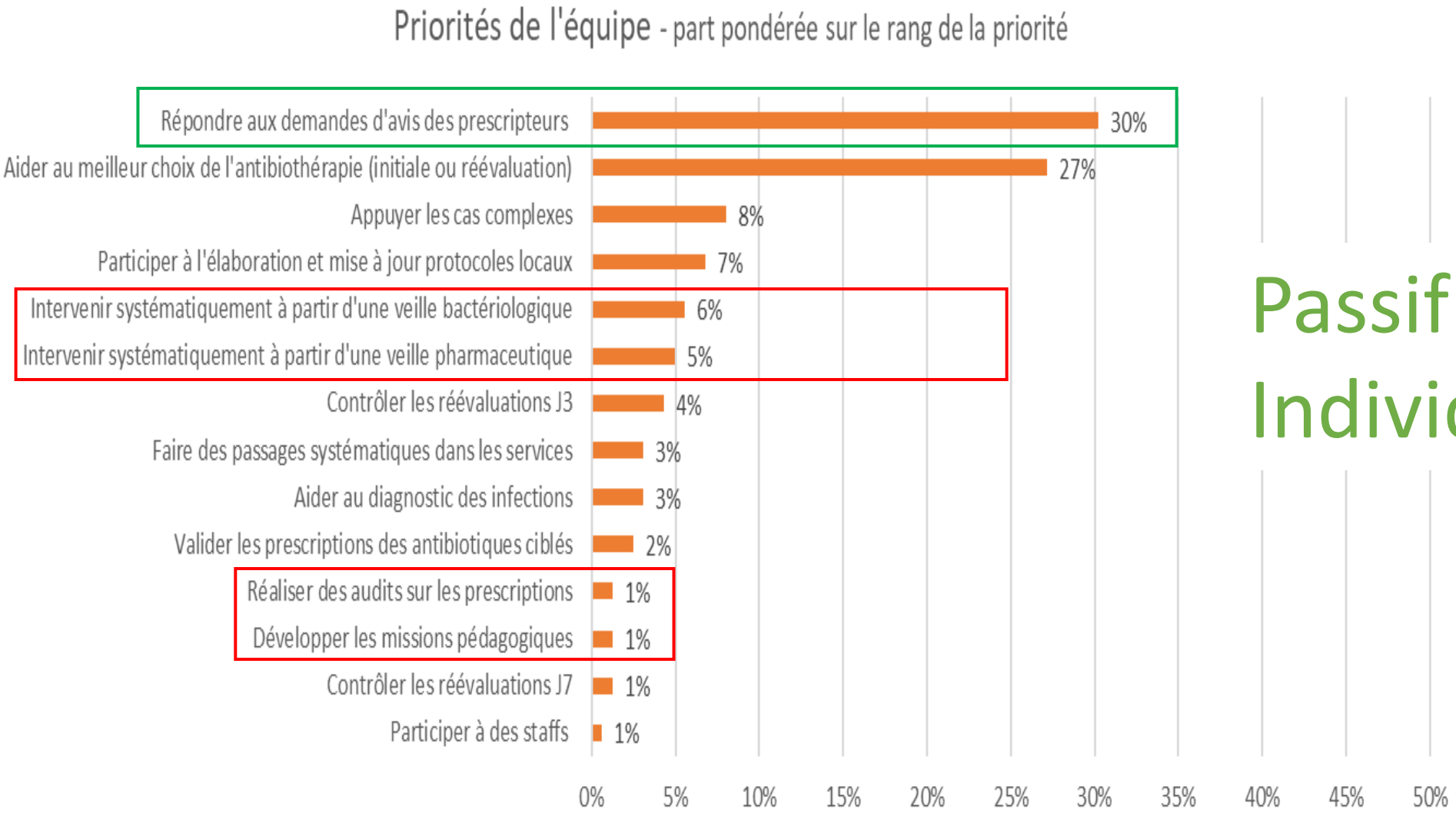
Individu vs collectif

Amélioration de la PEC des infections peu sévères

Amélioration de la PEC des infections sévères / complexes



Les priorités des équipes de bon usage antibiotique en France



Passif &
Individu centré

Perozziello et al. JAC 2019

Objectifs quantitatifs vs qualitatifs

1. Savoir s'abstenir

25-30% d'ATB prescrits dans les rhino-pharyngites en ville

Glinz D et al . JAC 2017

45% à 83% d'ATB prescrits dans les bactériuries asymptomatiques hôpital

Flokas ME et al . OFID 2017
Petty LA et al. JAMA int Med 2019

2. Raccourcir les durées

http://dx.doi.org/10.1016/j.medmal.2017.01.007

Propositions de la SPILF pour des antibiothérapies plus courtes

Objectifs quantitatifs vs qualitatifs

1. Savoir s'abstenir

3. Epargner les ATB à large spectre ?

« Large spectre »

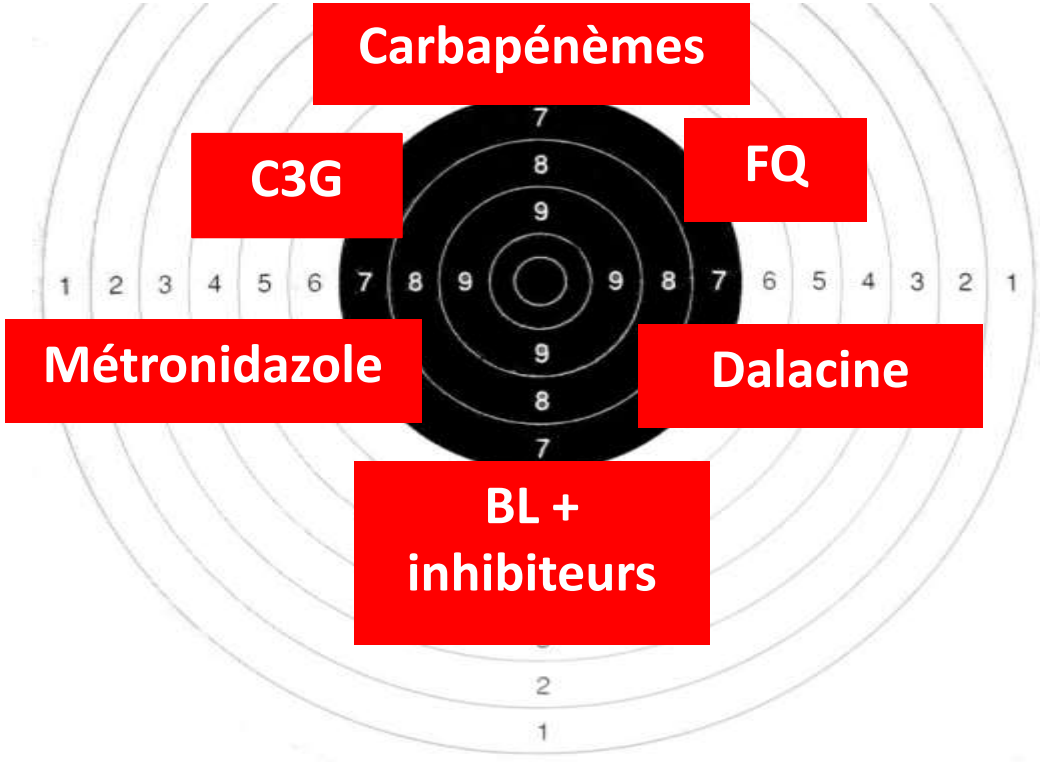
AAC vs C3G
Pip-Taz vs CP

2. Raccourcir les durées

Donskey et al. CID 2006
Kollef et al. Chest 2006
Weiss et al. CMI 2015
Dodds Ashley et al . CID 2014

Qualitatif écologique ?

Les ATB les plus polluants



« anaerobes friendly » ?

Flore dominante

10^9 à 10^{11} CFU/g de selles

Anaérobies (*Bacteroidetes, Clostridium, bifidobacteria*…)

Flore sous dominante

10^6 à 10^8 CFU/g de selles

E coli, Streptococcus, Enterococcus

Flore transitoire

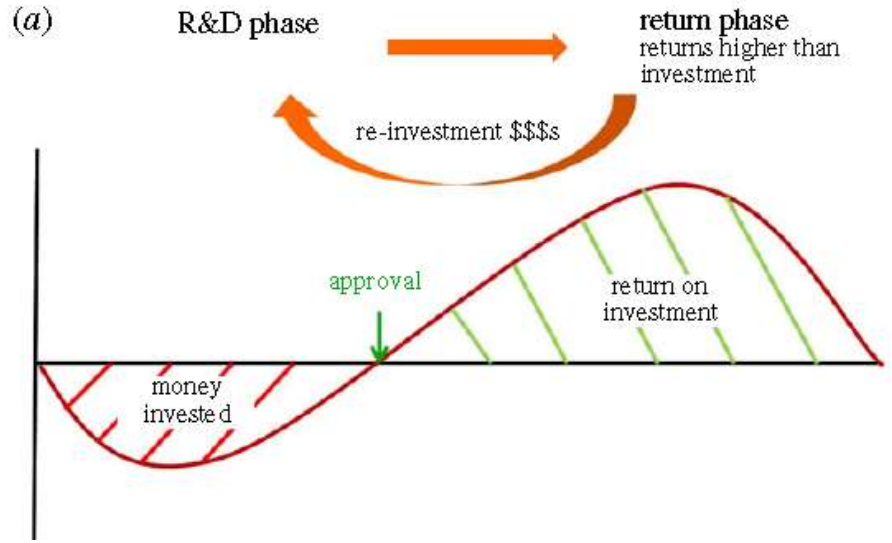
$<10^6$ CFU/g de selles

Klebsiella, Citrobacter

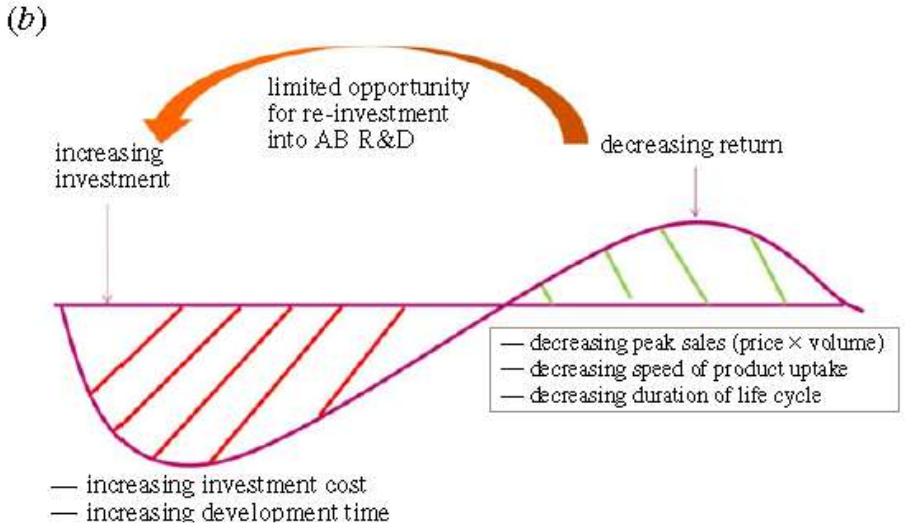
Pseudomonas

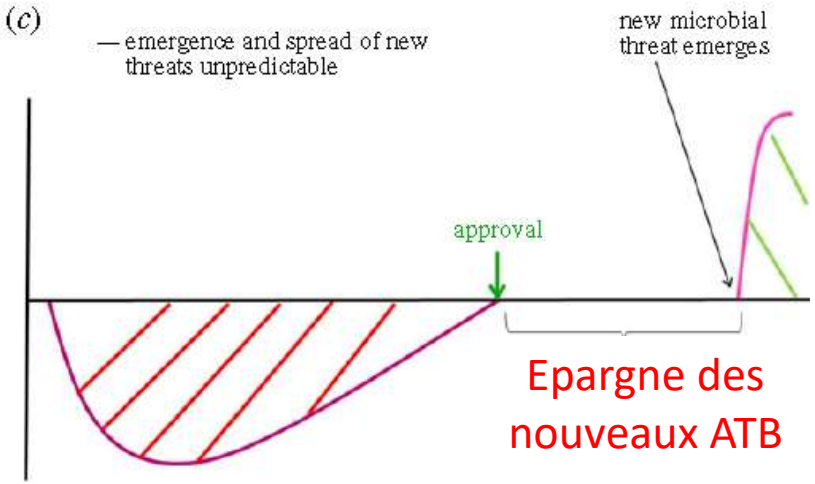
Faut-il épargner les nouveaux ATB ?

Modèle économique traditionnel



Modèle économique traditionnel ATB





Risque de déconnexion du modèle

Payne et al. Phil Trans R Soc B 2015

The Critical Role of the Staff Nurse in Antimicrobial Stewardship—Unrecognized, but Already There

Richard N. Olans,[1] Rita D. Olans,[2] and Alfred DeMaria Jr[3]

CID 2016:62 (1 January) • CLINICAL PRACTICE

[1]Hallmark Health System, Inc., Melrose-Wakefield Hospital, [2]MGH Institute of Health Professions - School of Nursing, Boston, and [3]Bureau of Infectious Disease, Massachusetts Department of Health, William A. Hinton State Laboratory Institute, Jamaica Plain, Massachusetts

An essential participant in antimicrobial stewardship who has been unrecognized and underutilized is the "staff nurse." Although the role of staff nurses has not formally been recognized in guidelines for implementing and operating antimicrobial stewardship programs (ASPs) or defined in the medical literature, they have always performed numerous functions that are integral to successful antimicrobial stewardship. Nurses are antibiotic first responders, central communicators, coordinators of care, as well as 24-hour monitors of patient status, safety, and response to antibiotic therapy. An operational analysis of inpatient admissions evaluates these nursing stewardship activities and analyzes the potential benefits of nurses' formal education about, and inclusion into, ASPs.

Impact of the implementation of a nurse-managed outpatient parenteral antibiotic therapy (OPAT) system in Baltimore: a case study demonstrating cost savings and reduction in re-admission rates

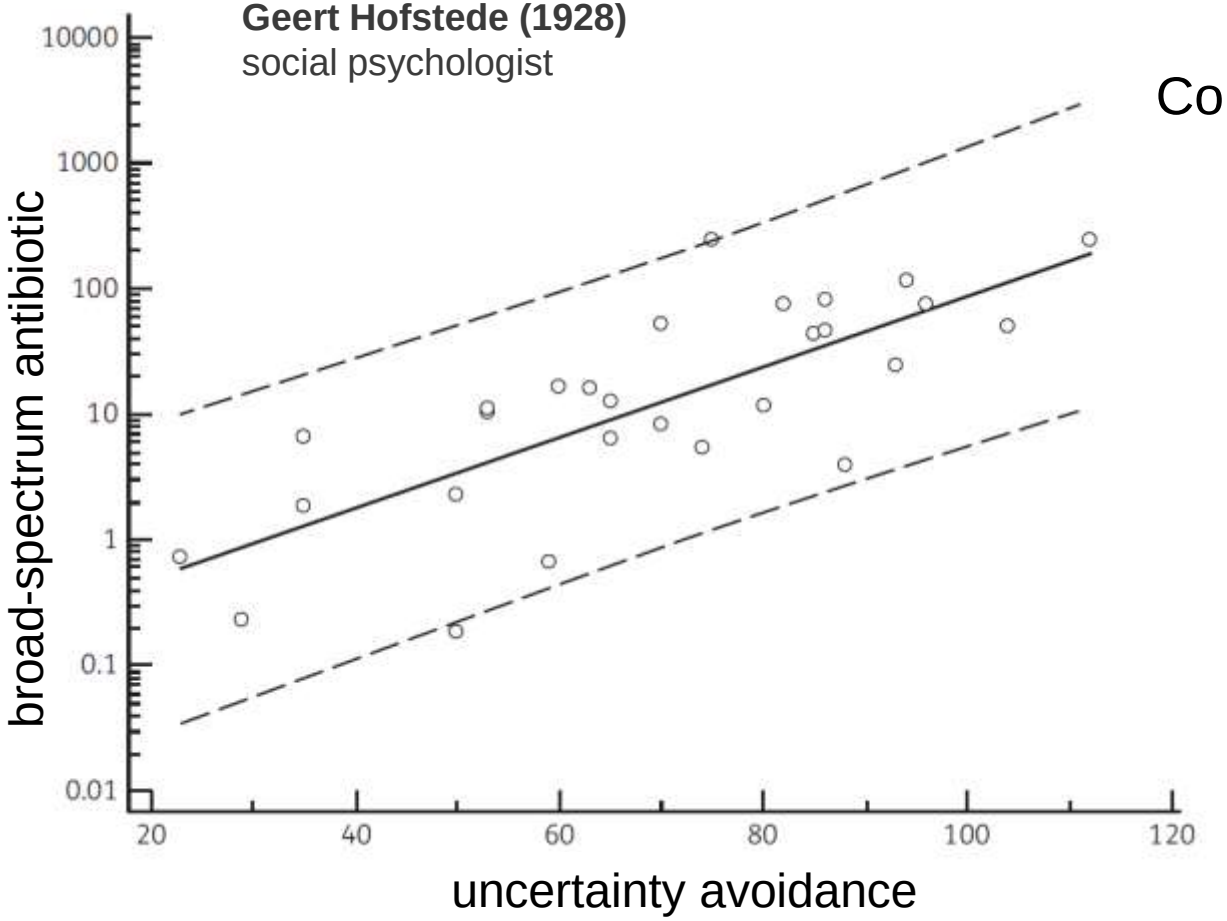
Omar Mansour[1,2], Jacqueline Heslin[3] and Jennifer L. Townsend[3*]

J Antimicrob Chemother 2018; **73**: 3181–3188

Broad-spectrum antibiotic use in Europe: more evidence of cultural influences on prescribing behaviour

https://geerthofstede.com

Geert Hofstede (1928)
social psychologist



Deals with a society's tolerance for uncertainty and ambiguity.

Correlation and regression analysis:

- Broad-spectrum ATB ratios (28 EU countries /ECDC)
- & national Hofstede cultural dimensions

A logarithmic model explained
58.6% of the variation
Broad-spectrum ATBr variability
solely using
national uncertainty avoidance scores (P 0.001).

Borg et al. JAC 2019

The Differences in Antibiotic Decision-making Between Acute Surgical and Acute Medical Teams: An Ethnographic Study of Culture and Team Dynamics

Ethnographic observational study of antibiotic decision-making in acute medical and surgical teams
London teaching hospital (2015 - 2017)
500 hours of direct observations, and face-to face interviews with 23 key informants
A qualitative grounded theory approach analyzed the emerging themes

In **medicine**, accepted norms of the decision-making process are characterized as:

collectivist (input from pharmacists, infectious disease, and medical microbiology teams)
rationalized, and policy-informed, with emphasis on de-escalation of therapy.

Challenge in antibiotic decision-making: **in the transition between the ED and inpatient teams**

In **surgery**, team priorities are split between 3 settings:

operating room, outpatient clinic, and ward

Challenges in antibiotic decision-making is perceived as a nonsurgical intervention that can be **delegated** to junior staff or other specialties.

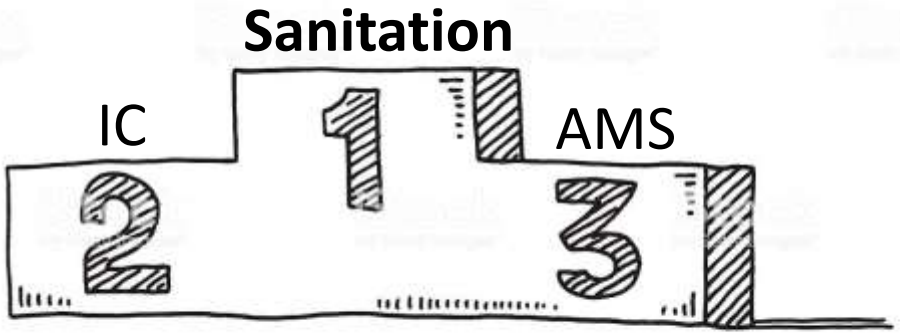
Charani et al. CID 2019

AMS in India

Abdul Ghafur
ID /AMS

- Antibiotics stewardship cannot be the only route ahead
- AMR is a complex challenge: technical and scientific challenge, but also a social, economic political challenge.
- Putting people at the centre of this fight is important, especially if we need to ameliorate the social and economic contributors

Tackling AMR in LMICs



"Improving sanitation and **involving the common people** in battling deadly resistant bacterial infections"

THE HINDU

Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach

C. Pulcini [1,2,*], F. Binda [1,2,3], A.S. Lamkang [4], A. Trett [4], E. Charani [5], D.A. Goff [6], S. Harbarth [7], S.L. Hinrichsen [8], G. Levy-Hara [9], M. Mendelson [10], D. Nathwani [11], R. Gunturu [12], S. Singh [13], A. Srinivasan [14], V. Thamlikitkul [15], K. Thursky [16], E. Vlieghe [17,18,19], H. Wertheim [20], M. Zeng [21], S. Gandra [4], R. Laxminarayan [4,22]

1) *Université de Lorraine, APEMAC, Nancy, France*
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3) *University of Milan, Department of Biomedical and Clinical Sciences «Luigi Sacco», Milan, Italy*
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6) *The Ohio State University Wexner Medical Center, Columbus, OH, USA*
7) *Geneva University Hospitals, Infection Control Program and WHO Collaborating Center, Faculty of Medicine, Geneva, Switzerland*
8) *Universidade Federal de Pernambuco (UFPE), Tropical Diseases Department, Recife, Brazil*
9) *Hospital Carlos G Durand, Unit of Infectious Diseases, Buenos Aires, Argentina*
10) *Groote Schuur Hospital, University of Cape Town, Department of Medicine, Division of Infectious Diseases & HIV Medicine, Cape Town, South Africa*
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18) *University of Antwerp, Global Health Institute, Antwerp, Belgium*
19) *Institute of Tropical Medicine, Department of Clinical Sciences, Antwerp, Belgium*
20) *Radboudumc, Department of Medical Microbiology and Radboud Center for Infectious Diseases, Nijmegen, The Netherlands*
21) *Children's Hospital of Fudan University, Department of Infectious Diseases, Shanghai, China*
22) *Princeton University, Princeton, NJ, USA*

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

ASP implementation core elements

Reporting & feedback

Quantity ATB
ATB susceptibility
Quality ATB

Displayed and real institutional priority

Standard staffing
Communicable Indicators

Monitoring /surveillance

Quantity ATB
ATB susceptibility
Quality ATB
Compliance

Accountability

Formal written strategy
Short & long terms targets

Formal written procedures of collaborations:
AS team, AST – leader,
AST –ATB committee,
AST – ICPT,
AST – other involved HCW

Organisation

Ward rounds
Meetings
AST availability
Community

Expertise

microbiology
Diagnosis
Treatment
Clinical

Formal documents

Up to date guidelines
Formulary
Plan of ATB administration
internal ATB procedures for AST

Education

Formal ressources
HCW
AST

Pulcini et al. CMI 2019

Sciences de l'Implémentation

Sciences de l'Implémentation pour la Prévention des Infections et le Bon Usage des Antibiotiques

Présentations :

- Introduction aux sciences de l'implémentation (fichier word, Gabriel Birgand)
- En quoi consistent les Sciences de l'implémentation ? 15 min (Gabriel Birgand)
- Comment évaluer les barrières et facilitateurs ? 45 min (Sylvain Delouvée, EHESS)
- Quelle stratégie d'implémentation choisir ? Exemple du CFIR 45 min (Walter Zingg, Genève)
- Comment former nos collègues ? 45 min (A.G. Venier, Bordeaux)
- Comprehensive Unit-based Safety Program (CUSP) de l'Agence for Healthcare Research and Quality. 45 min (Gabriel Birgand)
- Exemples d'implémentation science en prévention de l'infection. 45 min (Jean-Christophe Lucet)
- Exemples d'implémentation en Bon usage des antibiotiques 30 min (Jeroen Schouten, Radboud)

Prévention et Contrôle de l'infection

- Atelier 1 : Prévention des infections sur cathéters veineux centraux (Basé sur l'expérience Suisse) : Gabriel Birgand, Walter Zingg, Anne-Gaëlle Venier
- Atelier 2 : Prévention des complications post-chirurgicales : Checklist au bloc opératoire (Basé sur l'expérience Anglaise) : Gabriel Birgand, Jean-Christophe Lucet, Anne-Gaëlle Venier

Bon usage des antibiotiques

- Insuffler la culture de l'abstention thérapeutique et gérer l'incertitude. Nathan Peiffer Smadja
- Différer un traitement antibiotique, choisir une antibiothérapie probabiliste chez les patients à haut risque de multirésistance. Solen Kernéis
- Changer les habitudes en situation complexe. Serge Alfandari et Nahema Issa
- Désescalade chez le patient sévère (réanimation, hématologie), respect des durées courtes, arrêt de l'antibiothérapie si l'infection n'est pas confirmée, relais oral dans les infections complexes (endocardite, infection ostéo-articulaire). Serge Alfandari et Nahema Issa

Antimicrobial Stewardship at the Core of COVID-19 Response Efforts: Implications for Sustaining and Building Programs

Hasti Mazdeyasna[1] · Priya Nori[2] · Payal Patel[3] · Michelle Doll[4] · Emily Godbout[4] · Kimberly Lee[5] · Andrew J. Noda[5] · Gonzalo Bearman[4] · Michael P. Stevens[6]

Antimicrobial use, drug-resistant infections and COVID-19

Timothy M. Rawson, Damien Ming, Raheelah Ahmad, Luke S. P. Moore and Alison H. Holmes

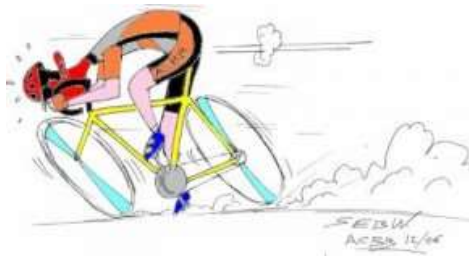
COVID-19: don't neglect antimicrobial stewardship principles!

B.D. Huttner [1,2,*], G. Catho [2], J.R. Pano-Pardo [4], C. Pulcini [5,6], J. Schouten [3]

Involving antimicrobial stewardship programs in COVID-19 response efforts: All hands on deck

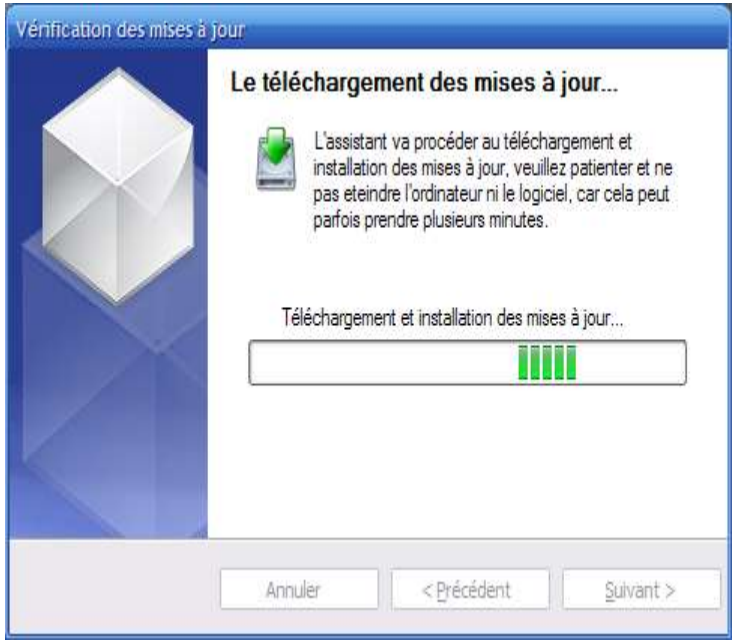
Michael P. Stevens MD, MPH[1], Payal K. Patel MD, MPH[2] and Priya Nori MD[3]

Conclusion



Squeezing the Resistance Balloon at Multiple Sites

Rahal et al. Clin Infect Dis 2002



- Reconfiguration du schéma de pensée dans l'adaptabilité et la dualité
  - L'hôpital et la ville
  - L'individu et le collectif
  - Le quantitatif vs le qualitatif
  - Le travail des synergie d'équipes
  - La stratégie d'approche et l'implémentation