Optimisation de la prescription des antibiotiques, place des équipes mobiles d'infectiologie

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Préambule / sémantique

- **Optimisation de la prescription des antibiotiques**
  - // quelles sont les interventions les plus efficaces?
  - // moyens contraints/constants voire décroissants

- **« Place des équipes mobiles d'infectiologie »**
  - Equipe vs médecin référent ATB
  - M comme mobile, M comme multidisciplinaire
  - Infectiologie vs Antibiothérapie

Les interventions des équipes mobiles

	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

Typologie des interventions

Persuasive interventions:

- Educational materials
- Educational meetings
- Local consensus processes
- Educational outreach visits
- Local opinion leaders
- Reminders provided verbally on paper or on computer
- Audit and feedback

Restrictive interventions:

- Selective reporting of laboratory susceptibilities
- Formulary restriction
- Requiring prior authorization of prescriptions
- Therapeutic substitutions
- Automatic stop orders
- Antibiotic policy changes; cycling, rotation, recycling

Structural interventions:

- Changing from paper to computerized records
- Computerized decision support systems
- Rapid laboratory testing

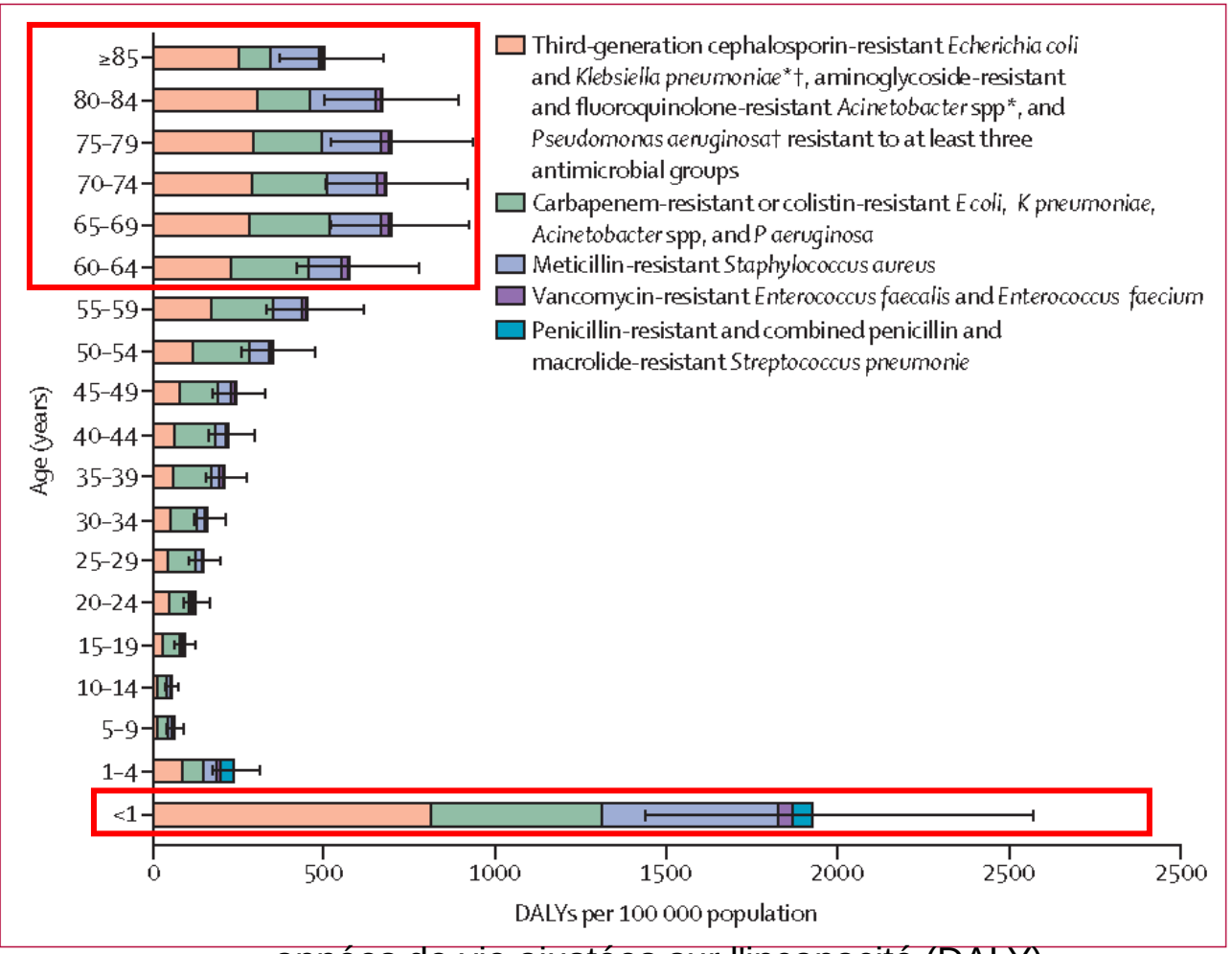
Davey et al . Cochrane 2011

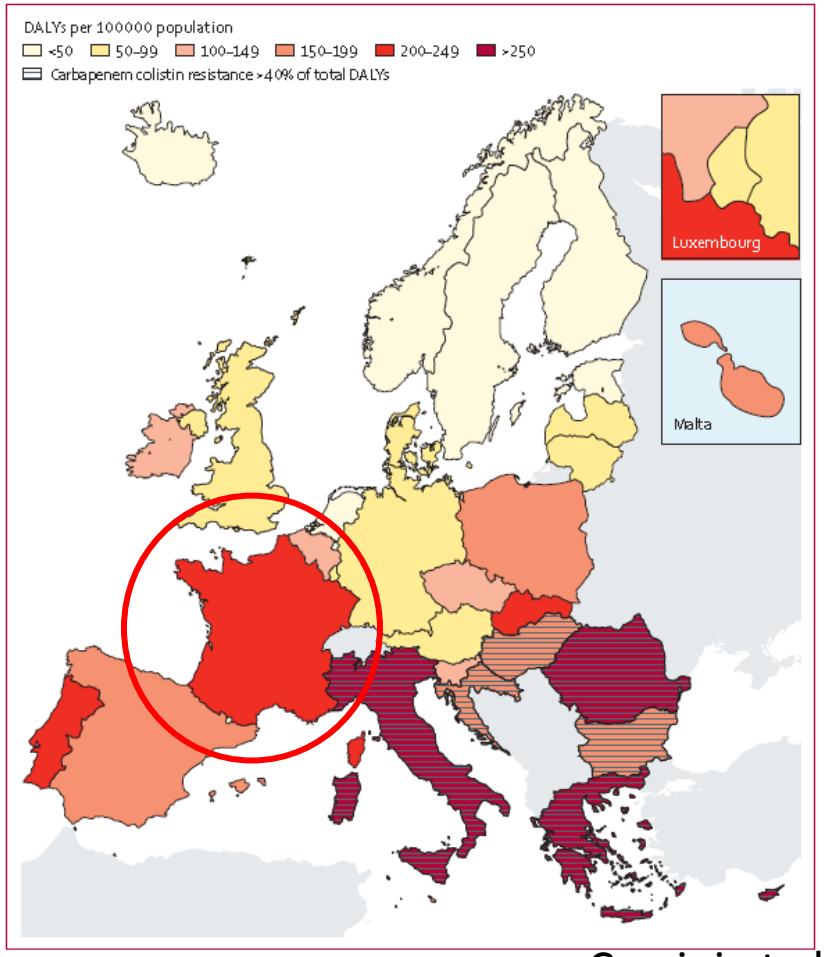
L’enjeu, en termes de morbi-mortalité

33.110 (28.480–38.430) attributable deaths

EARS-Net

CE 2015





années de vie ajustées sur l'incapacité (DALY)

Cassini et al. Lancet ID 2018

Quelle est la finalité des équipes mobiles

- Quels facteurs pour déterminer l'impact du conseil antibiotiques?

Niveau Collectif			Niveau individuel
Antibiotiques	**Microbiologique**	**Financier**	**Patient**
Prescriptions conformes aux recommandations	Taux de résistance	Maîtrise ou réduction des coûts	Mortalité
Volumes d'antibiotiques	Incidence des Clostridium difficile		Durée de séjour
Durée des traitements antibiotiques			Réhospitalisation
Réduction de certains antibiotiques			Délai d'initiation d'un traitement adapté

Nagel JL., Clin Infect Dis 2014

« …optimisation de la prescription ATB »

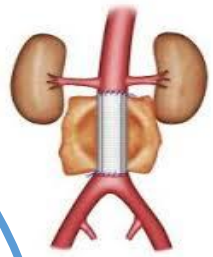
The primary goal is to achieve optimum **clinical outcomes** and ensure **cost-effectiveness** of therapy while keeping to a minimum unintended consequences of anti microbial use, including **toxic effects**, **selection of pathogenic organisms**, and the **emergence of resistance**

Dellit TH., Clin Infect Dis 2007

Optimisation de la prescription antibiotique

Amélioration de la PEC des infections peu sévères

Amélioration de la PEC des infections sévères / complexes



Critères médico-économiques et écologiques

Critères médicaux, mortalité

Exemples d’évaluations d’interventions

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

David Baur*, Beryl Primrose Gladstone*, Francesco Burkert, Elena Carrara, Federico Foschi, Stefanie Döbele, Evelina Tacconelli

	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

Effet de l'AMS sur la mortalité

Variables	OR (95% CI)	*P* Value
14-day mortality		
Age >60 y	2.97 (1.51–5.87)	.002
Pitt score >2	3.04 (1.74–5.33)	<.001
High-risk source[a]	2.80 (1.32–5.92)	.007
Intervention	0.49 (.28–.87)	.016
30-day mortality		
Age >60 y	3.48 (1.89–6.41)	<.001
Pitt score >2	2.34 (1.40–3.92)	.001
High-risk source[a]	3.11 (1.54–6.26)	.001
Intervention	0.59 (.36–.97)	.04

Dans les bactériémies à *Staphylococcus aureus*

High-risk source includes endovascular sources different than catheter, endocarditis, nervous central system infections, intra-abdominal infections, and respiratory tract infection

Lopez-Cortes et al. CID 2013

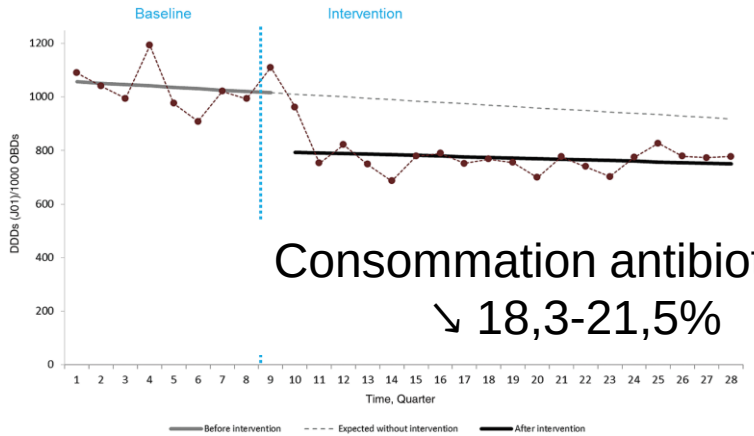
Ce ne sont pas des choses très compliquées

	Preintervention Period	Intervention Period	Adjusted OR for Adherence to QCI (95% CI)[a]	*P* Value
Follow-up blood culture	131/214 (61.2)	159/198 (80.3)	2.83 (1.78–4.49)[b]	<.001
Source control	86/122 (70.2)	105/115 (91.3)	4.56 (2.12–9.79)[c]	<.001
Echocardiography	76/144 (52.8)	74/101 (73.3)	2.50 (1.42–4.41)[d]	.002
Early cloxacillin in MSSA	120/211 (56.9)	124/174 (71.3)	1.79 (1.15–2.78)[e]	.009
Vancomycin dosing	23/49 (46.9)	30/54 (55.6)	1.42 (.65–3.10)[f]	.38
Treatment duration	151/207 (72.9)	161/189 (85.2)	2.13 (1.24–3.64)[g]	.006

The intervention consisted of a set of written recommendations according to the 6 aspects selected as QCIs provided in a structured form by an infectious diseases specialist at each hospital

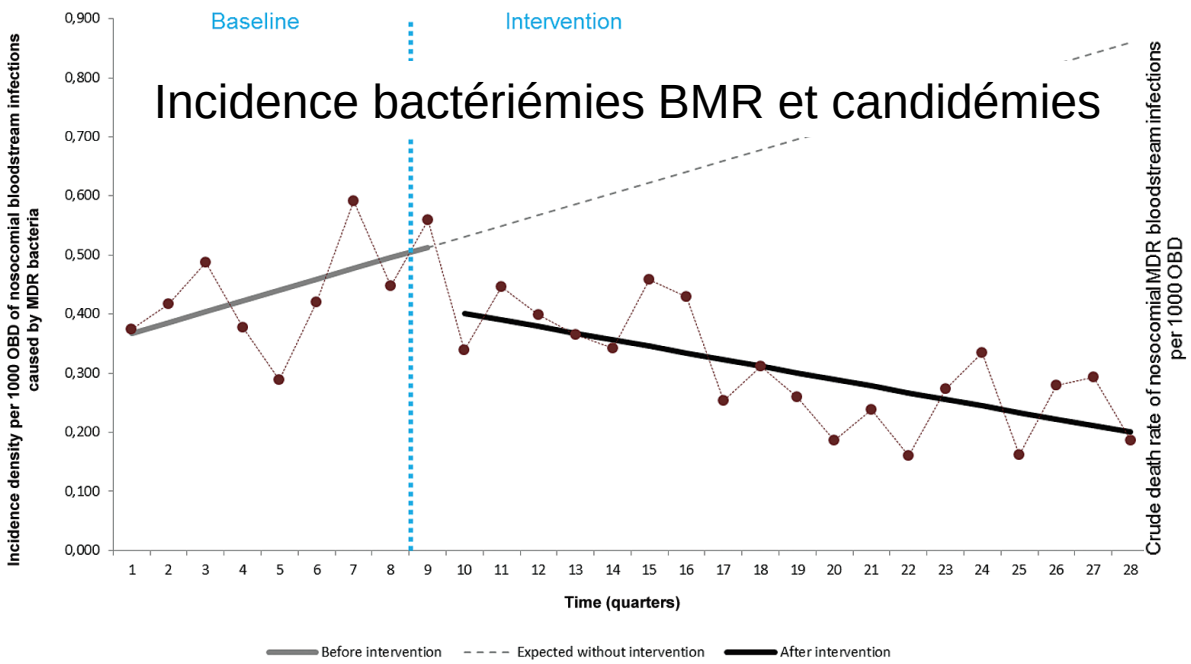
Lopez-Cortes et al. CID 2013

Effet de l'AMS sur la mortalité // résistance

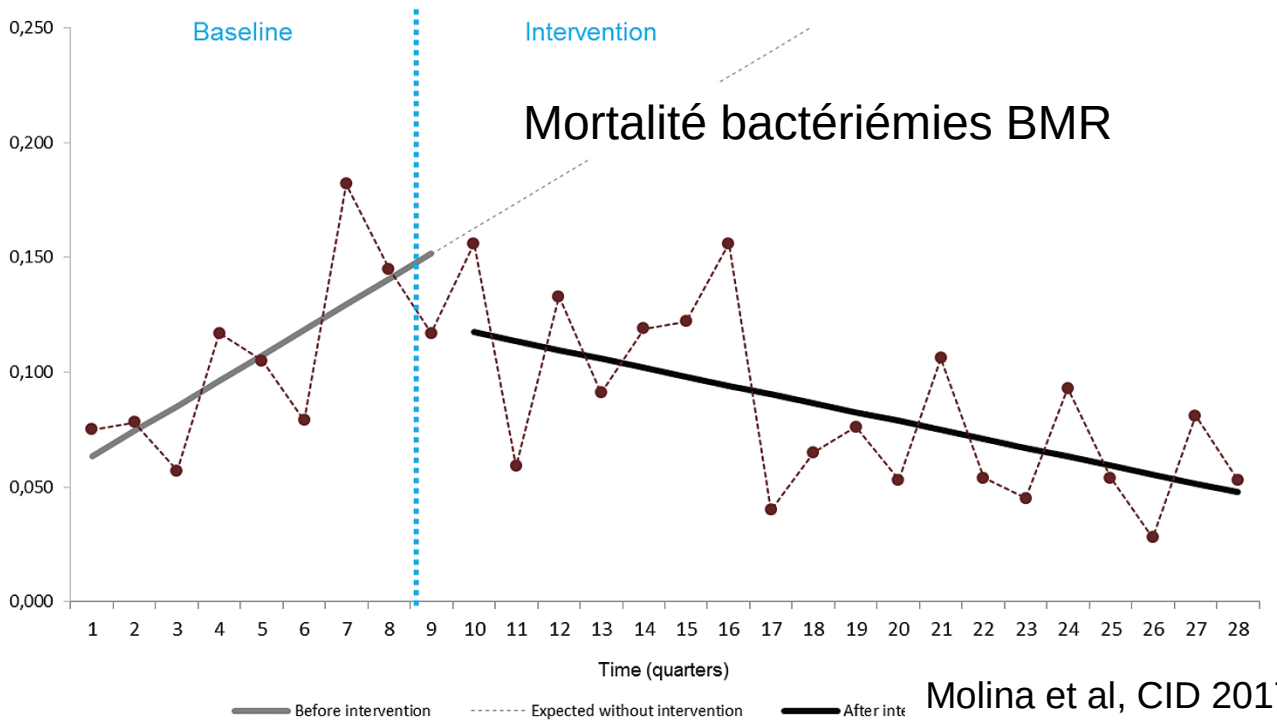


Consommation antibiotiques
↘ 18,3-21,5%

Quasi-experimental intervention study
Interrupted time-series analysis
Multifaceted educational intervention (10 counselors)
Over a 5-year period in a teaching hospital
Peer-to-peer educational



Incidence bactériémies BMR et candidémies



Mortalité bactériémies BMR

Molina et al, CID 2017

AMS aux urgences

	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

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 aux urgences

Mortalité à J14 : multivariée

	aHR (95% CI)	p
Age	1.01 (1.00-1.03)	0.05
qSOFA ≥ 2	1.68 (1.15-2.45)	0.007
Lactate > 2	2.13 (1.39-3.25)	<0.001
Source de l'infection	2.07 (1.42-3.02)	<0.001
Post phase	0.64 (0.43-0.94)	0.026

Mais intervention : 13 médecins 24/24, 7/7

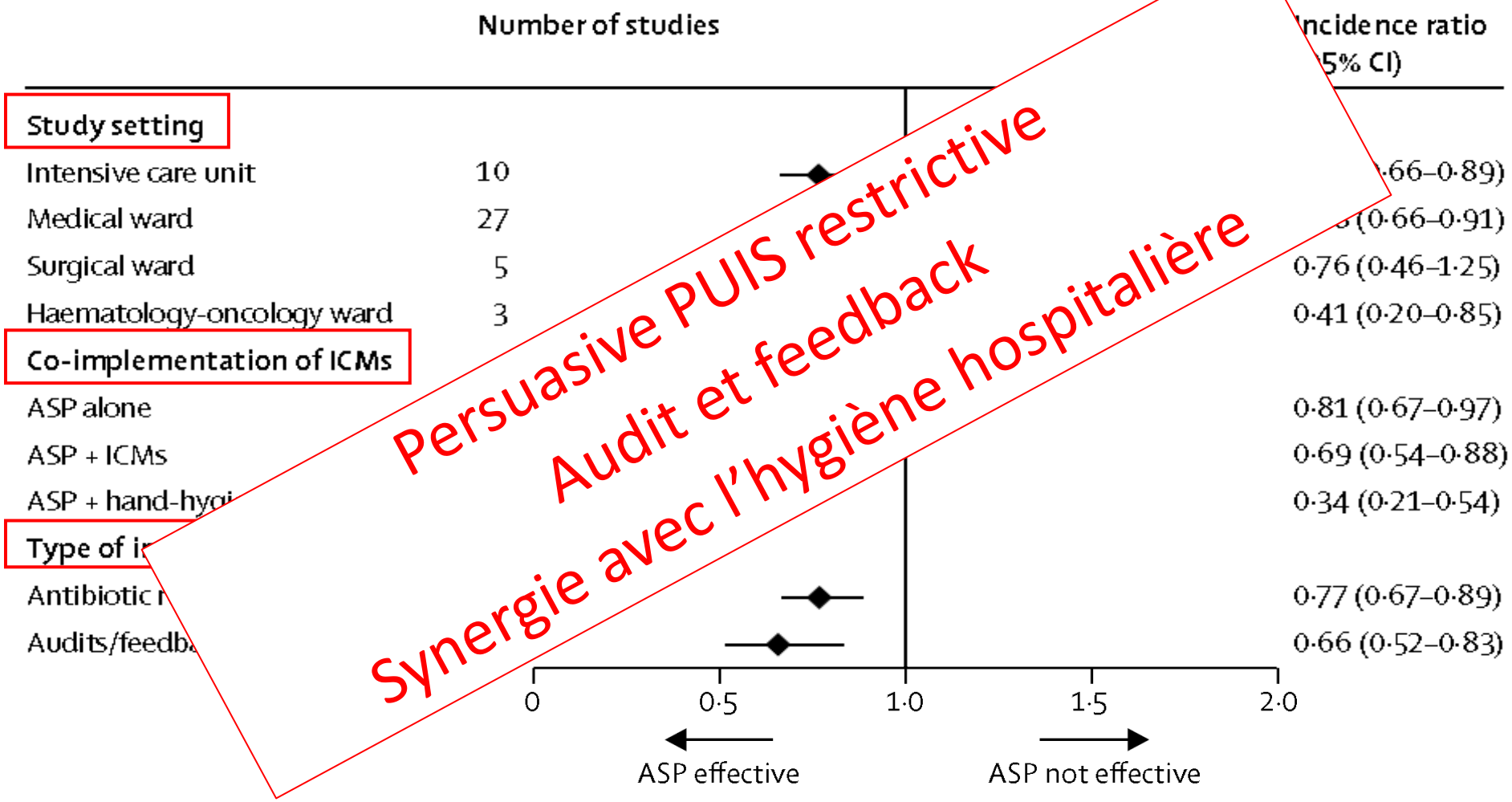
Viale et al. CID 2017

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 résistance bactérienne



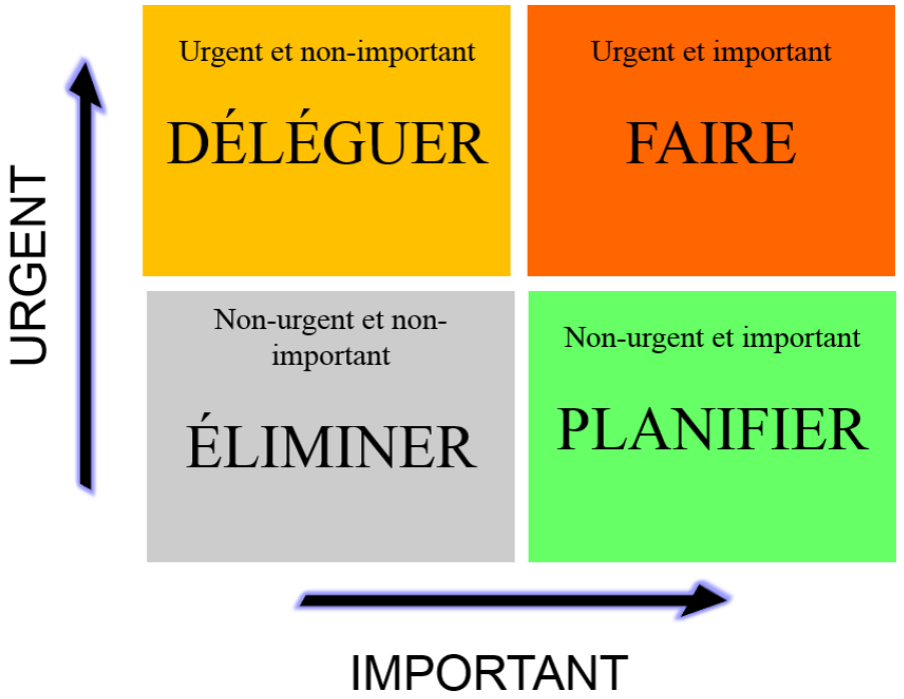
Persuasive PUIS restrictive

Audit et feedback

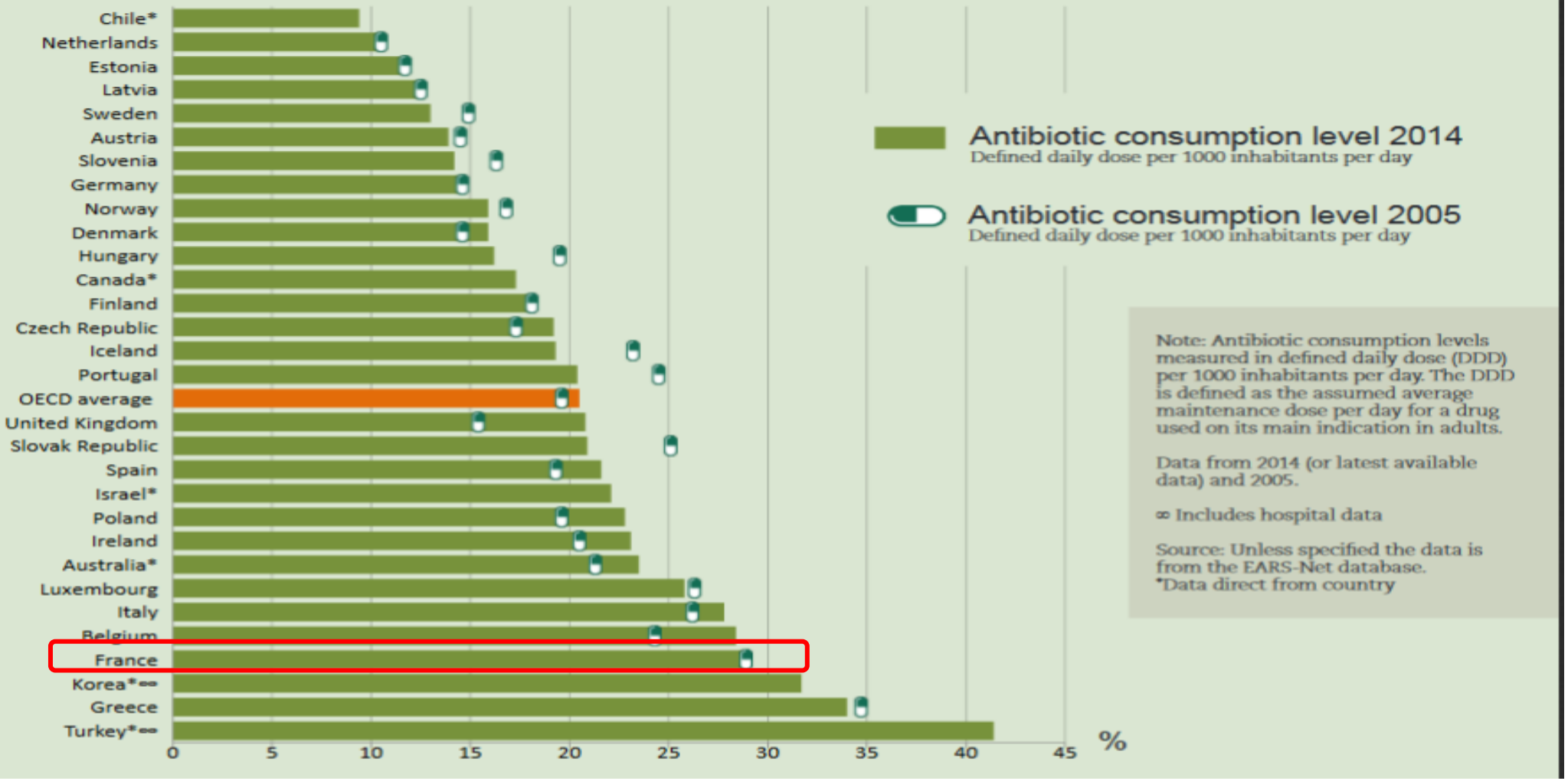
Synergie avec l'hygiène hospitalière

Baur et al. LID 2017

Questions existentielles



Human consumption of antibiotics remained substantially stable between 2005 and 2014



Données de consommation ATB - ANSM 2018

EN SANTÉ HUMAINE EN ÉTABLISSEMENTS DE SANTÉ (HÔPITAUX ET CLINIQUES)

Dans les établissements de santé

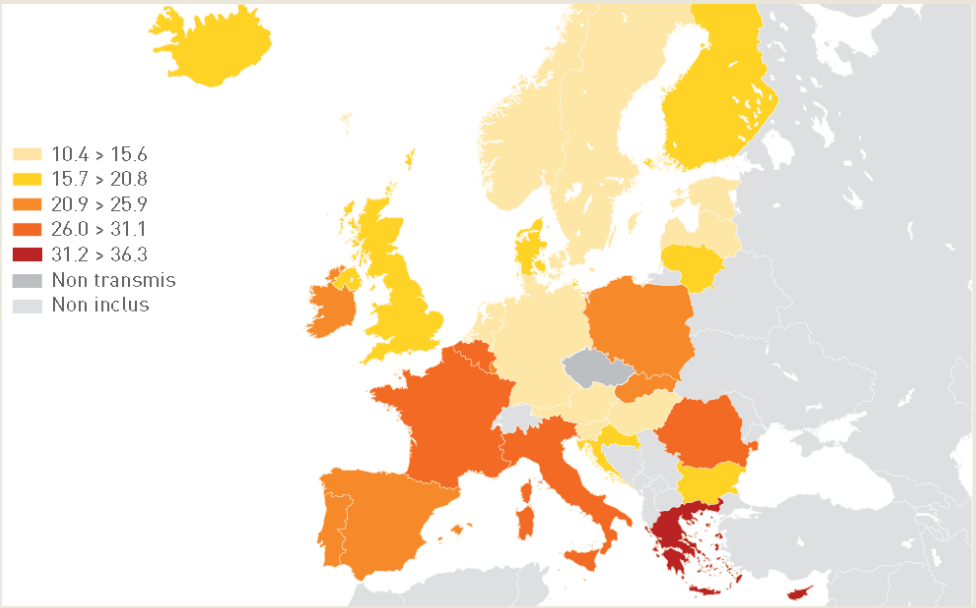
2007 : 2,2 doses[1] / 1 000 habitants / jour

2017 : 2,1 doses[1] / 1 000 habitants / jour

En 10 ans, la consommation d'antibiotiques en établissements de santé est plutôt stable.

Source : ANSM

CONSOMMATION D'ANTIBIOTIQUES EN SANTÉ HUMAINE (EN VILLE) EN 2016



Source : Esac-Net / ANSM

EN SANTÉ HUMAINE EN VILLE

Dans la communauté

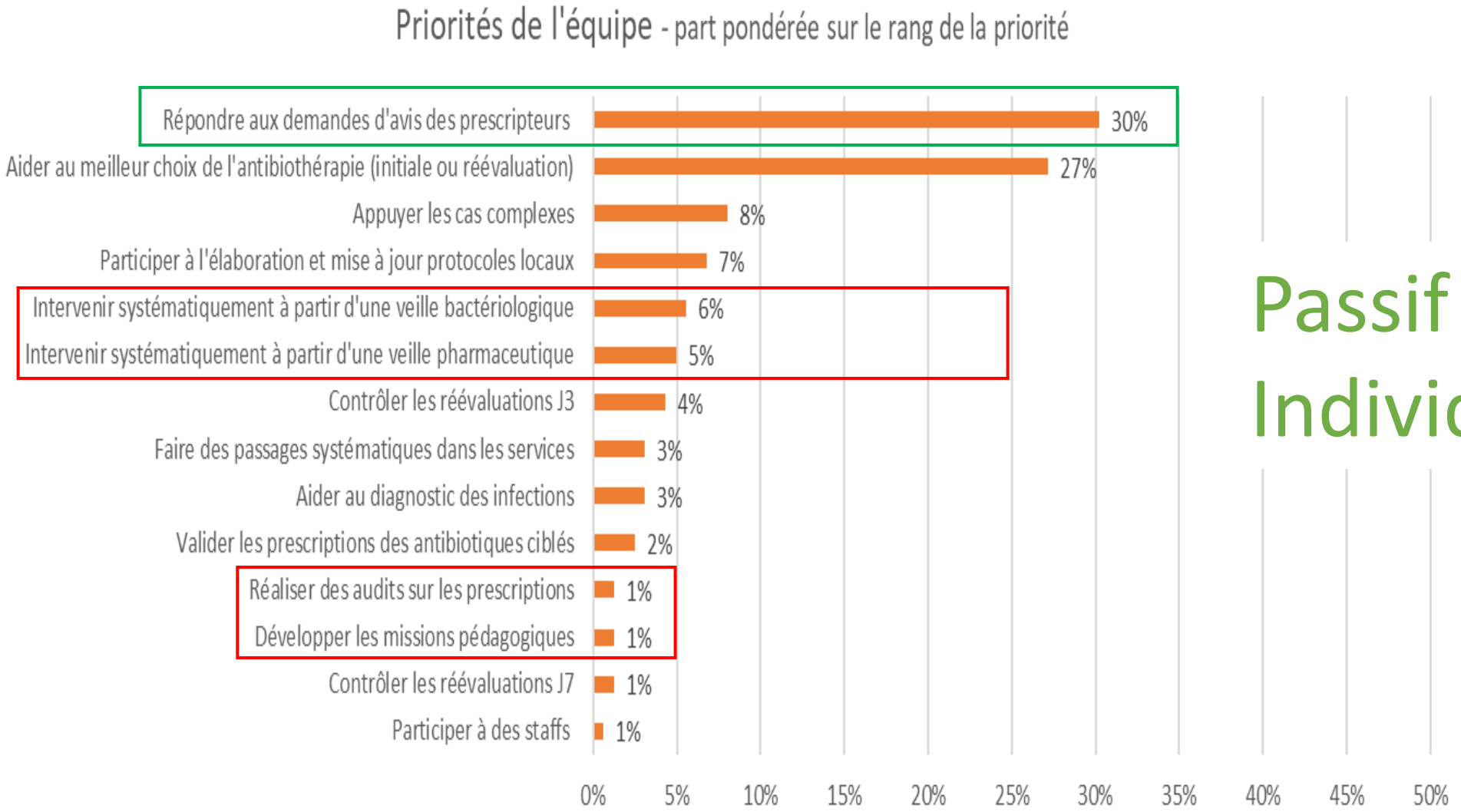
2007 : 28,6 doses[1] / 1 000 habitants / jour

2017 : 29,2 doses[1] / 1 000 habitants / jour

En 10 ans, la consommation d'antibiotiques en ville s'inscrit à la hausse.

Source : ANSM

Les priorités des équipes de bon usage antibiotique en France



Passif &
Individu centré

Perozziello et al. under review

Objectifs quantitatifs ?

1. Ne pas démarrer, à chaque fois que possible

2. Raccourcir les durées

Objectifs quantitatifs ?

1. Ne pas démarrer, à chaque fois que possible

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

Glinz D et al . JAC 2017

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

Flokas ME et al . OFID 2017

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 ou qualitatifs ?

1. Ne pas démarrer, à chaque fois que possible

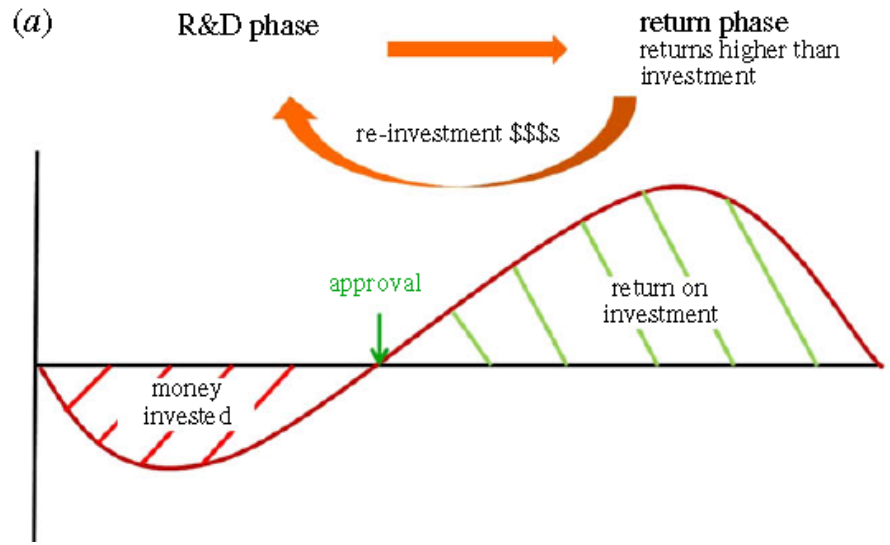
3. Epargner les ATB à large spectre ?

« Large spectre »

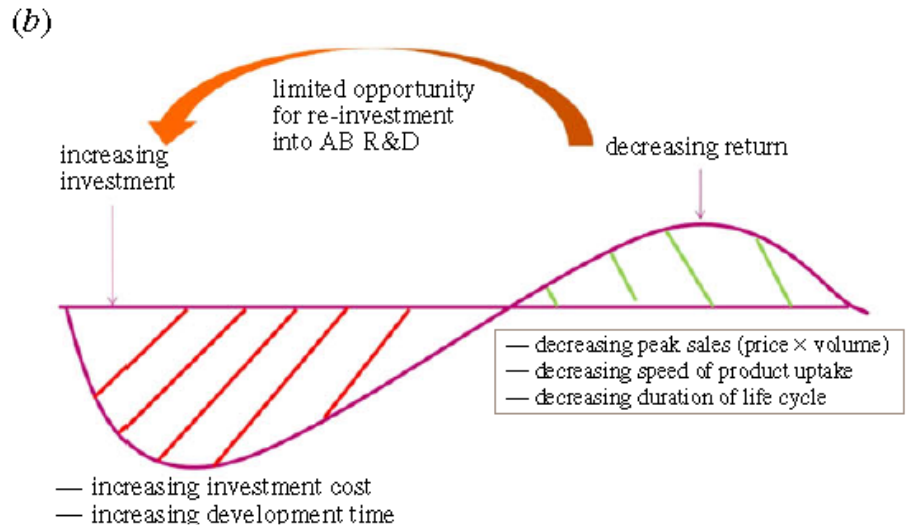
2. Raccourcir les durées

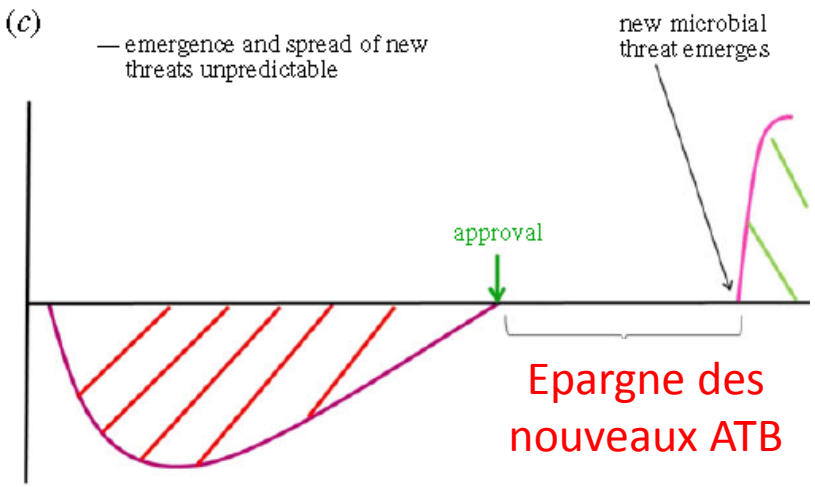
Faut-il épargner les nouveaux ATB ?

Modèle économique traditionnel



Modèle économique traditionnel ATB





Risque de déconnexion du modèle

Payne et al. Phil Trans R Soc B 2015

Avoir notion de la cascade de l'étiquette « allergique aux BL » et de ses conséquences

10 % d'allergies rapportées aux β-lactamines

→ **10% de réelles allergies**

→ **10% d'hypersensibilités bloquantes**

Macy E et al. J Allergy Clin Immunol 2013 & 2014

- **Utilisation d'alternatives souvent plus « polluantes »** — Macy et al. JACI 2014
- **Perte de chance sur le pronostic de l'infection / mortalité** — Blumenthal et al. Plos One 2016, Turner OFID 2018, Gary Huang CID 2018
- **Impact délétère aussi en antibioprophylaxie, +50% ISO** — Blummenthal et al. CID 2018

Interventions réduisent l'usage des alternatives à large spectre (formation, délégation de tâches)

Trubiano et al. CID 2017 , Leis JA et al. CID 2017

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*]

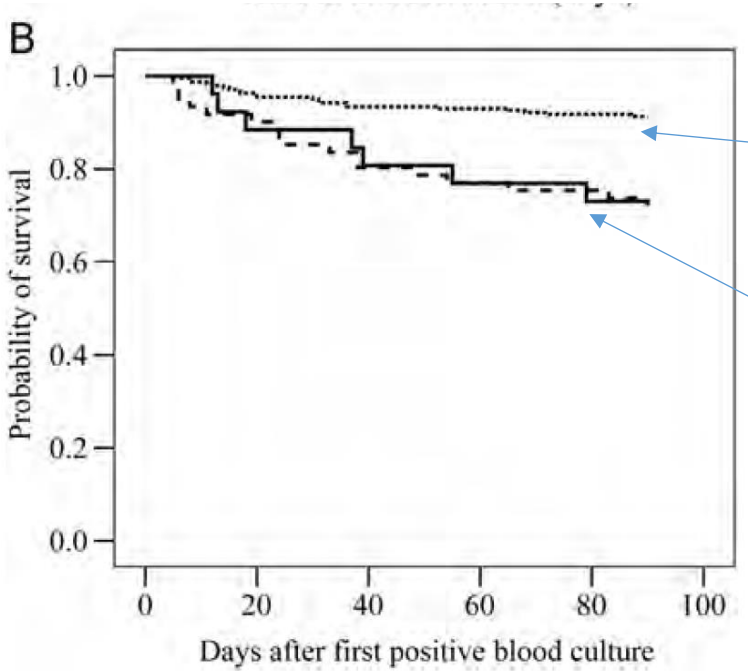
J Antimicrob Chemother 2018; **73**: 3181–3188

Se méfier des avis téléphoniques

Survie à J90

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Negative prognostic impact				
Pneumonia	2.31 (1.23–4.33)	.008	2.74 (1.49–5.05)	.001
ICU within 3 d	1.96 (1.00–3.83)	.046	2.28 (1.19–4.15)	.012
Corticosteroid therapy[b]	5.48 (1.93–15.6)	<.0001	2.98 (1.29–6.85)	.01
Telephone IDS within 1 wk	3.21 (1.63–6.33)	<.0001	2.31 (1.22–4.38)	.01
No IDS consultation within 1 wk	2.51 (.99–6.37)	.045	3.56 (1.59–7.94)	.002

- Finlande
- Etude rétrospective
- 342 bactériémies à SAMS
- Suivi à 90 jours
- Analyse selon
  - Avis au lit du patient (72%)
  - Avis téléphonique (18%)
  - Aucun avis donné (10%)
- Au moins un ATB actif à J0

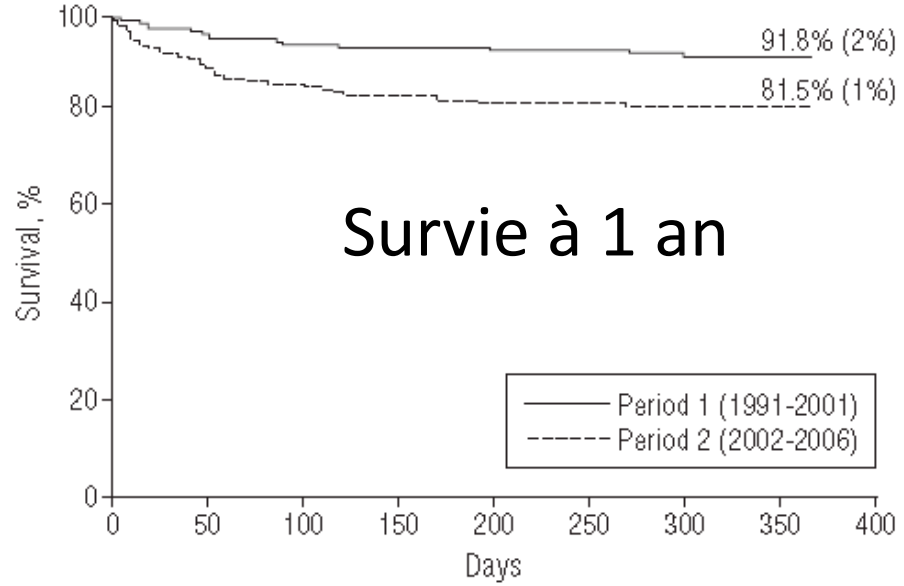


Bedside

Telephone
No IDS cs

Forsblom, Clin Infect Dis 2013

Staff, RCP d'infectiologie



Definite IE due to common or unknown pathogens, patients in cardiology department, La Timone Marseille, France:

-1991-2001: Multidisciplinary team, management not standardized. 1994: standardized diagnostic kit= 173 cases
-VS 2001-2006: Consensual and standardized management (ATB, surgery) and Follow-up = 160 cases

The rate of administration of an appropriate antimicrobial agent increased significantly from 31.6% during period 1 to 95% during period 2 (*P*.001).

1 year mortality: 18.5% to 8.2% (HR, 0.41; 95% CI 0.21-0.79 [*P*=.008]).
Reduction in-hospital mortality: 12.7% vs 4.4%, respectively; *P*=.007

Table 5. Predictors of 1-Year Mortality (Cox Multivariable Analysis)

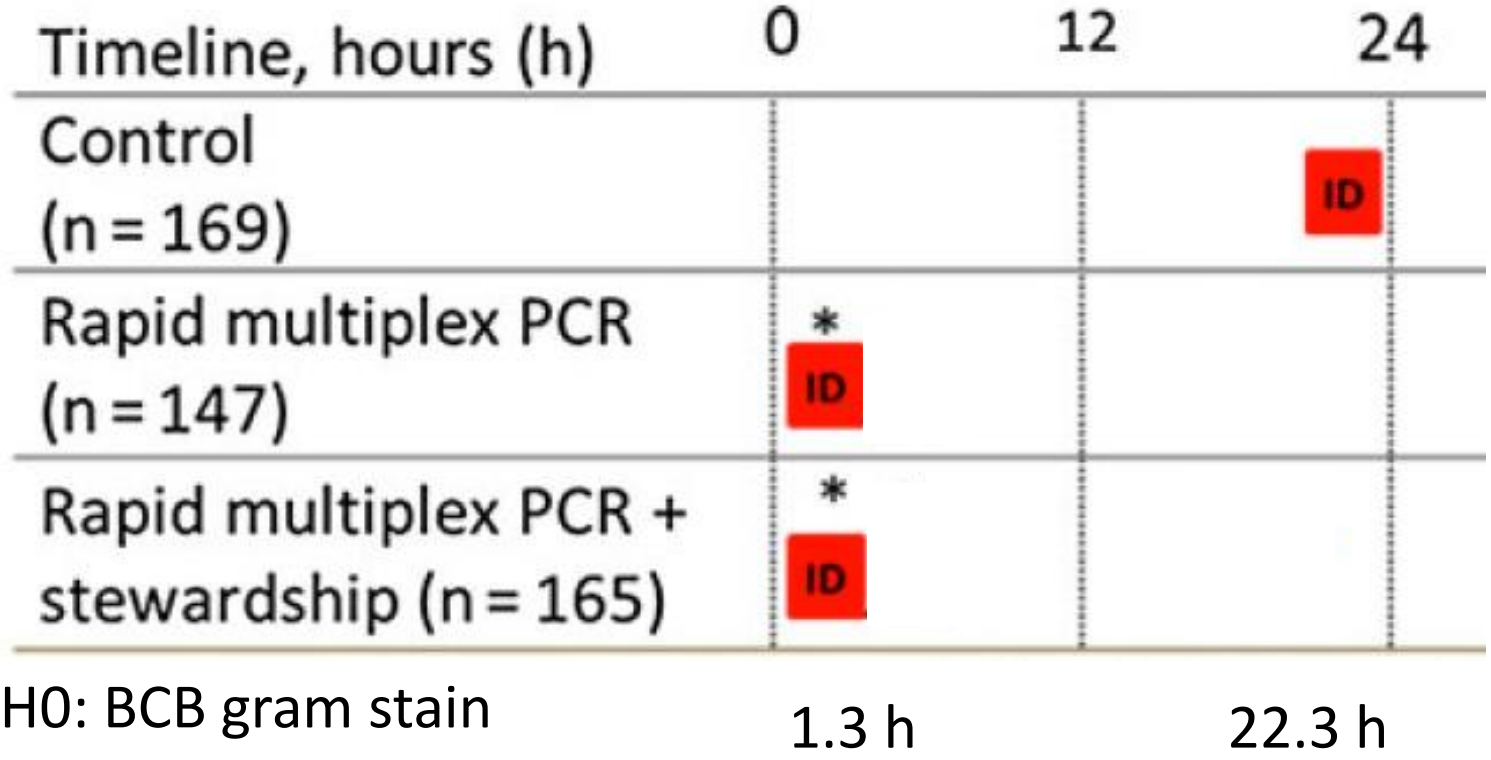
Predictor	Adjusted HR (95% CI)	*P* Value
Age, y	1.04 (1.02-1.08)	.001
Male sex	0.64 (0.32-1.28)	.21
Charlson comorbidity index >2	1.20 (0.49-2.96)	.69
Presumably healthy valves	0.57 (0.25-1.29)	.18
Mechanical prosthetic valve	2.70 (1.13-6.40)	.03
Renal failure	1.21 (0.60-2.44)	.60
Staphylococcus aureus	3.18 (1.29-7.84)	.01
Enterococci	2.69 (0.97-7.43)	.06
Nondigestive streptococci	0.38 (0.08-1.79)	.22
IE of unknown etiology	2.49 (0.95-6.53)	.06
Acute heart failure	2.04 (1.01-4.15)	.048
Stroke	2.92 (1.27-6.73)	.01
Abscess	0.64 (0.28-1.47)	.29
Valvular surgery	0.82 (0.40-1.67)	.58
Calendar year	0.99 (0.89-1.10)	.85
Period 2 (2002-2006)	0.26 (0.09-0.76)	.01

Bothelo-Nevers E Archives Intern Med 2009

Implication dans l'implementation des nouveaux tests DG

FilmArray Blood Culture ID Panel

Randomized clinical trial, n=617 patients, Mayo Clinic, 2013-2014



↗ Narrow-spectrum BL use (cefazolin, nafcillin, oxacillin)

↘ Broad-spectrum BL use (piperacillin-tazobactam)

Time from Gram stain to appropriate ATB shortest in the rmPCR/AS group: 21 hours vs control 34 h vs rmPCR 38 hours, P < .001

Banerjee et al . CID 2015

Bon usage antibiotique et dimensions culturelles

Individualism
The extent to which people feel independent, as opposed to being interdependent as members of larger wholes.

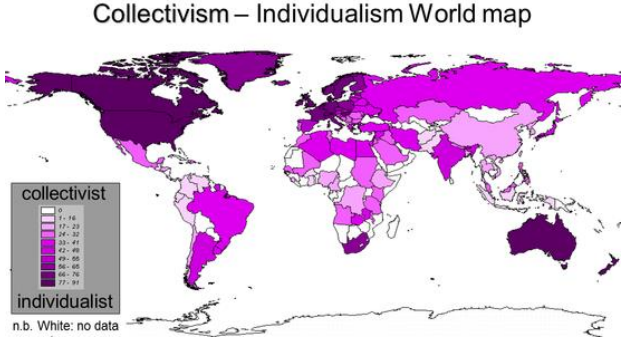
Power Distance
The extent to which the less powerful members of organizations and institutions (like the family) accept and expect that power is distributed unequally

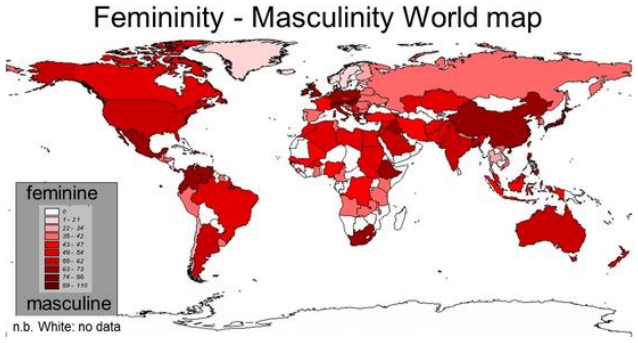
Masculinity
The extent to which the use of force in endorsed socially.

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

Long-term orientation
deals with change.

Indulgence
About the good things in life.





https://geerthofstede.com

Approche culturelle et qualitative

RESEARCH ARTICLE

Investigating the cultural and contextual determinants of antimicrobial stewardship programmes across low-, middle- and high-income countries—A qualitative study

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

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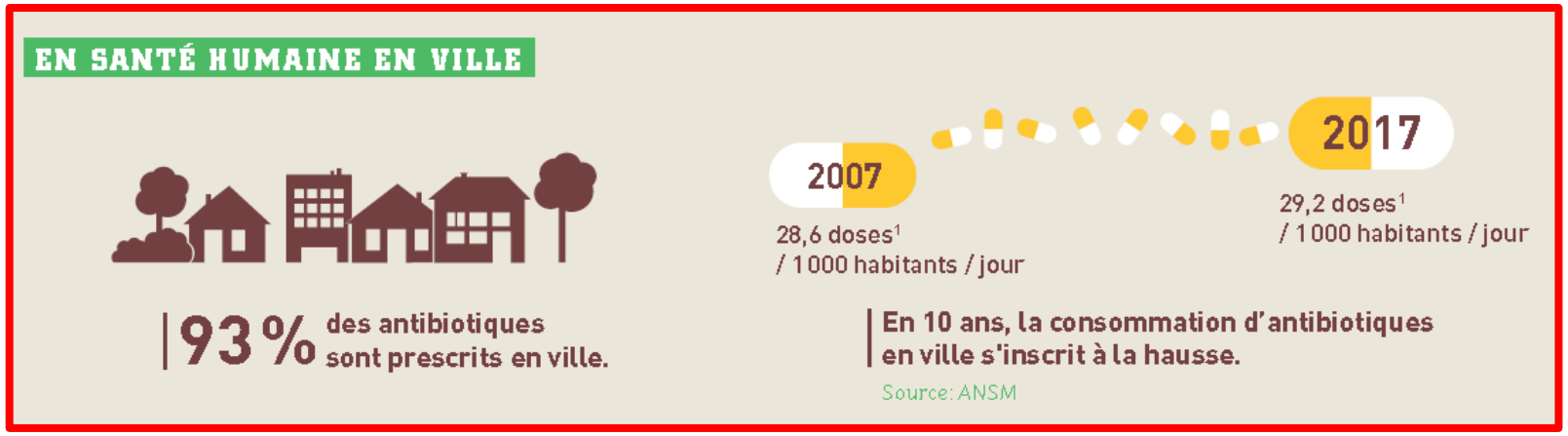
4 KEY ISSUES

1. IN SOME COUNTRIES ACCESS TO ANTIBIOTICS IS TOO EASY
2. PROFESSIONAL BOUNDARIES AND RESPECT FOR HIERARCHIES CAN LIMIT WHO CAN PARTICIPATE IN DECISIONS ON ANTIBIOTIC PRESCRIBING
3. THE USE OF ANTIBIOTICS IN SURGERY NEEDS TO BE OPTIMISED
4. THERE IS A NEED TO IMPROVE THE SUPPORT FROM GOVERNMENTS AND LOCAL AUTHORITIES



ANTIBIOCLIC
Antibiothérapie rationnelle en soins primaires

> 9.500 connexions / jour

→ Impact favorable sur :
Choix molécules / reco
Durée ttt

P228 & 229, RICAI 2017

Indépendant de l'industrie
Comité d'experts : généralistes universitaires et infectiologues hospitaliers
Mises à jour au gré des recommandations

Systèmes informatiques d'aide à la décision dans le domaine de l'antibiothérapie

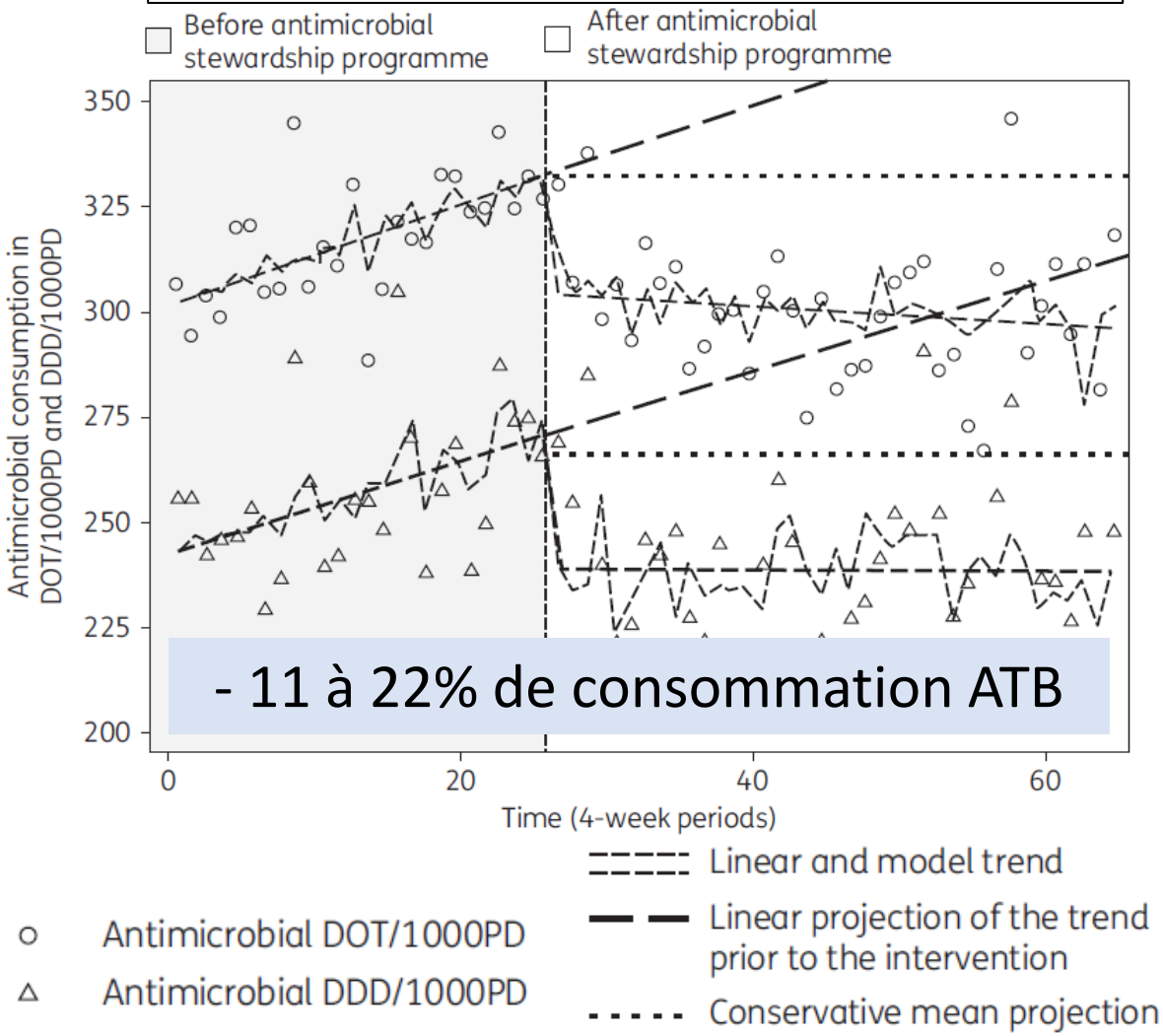
Domain 1: Development	Domain 2: Feasibility and Piloting
Literature describing a system should demonstrate: A definition of stakeholder behaviours that are being targeted and how stakeholders have been engaged with during the development phase A rationale for how the intervention may influence these behaviours An outline of how the system was developed	**Literature describing a system should outline:** How pilot testing was performed and the findings of this An understanding of the mechanism of behaviour change witnessed and how the intervention may be having its effect
Domain 3: Evaluation	**Domain 4: Implementation**
Literature describing a system should demonstrate: Efficacy testing in a 'real-world' setting High levels of control maintained to confirm internal validity of intervention Confirm how the intervention changes practice and quantify its impact	**Literature describing a system should outline:** How it was tested in the real world with real-world providers Strategies for implementation and adoption of intervention that were used and how these may have impacted on observations Plans for (or evidence of) long-term surveillance / follow up of the system

CDSS characteristics	*n* (%)
System setting	
Primary care	11 (29)
Secondary care	27 (71)
Types of decision support	
Antibiotic prescribing	29 (76)
Physician feedback	1 (3)
Alerts / prompts	7 (18)
Dose optimization	3 (8)
De-escalation	2 (5)
Surveillance	2 (5)
CDSS Platform	
Integrated into EMR	28 (74)
On PDA device	3 (8)
Web-based application	5 (13)
Stand-alone software	2 (5)
System Attributes	
Rule based[a]	29 (76)
Causal probabilistic networks	1 (3)
Drug-bug logic	1 (3)
Pharmacokinetic modelling[a]	2 (5)
Fuzzy cognitive mapping	1 (3)
Guidelines	2 (5)
Predictive models	1 (3)
N/A	2 (5)

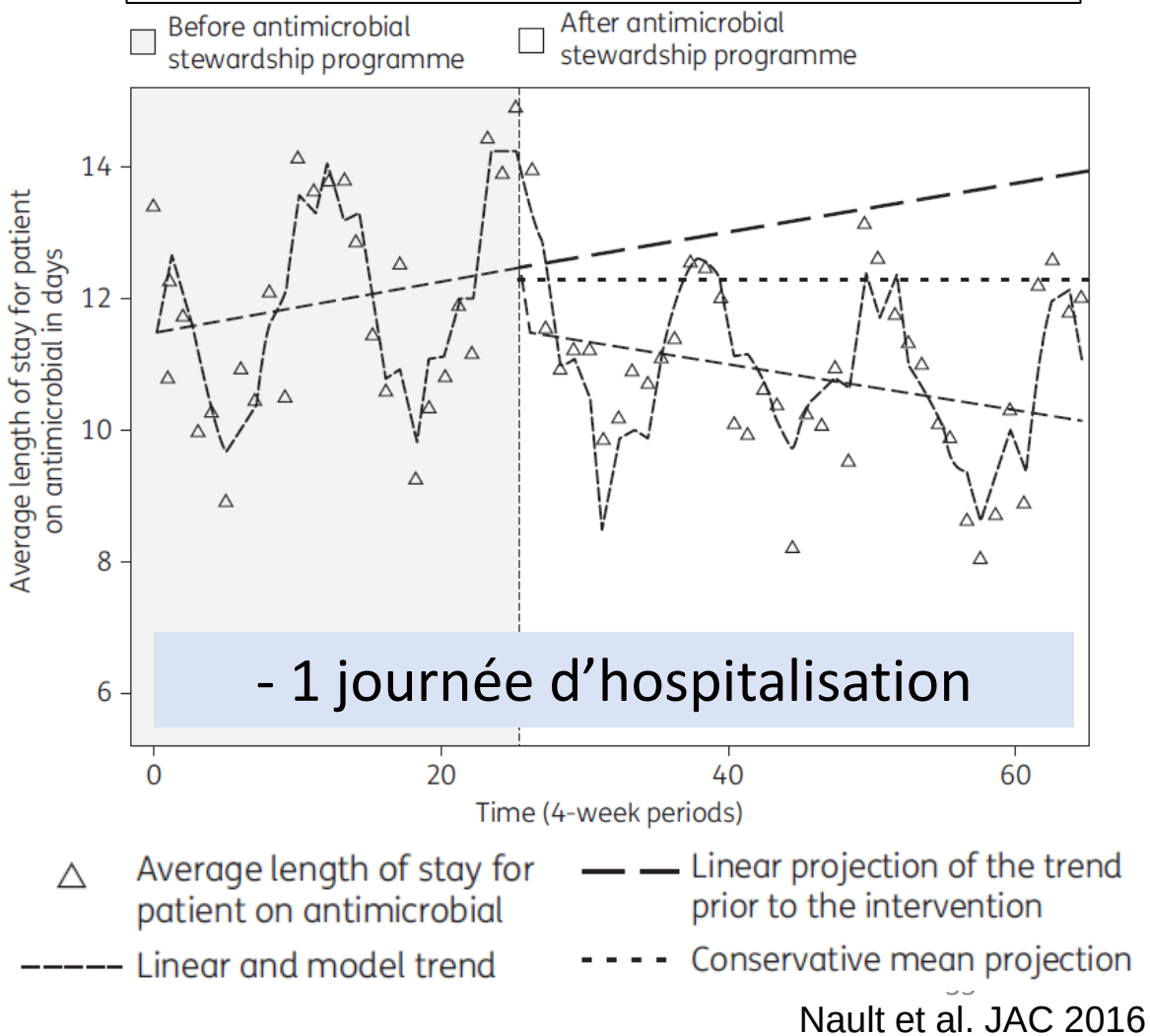
Rawson TW et al. CMI 2017

Système d'outils d'aide à la decision à l'hôpital

Consommation antibiotique



Durée de séjour hospitalier



Nault et al. JAC 2016

Evaluation of a machine learning capability for a clinical decision support system to enhance antimicrobial stewardship programs

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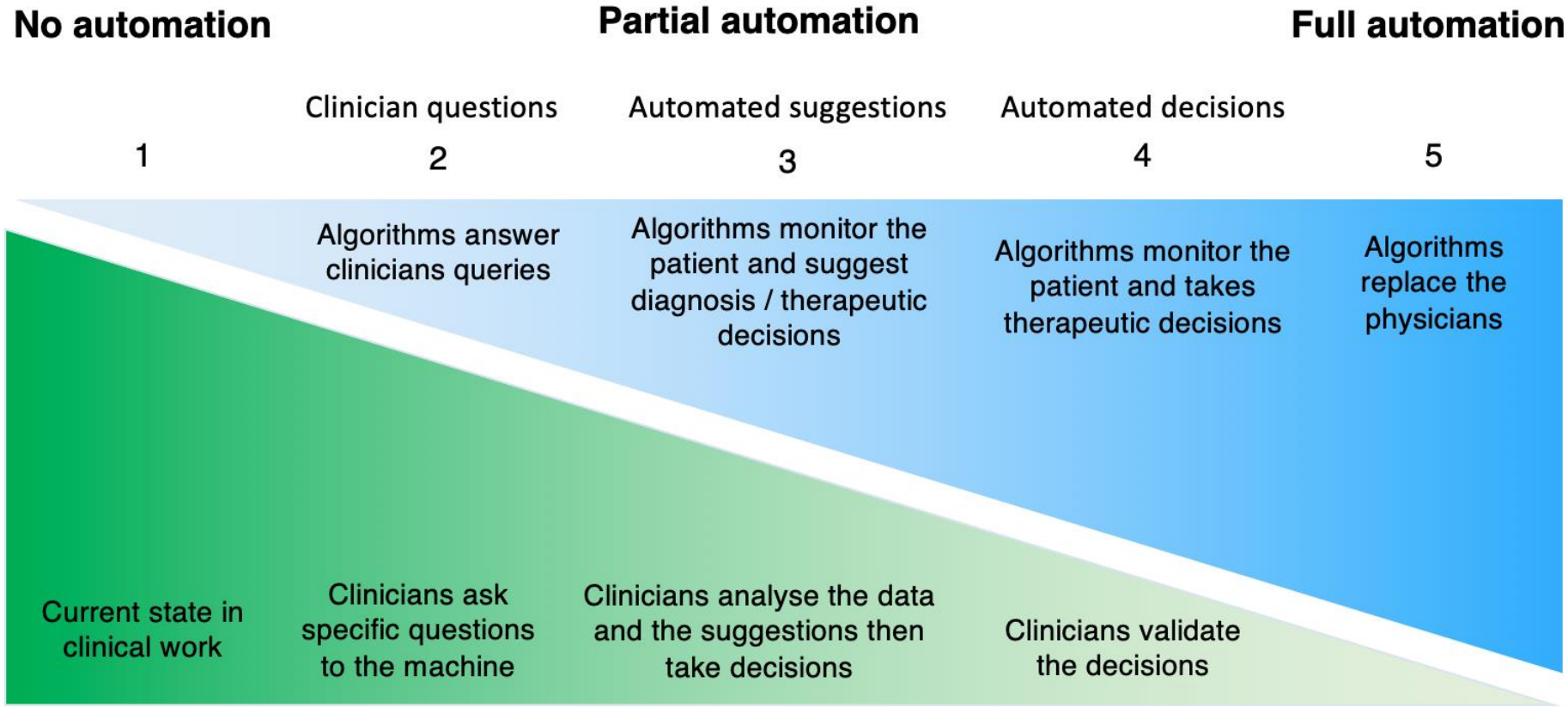
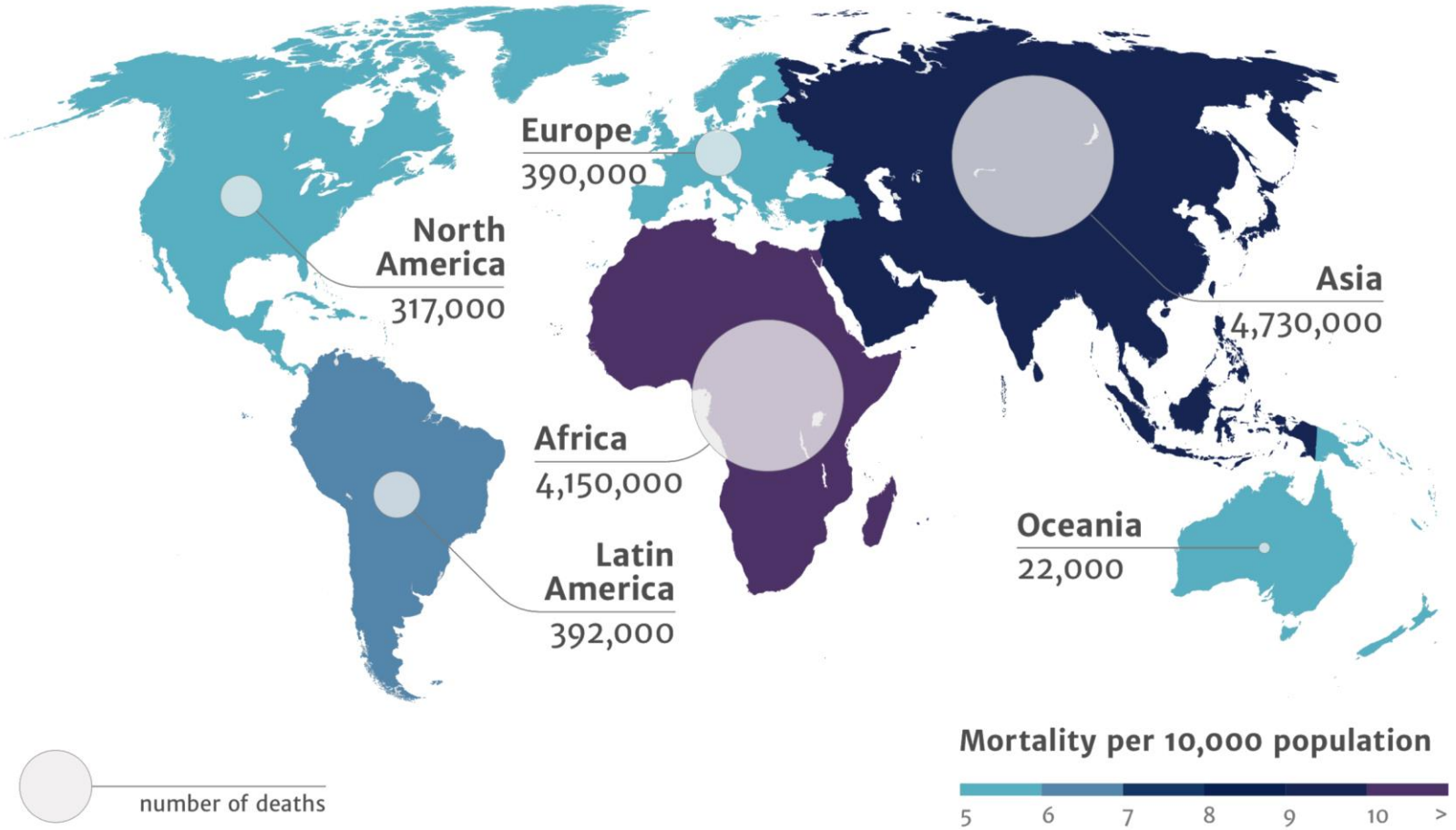
Artificial intelligence in medicine 2016



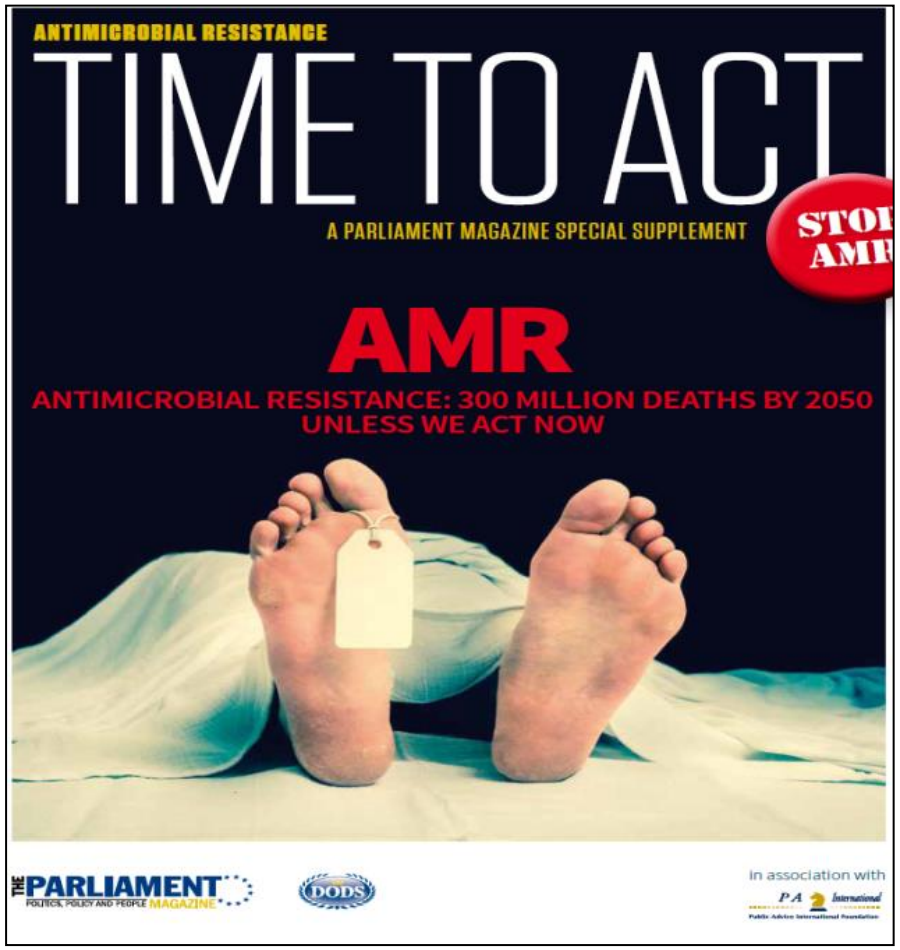
S'intéresser au sud et à l'est



Review on Antimicrobial Resistance 2014

Klein E et al. PNAS 2018

Implication citoyenne, un élan européen



Effective education, better outcome

Personal tragedy, collective responsibility

The need for a precautionary approach

The increasing use of antibiotics is driving resistance and creating a global health threat

"To win the war against AMR, we must stop doling out antibiotics like sweets"
Lord Jim O'Neill, Chairman of the UK Review on AMR

The Silent Tsunami

The relentless spread of antimicrobial resistance across the world has highlighted the need for a strong, global response to the crisis

75 per cent of all antimicrobials in Europe and the US are used in animal husbandry

2002 Plan Kouchner

2007 Plan d'alerte ATB 2

2011 Plan d'alerte ATB 3

2012 ICATB - 2

2013 Réf. ATB dans les ES privés

2015 Task force, PROPIAS

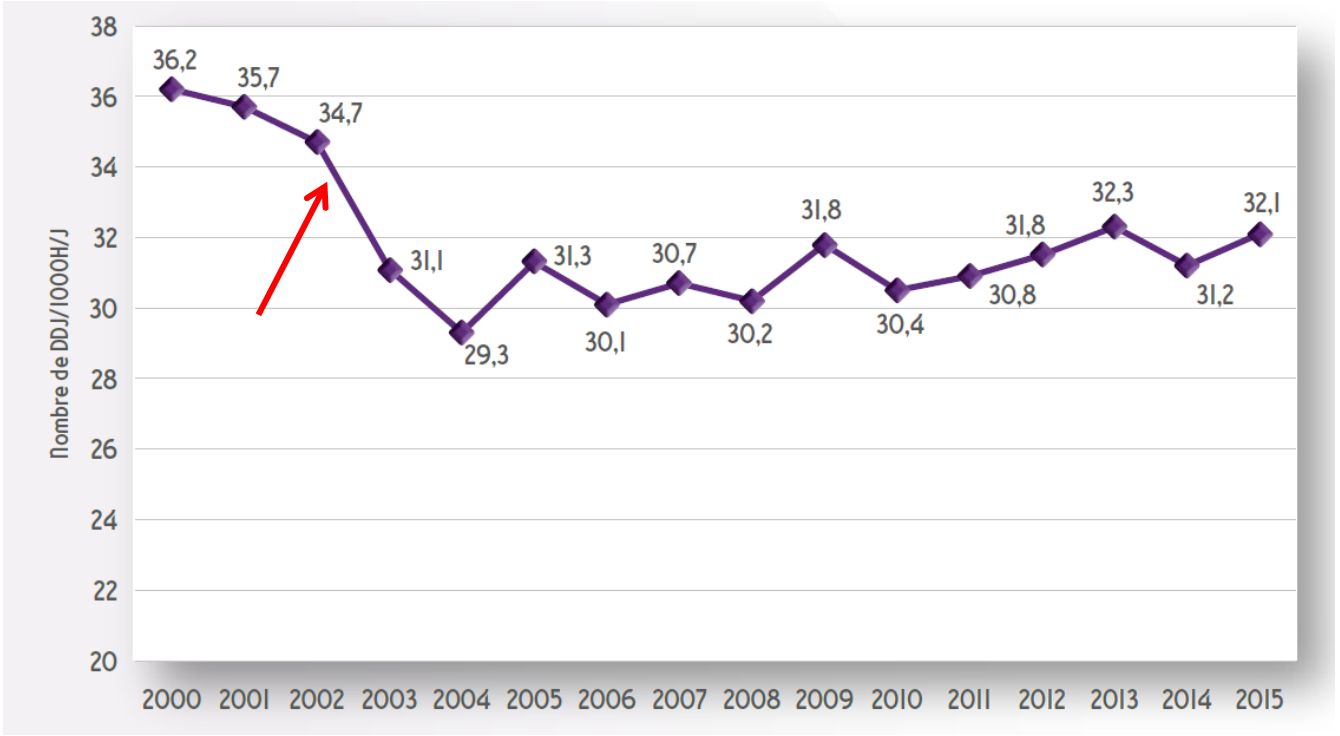
2016 Programme interministériel

2017 CPIAS vs Ref. ATB de l'ARS

?

Impact sur les consommations ATB?

Impact sur la résistance bactérienne?



Les « petites phrases »

Propositions personnelles :

« Les antibiotiques, c’est pas des anxiolytiques »

« Une semaine d’augmentin, c’est pas anodin »

« La tazo, c’est pas une benzo »

« Il faut savoir préserver nos amis les anaérobies »

Conclusion

Squeezing the Resistance Balloon at Multiple Sites

Rahal et al. Clin Infect Dis 2002