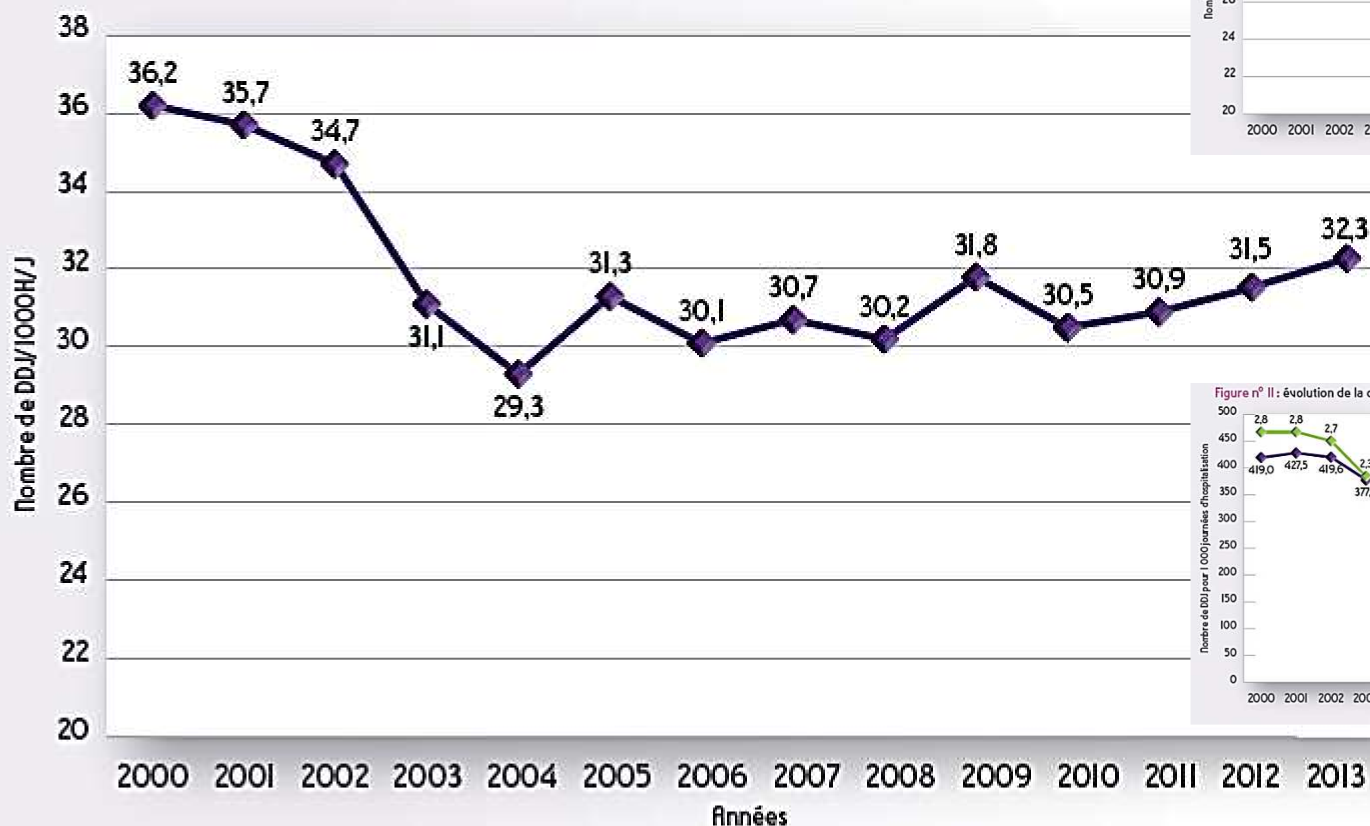
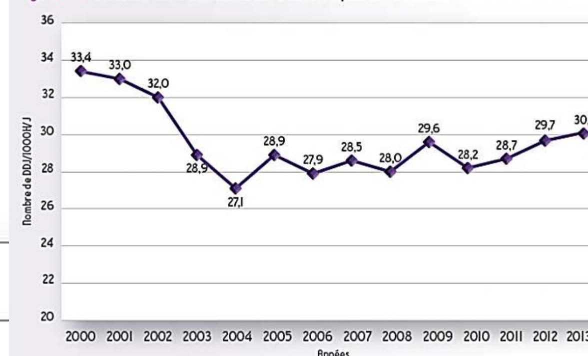
Améliorer la prescription des antibiotiques sur le terrain

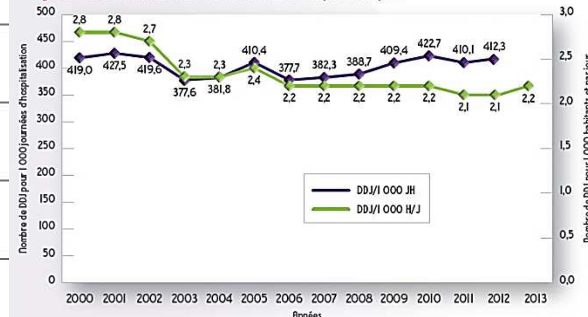
P. Lesprit
Infectiologie transversale
Hôpital Foch

L'évolution des consommations d'antibiotiques en France entre 2000 et 2013

ansm
Agence nationale de sécurité du médicament et des produits de santé







Prévalence des traitements antibiotiques dans les établissements de santé, France 2001-2012

	2001	2006	2012
Médecine	26	26.2	26.7
Chirurgie	27.1	27.8	25.7
Réanimation	47.3	50	48.8
Court séjour	25.2	25.4	25.0

www.invs.sante.fr

Utilisation inappropriée des antibiotiques à l'hôpital

Amphia hospital, Pays Bas

321 → 426 DDJ/1000 j (+32%)

Antibiothérapie 22.9%

Inappropriée 37.4%

Indiquée/non prescrite 0.6%

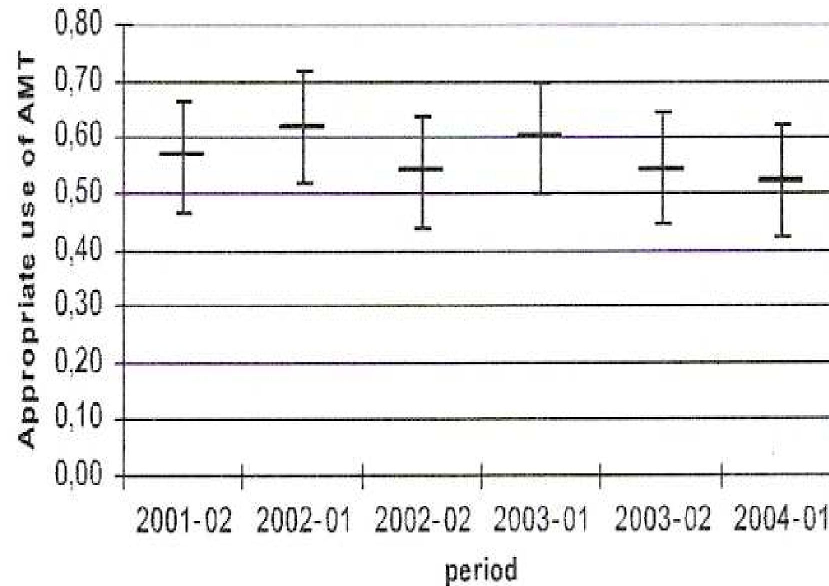


FIG. 2. Appropriateness of use of AMT (95% confidence interval) in six surveys between 2001 and 2004.

Willemsen I. et al, Antimicrob Agents Chemother 2007

Antibiotic misuse: a prospective clinical audit in a French university hospital

- 122 IDS consultations
- Antibiotic unnecessary or inappropriate=78 (64%)
- Antibiotic unnecessary= 42 (34%)
- Misdiagnosis

Clinical=41

Microbiological=32

Imaging=19

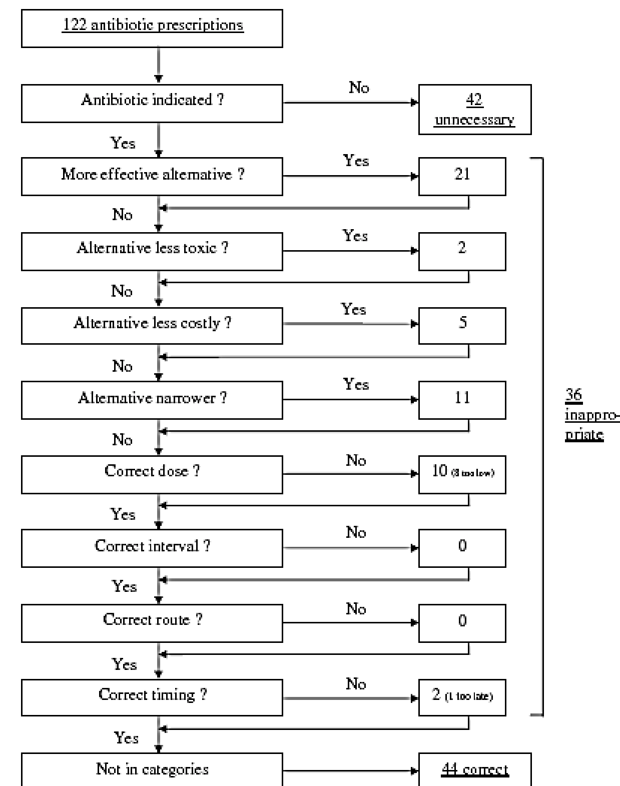


Fig. 1 Antibiotic treatments considered inappropriate by the infectious diseases specialist. Prescriptions can be inappropriate for several reasons simultaneously and can consequently appear in more than one category

Pulcini C. et al, Eur J Clin Microbiol Infect Dis 2007

14e Conférence de Consensus

Comment améliorer la qualité de l'antibiothérapie dans les établissements de soins ?

Qualité = préserver l'intérêt collectif sans nuire à l'intérêt individuel du patient

6 objectifs principaux :

- Un diagnostic précis et précoce
- Une bonne indication thérapeutique, un traitement adapté, réévalué cliniquement et microbiologiquement, de durée appropriée
- Le meilleur rapport bénéfice/risque individuel et collectif par le choix du traitement dont les effets indésirables sont les plus faibles à efficacité égale, assurant l'impact écologique le plus faible
- Une décision médicale fondée sur les meilleures preuves scientifiques disponibles
- La prise en compte des préférences du patient
- La maîtrise de l'émergence des bactéries multi-résistantes

Méd Mal Infect 2002

14e Conférence de Consensus

Comment améliorer la qualité de l'antibiothérapie dans les établissements de soins ?

Outils d'amélioration

Référentiels et recommandations

Production, utilisation et circulation des informations (informatisation)

Formation

Outils d'évaluation

Présence des structures

Audit clinique de la prescription

Consommation des antibiotiques

Résistance aux antibiotiques

Acteurs

Clinicien en charge du patient

Clinicien référent en infectiologie

Microbiologiste

Responsable de l'EOHH

Pharmacien

Correspondants des services cliniques

L'administration

Structures

Commission des anti-infectieux

Equipe opérationnelle en infectiologie

Méd Mal Infect 2002

Plan national d'alerte sur les antibiotiques 2011-2016

La réduction durable de la consommation globale d'antibiotiques s'impose comme un enjeu fort de santé publique pour réduire la pression de sélection globale qui s'exerce sur les bactéries. Une réponse visible face au péril que représentent les bactéries multi résistantes aux antibiotiques est de fixer un objectif de réduction de la consommation pour la durée du plan, celui-ci pourrait être de l'ordre de 25% sur cinq ans comme le préconisent les experts. L'atteinte de cet objectif doit être le résultat d'une stratégie de juste utilisation des antibiotiques.

Programme d'interventions successives

Hôpital 250 lits
AMT n=6

Table 1. Variations in use of intravenous antibiotics after implementation of successive intervention steps for optimizing the quality of antimicrobial prescription in the hospital.

	Consumption, divided daily doses per 1000 patient-days[a]				
Antibiotic	Period 1: baseline	Period 2: initial intervention	Period 3: education phase	Period 4: active control phase	*P* for period 4 vs. period 1[b]
Amikacin	40.18	25.40[c]	26.22	32.04	NS
AMP-SUL	24.75	17.05	18.82	22.90	NS
→ Carbapenem	13.54	7.79	6.39	6.18	.03
Cefepime	3.86	3.31	8.96[d]	8.80	NS
Ceftazidime	29.46	21.67	24.60	30.50	NS
→ Ceftriaxone	62.85	35.63[c]	26.63	11.77	<.0001
Cefuroxime	9.48	4.83	4.77	2.88	.04
→ Cephalothin	80.68	62.59	59.54	45.43	<.0001
Ciprofloxacin	16.02	14.11	12.75	17.54	NS
Clarithromycin	7.87	3.49	3.10	3.02	NS
→ Clindamycin	42.75	31.14	19.66	21.99	.003
Gentamicin	51.13	43.03	33.04	36.72	NS
Metronidazole	19.78	15.20	17.85	15.87	NS
Vancomycin	28.53	27.81	24.98	20.70	NS
Total	430.89	313.06[c]	287.31	276.35	<.0001

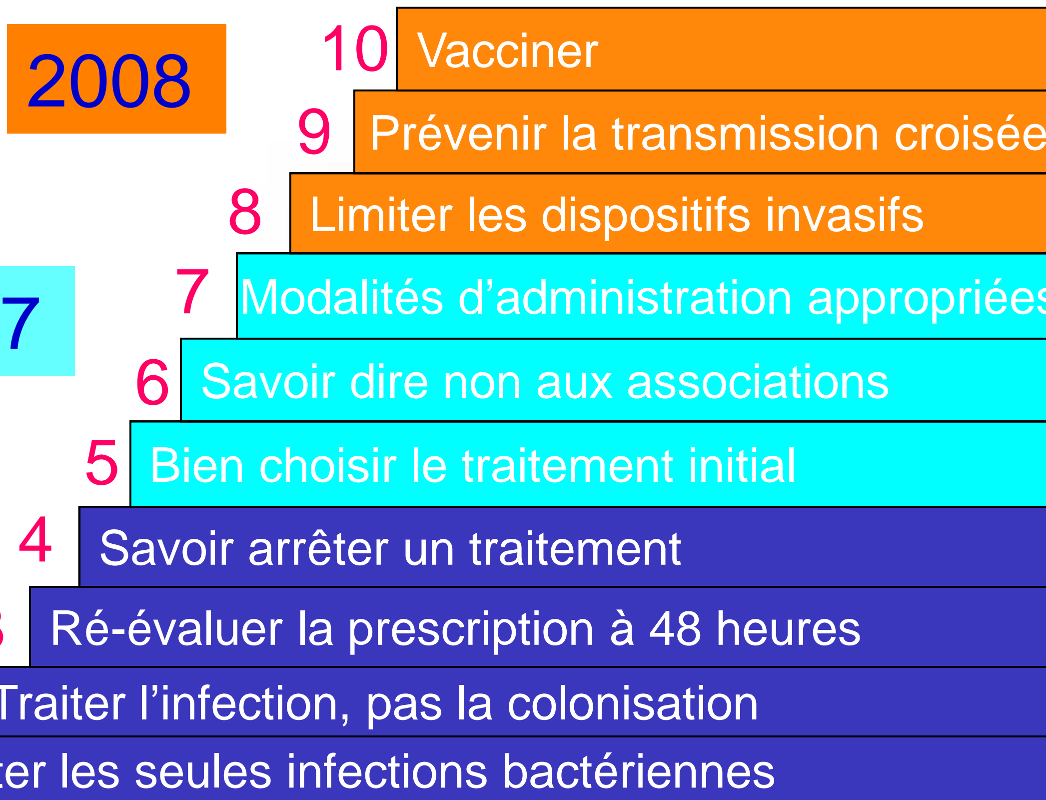
↓36%

NOTE. AMP-SUL, aminopenicillin-sulbactam; NS, not significant.
[a] See the section "Program design" in Methods for detailed definitions.
[b] Determined by χ^2 test.
[c] Significant decrease was observed between period 1 and period 2 ($P<.05$).
[d] Significant increase was observed between period 2 and period 3 ($P<.05$).

Bentar C, Clin Infect Dis 2003

Préserver l’efficacité des antibiotiques à l’hôpital

3 volets, 10 messages clés



2008

2007

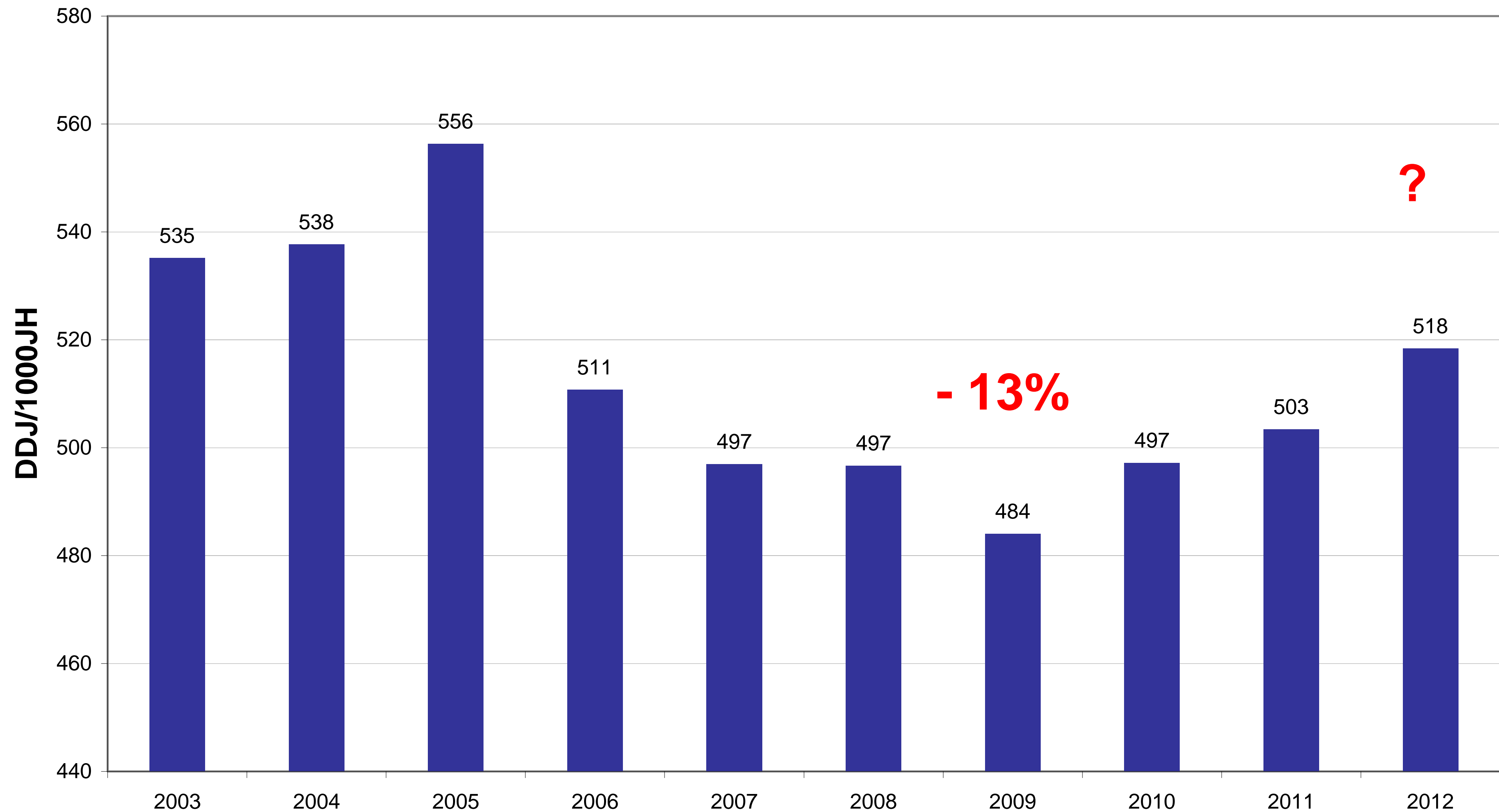
2006

Prévenir les infections

Mieux utiliser les antibiotiques

Savoir dire non aux antibiotiques

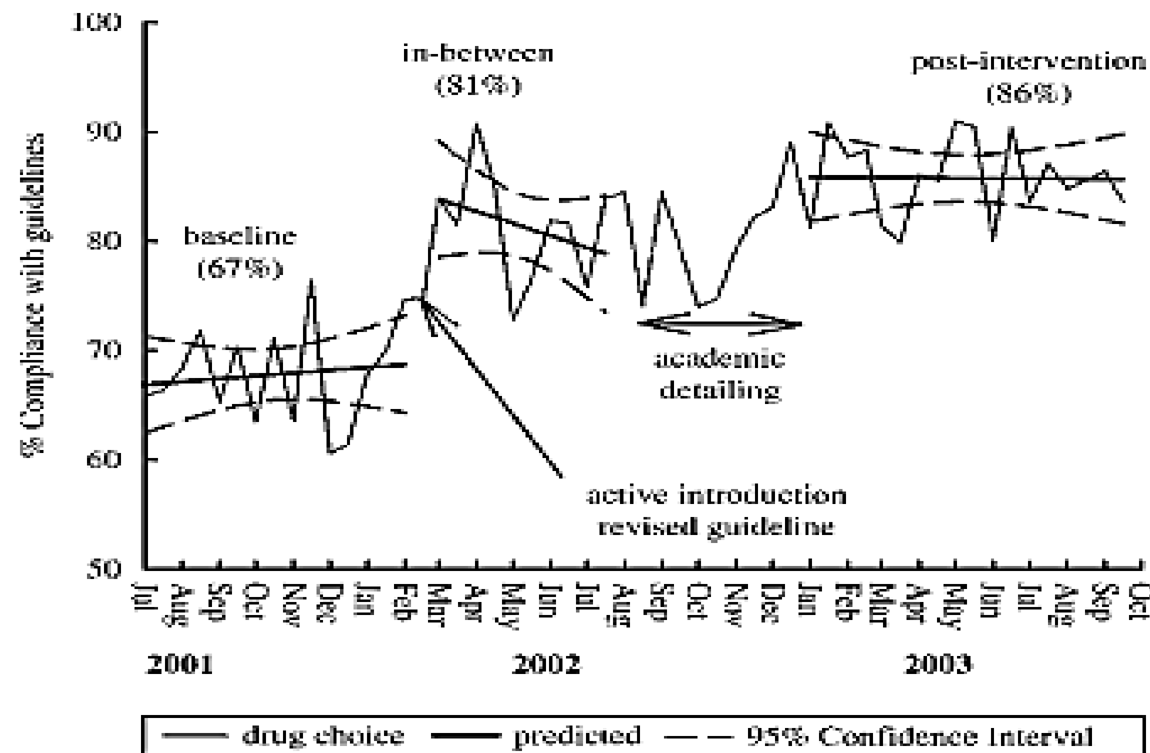
Evolution de la consommation des antibiotiques dans les hôpitaux de l'AP-HP



S Fournier/EOH/DMA/Juin 2013

Source AGEPS – EMER – ESBUI – Service EPBU

Improving compliance with hospital antibiotic guidelines: a time-series intervention analysis



*predicted regression lines are produced with segmented regression analysis of the observed drug choice data; (67%) level of compliance to guidelines at baseline, in-between (81%), and post-intervention (86%).

Figure 2. Percentage compliance with antibiotic guidelines, 1 July 2001–30 September 2003.

Mol P, J Antimicrob Chemother 2005

Impact of an intervention in the management and outcome of *S. aureus* bacteremia

Table 4. Adherence to Quality-of-Care Indicators

Quality-of-Care Indicator	Preintervention Period	Intervention Period	Median Improvement in Percentage of Adherence to QCI (IQR)	Relative Risk for Adherence to CQI (95% CI)	*P* Value	Adjusted OR for Adherence to QCI (95% CI)[a]	*P* Value
Follow-up blood culture	131/214 (61.2)	159/198 (80.3)	25 (5.9–54.4)	1.31 (1.15–1.49)	<.001	2.83 (1.78–4.49)[b]	<.001
Source control	86/122 (70.2)	105/115 (91.3)	22 (10.2–50)	1.29 (1.13–1.49)	<.001	4.56 (2.12–9.79)[c]	<.001
Echocardiography	76/144 (52.8)	74/101 (73.3)	18.8 (0–65.7)	1.38 (1.13–1.68)	.001	2.50 (1.42–4.41)[d]	.002
Early cloxacillin in MSSA	120/211 (56.9)	124/174 (71.3)	11.1 (0–51.1)	1.25 (1.07–1.45)	.014	1.79 (1.15–2.78)[e]	.009
Vancomycin dosing	23/49 (46.9)	30/54 (55.6)	20 (0–54.3)	1.18 (.80–1.73)	.38	1.42 (.65–3.10)[f]	.38
Treatment duration	151/207 (72.9)	161/189 (85.2)	10.2 (2–20.2)	1.16 (1.05–1.29)	.003	2.13 (1.24–3.64)[g]	.006

Table 7. Multivariate Analyses of Variables Associated With 14- and 30-Day Mortality Among Patients With *Staphylococcus aureus* Bacteremia

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

López-Cortés LE. et al, Clin Infect Dis 2013

Appropriate Antibiotic Use for Urinary Tract Infections Reduces Length of Hospital Stay

Table 1. Baseline Characteristics of Hospitalized Patients With a Complicated Urinary Tract Infection

Characteristic	Total (N = 1252)[a]
Age, y, mean (SD)	63.1 (21.5)[b]
Male sex	513 (41.0)
Urological comorbidity (anatomical and/or functional abnormalities of urinary tract)	286 (22.9)
Comorbidity, other (cardiovascular disease, diabetes mellitus, immunocompromising disease, kidney disease)	610 (48.8)
Urinary catheter	215 (17.2)
Febrile UTI; nonfebrile UTI	1083 (86.6); 167 (13.4)
Internal medicine ward; urology ward	890 (71.1); 362 (28.9)
Patients treated in university hospital	292 (23.3)
Length of hospital stay, d, mean (SD)	8.0 (8.2)
ICU admission necessary	36 (2.9)
In-hospital mortality	32 (2.6)
QIs for appropriate antibiotic use:	
1. Perform a urine culture before starting treatment	n = 1250 1003 (80.2)[b]
2A. Prescribe empirical treatment in accordance with the national guideline	n = 1167 765 (65.6)
2B. Prescribe empirical treatment in accordance with the local hospital guideline	n = 983 455 (46.3)
3. Switch from intravenous to oral treatment within 72 hours of starting treatment	n = 543 295 (54.3)
4. Tailor antibiotic treatment on the basis of culture result	n = 851 610 (71.7)

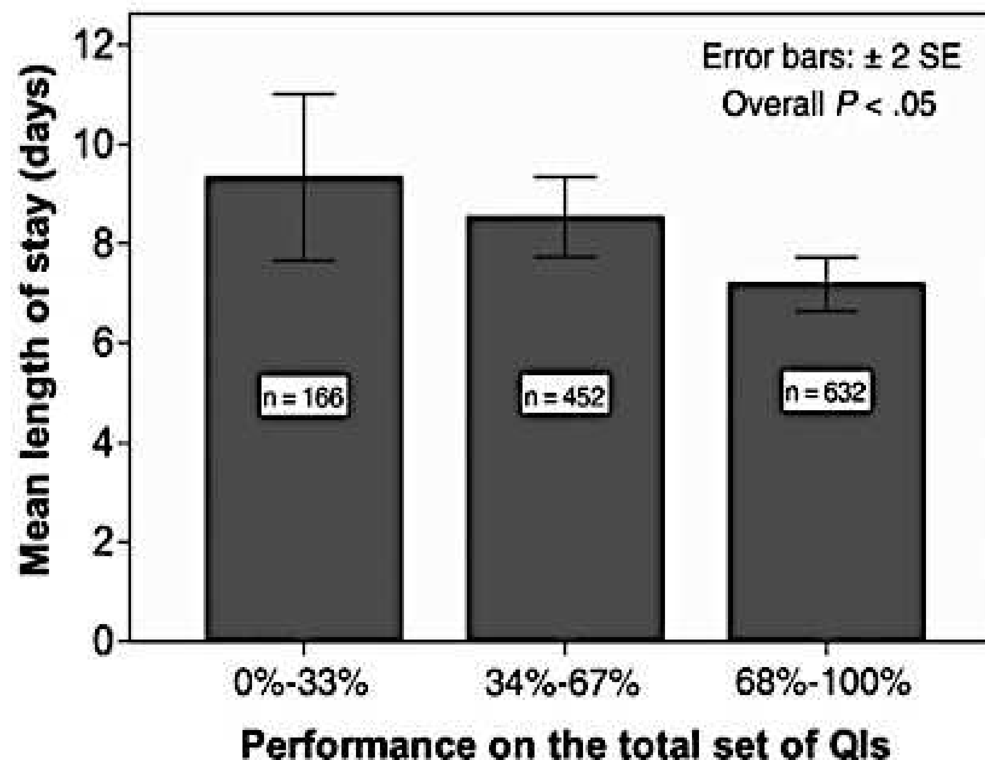


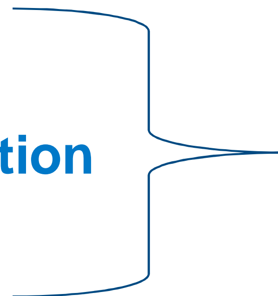
Figure 1. Performance on the total set of quality indicators (proportion of appropriate antibiotic use) and length of hospital stay. Abbreviations: QI, quality indicator; SE, standard error.

Spoorenberg V, Clin Infect Dis 2014

Juste utilisation des antibiotiques : une vraie marge d'amélioration …

- 25-50% des patients reçoivent un antibiotique pendant leur séjour
- 25-50% des prescriptions peuvent être améliorées
- Prescription adaptée =

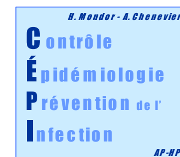
✓ Indication
✓ Molécule
✓ Modalité d'administration
✓ Posologie
✓ Durée



Réévaluer à J3 et à J7 et tracer dans le dossier médical

- La maîtrise de la prescription des antibiotiques est un volet essentiel du programme de lutte contre les infections et de la maîtrise de la résistance aux antibiotiques

Commission des Anti-Infectieux



Résultat de la requête sur les patients en cours d'hospitalisation recevant des antibiotiques contrôlés

(Amiklin, Axepim, Ciflox, Fortum, Oflocet, Targocid, Tavanic, Tazocilline, Tienam, Vancocine, Zyvoxid , Claforan , Rocéphine, Augmentin, Gentalline)

Il y a 59 résultats.

US	NIP	NOM	PRENOM	DDN	SEXE	ANTIBIOTIQUE	PRESCRIT_LE	D
AC1						OFLOXACINE MERCK 200MG CPR	07/05/09	1 m
AC1						OFLOXACINE MERCK 200MG CPR	13/05/09	1 m
AC2						AUGMENTIN 1G/125MG AD SACH	13/05/09	1 s
CE2						OFLOCET 200MG CPR	14/05/09	2 s
CE2						AUGMENTIN 1G-200MG IV PDR INJ	16/05/09	7 j
CE2						AUGMENTIN 500MG/62,5MG PDR - AC	15/05/09	1 s
CH2						AUGMENTIN 1G/125MG AD SACH	12/05/09	1 m
CY1						OFLOCET 200MG /40ML SOL INJ POCHE	13/05/09	1 m
FI2						VANCOMYCINE MERCK 500MG PDR INJ	14/05/09	10 j
ME1						OFLOXACINE MERCK 200MG CPR	17/05/09	5 j
UMG						AUGMENTIN 1G/125MG AD SACH	14/05/09	6 j
UMG						OFLOCET 200MG /40ML SOL INJ POCHE	17/05/09	5 j
UMG						AUGMENTIN 1G/125MG AD SACH	12/05/09	7 j
03A						OFLOXACINE MERCK 200MG CPR	18/05/09	2 s
03C						OFLOXACINE MERCK 200MG CPR	11/05/09	3 s
03C						AUGMENTIN 1G-200MG IV PDR INJ	17/05/09	10 j
03C						OFLOXACINE MERCK 200MG CPR	13/05/09	2 s
03C						OFLOXACINE MERCK 200MG CPR	14/05/09	1 s
03D						OFLOXACINE MERCK 200MG CPR	18/05/09	1 s
03D						AUGMENTIN 1G/125MG AD SACH	16/05/09	1 s
04D						AUGMENTIN 1G-200MG IV PDR INJ	15/05/09	5 j
04D						AUGMENTIN 1G/125MG AD SACH	17/05/09	1 s
04D						AUGMENTIN 1G-200MG IV PDR INJ	18/05/09	7 j
05A						AUGMENTIN 1G-200MG IV PDR INJ	18/05/09	1 s
05C						AUGMENTIN 1G/125MG AD SACH	18/05/09	8 j
06D						AUGMENTIN 1G-200MG IV PDR INJ	15/05/09	7 j
06I						VANCOMYCINE MERCK 500MG PDR INJ	15/05/09	7 j
06I						VANCOMYCINE MERCK 500MG PDR INJ	14/05/09	15 j
06I						OFLOCET 200MG CPR	29/04/09	1 m
06T						GENTAMICINE 80MG/2ML INJ	18/05/09	2 j
07H						OFLOXACINE MERCK 200MG CPR	15/05/09	5 j
07O						VANCOMYCINE MERCK 1G PDR INJ	18/05/09	1 s
08G						AUGMENTIN 500MG/62,5MG PDR - AC	14/05/09	7 j
08G						VANCOMYCINE MERCK 1G PDR INJ	18/05/09	1 j
08G						VANCOMYCINE MERCK 500MG PDR INJ	19/05/09	4 j
08H						OFLOXACINE MERCK 200MG CPR	15/05/09	7 j
09B						AUGMENTIN 500MG/62,5MG PDR - AC	13/05/09	8 j
10C						GENTAMICINE 80MG/2ML INJ	18/05/09	13 j
10C						OFLOXACINE MERCK 200MG CPR	19/05/09	8 j
11U						GENTAMICINE 80MG/2ML INJ	12/05/09	2 s
11U						VANCOMYCINE MERCK 1G PDR INJ	18/05/09	1 m
13C						AUGMENTIN 1G/125MG AD SACH	14/05/09	1 s
13C						CEFOTAXIME PANPH 1G PDR INJ IM IV	16/05/09	10 j
13D						AUGMENTIN 500MG/62,5MG PDR - AC	16/05/09	1 s
13D						OFLOXACINE MERCK 200MG CPR	18/05/09	2 j
13D						CEFOTAXIME PANPH 1G PDR INJ IM IV	13/05/09	1 s
14A						TAZOCILLINE 4G/0,5G PDR LYO	18/05/09	1 s
14A						AUGMENTIN 1G-200MG IV PDR INJ	15/05/09	17 j
14A						CEFOTAXIME PANPH 1G PDR INJ IM IV	17/05/09	1 s
14A						AUGMENTIN 1G-200MG IV PDR INJ	15/05/09	17 j
14A						TAZOCILLINE 4G/0,5G PDR LYO	13/05/09	10 j
14A						VANCOMYCINE MERCK 1G PDR INJ	13/05/09	10 j
14C						AUGMENTIN 1G/125MG AD SACH	15/05/09	10 j
15C						GENTAMICINE 160MG/2ML INJ -HM	18/05/09	4 j

2006

Mise en place d’une requête informatisée

Services de médecine et chirurgie

Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkp062

JAC

Impact of a computer-generated alert system prompting review of antibiotic use in hospitals

Philippe Lesprit[1*], Trung Duong[2], Emmanuelle Girou[1], François Hemery[2] and Christian Brun-Buisson[3]

Objectives: The aim of this study was to measure the impact on antibiotic use of a computer-generated alert prompting post-prescription review and direct counselling in hospital wards.

Methods: A computer-generated alert on new prescriptions of 15 antibiotics was reviewed weekly by an infectious disease physician for 41 weeks. During the first 6 months of the study, criteria selected for potential intervention were: (i) a planned duration of treatment of ≥10 days; (ii) discordance between the spectrum of the prescribed antibiotic and available microbiological results; or (iii) prescriptions of broad-spectrum β-lactams, fluoroquinolones, glycopeptides or linezolid. During the following 5 months, the alert was restricted to any prescription of the 15 antibiotics in the 9 wards where overall antibiotic use had not decreased in the past year.

Results: We analysed 2385 prescriptions, 932 (39%) of which generated an alert for potential intervention. Among the latter, 482 (51.7%) prescriptions prompted direct counselling, mainly for shortening the planned duration of therapy (18.9%), withdrawing antibiotics (16.2%) or streamlining therapy (15.5%). The attending physicians' compliance with the recommendations was 80%. The overall median (interquartile range) days of therapy prescribed by the attending physicians was reduced from an initial duration of 8 (7–14) to 7 (6–11) days ($P \leq 0.0001$), resulting in 26.5% less antibiotic days prescribed. The time required for the intervention was 6 h per week.

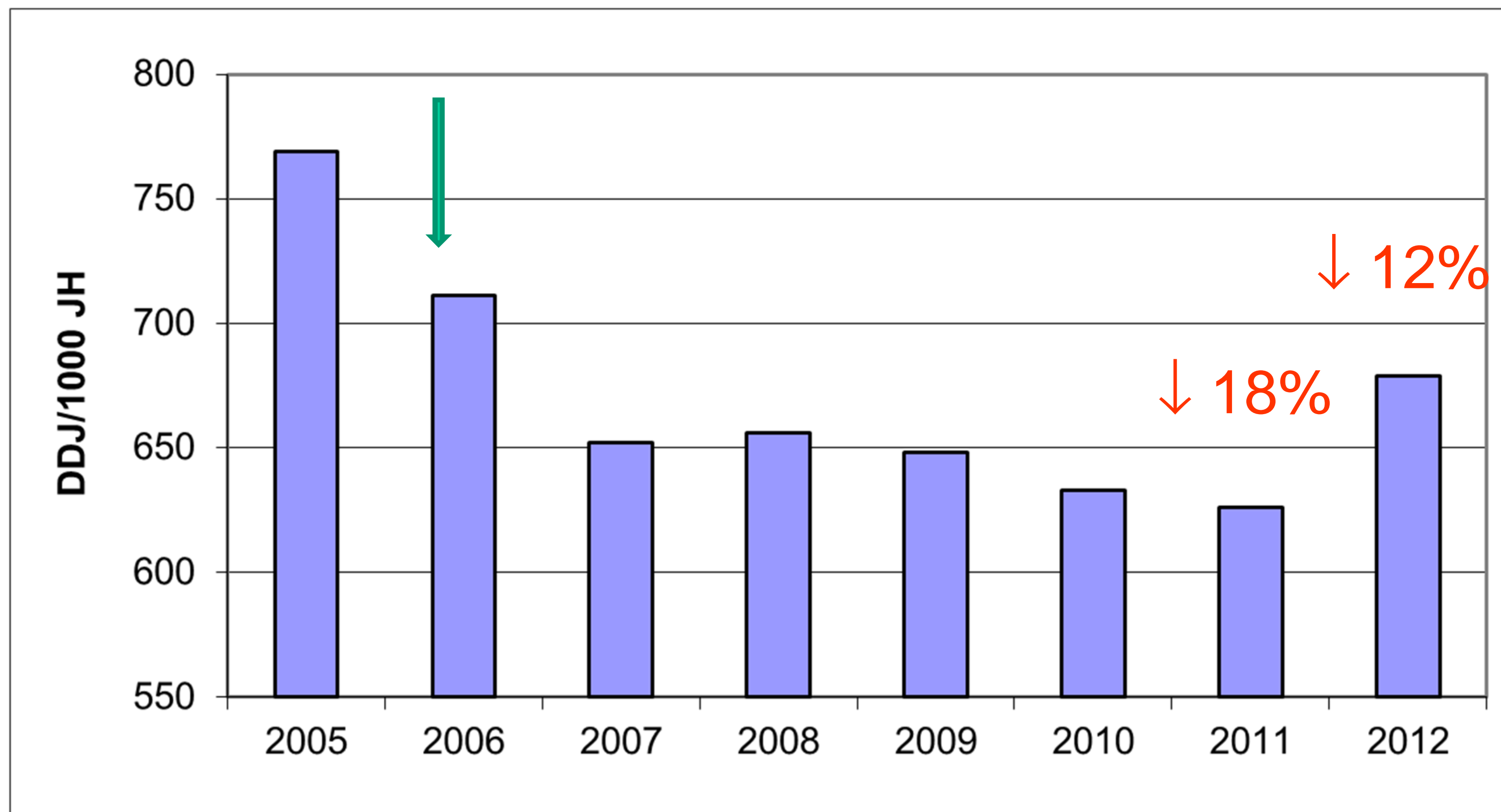
Conclusions: This computer-prompted post-prescription review led physicians to modify one half of the antibiotic courses initially prescribed and was well accepted by the majority, although they had not requested counselling.

Clinical impact

	Intervention group (n=376)	Control group (n=377)	P
Length of stay, median (IQR)			
Overall	15 (9-25)	15 (9-27)	0.95
Community-acquired inf.	5 (3-10)	6 (3-14)	**0.06**
In-hospital mortality (%)	37 (9.8)	38 (10.1)	0.91
ICU admission within 7 days (%)	7 (1.9)	6 (1.6)	0.78
New course of antibiotic therapy (%)	17 (4.5)	25 (6.6)	0.21
Antibiotic treatment for **relapsing infection** (%)	13 (3.4)	30 (7.9)	**0.01**

Lesprit P. et al, Clin Microbiol Infect 2012

Evolution de la consommation globale d'antibiotiques, Henri Mondor



24th ECCMID Barcelona, Spain 10 – 13 May 2014

Appropriateness of therapy

Variable	**Intervention group**	**Control group**	P
D1			
Antibiotic indicated	89 (72.4)	96 (78.0)	0.30
Optimal drug	61/89 (69.5)	62/96 (64.6)	0.57
Optimal administration	81/89 (91.0)	87/96 (90.6)	0.93
Optimal dosing	68/89 (76.4)	78/96 (81.2)	0.42
D3-4			
Antibiotic indicated	109 (88.6)	97 (78.9)	**0.04**
Optimal drug	82/105 (78.1)	61/99 (61.6)	**0.01**
Optimal administration	77/81 (95.1)	79/87 (90.8)	0.28
Optimal dosing	74/81 (91.6))	77/87 (88.5)	0.54
Optimal duration	72 (58.5)	55 (44.7)	**0.03**
Median duration (IQR)	7 (3-14)	10 (7-16)	**0.003**

Lesprit P. et al, Clin Microbiol Infect 2014

Audit and Feedback to Reduce Broad-Spectrum Antibiotic Use among Intensive Care Unit Patients: A Controlled Interrupted Time Series Analysis

- 3 ICU, 48 lits
- Audit : > 3 jours d'ATB spectre large (C3G, pénicillines + inhibiteurs, carbapénèmes, quinolones, vancomycine)
- J3 et J10
- EMA : binôme pharmacien/infectiologue
- Sur 12 mois : 717 prescriptions, modification 34%, compliance 82%
- Modifications : arrêt 56%, changement 26%, autres 8%

Elligsen M. et al, Infect Control Hosp Epidemiol 2012

Audit and Feedback to Reduce Broad-Spectrum Antibiotic Use among Intensive Care Unit Patients: A Controlled Interrupted Time Series Analysis

Autres effets :

• Consommation globale :
1134 -> 985 j/1000 pts (p=0.003)

• Mortalité :
13.1% -> 14.4% (p=0.20)

• Coût ATB :
- 95 000 $ (-23.7%)

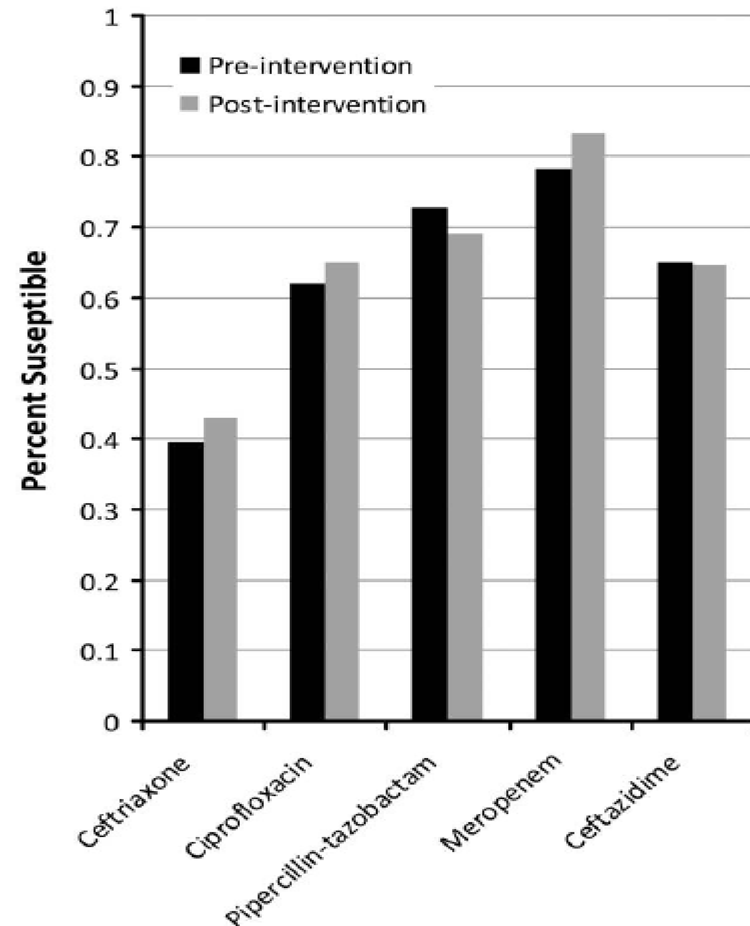


FIGURE 3. Overall susceptibility of gram-negative bacteria isolated from intensive care unit patients during the preintervention period versus during the postintervention period. The increase in meropenem susceptibility (from 78.2% to 83.4% of isolates) was statistically significant ($P = .03$).

Elligsen M. et al, Infect Control Hosp Epidemiol 2012

Impact of infectious diseases specialists on antibiotic prescribing in hospitals

- 31 studies (RCT, before/after controlled, ITS = 7)
- Wide range of infections, hospital settings and types of antibiotic prescriptions
- Quality of evidence: moderately high
- IDS intervention: significant improvement of the appropriateness of antibiotics in almost all studies (56-98%)
- Nearly all studies showed a reduction in antibiotic use

  (-11% to -45%)
- Several studies also showed that IDS intervention was associated with reduced length of stay, decreased mortality, a reduction in prevalence of multiresistant bacteria, as well as lowering the overall costs of antibiotics

Pulcini C. et al, Clin Microbiol Infect 2014

14e Conférence de Consensus
Comment améliorer la qualité de l'antibiothérapie dans les établissements de soins ?

Les éléments cardinaux d'une bonne politique des antibiotiques

- La liste des antibiotiques disponibles
- Les référentiels
- La réévaluation des traitements
- Les ordonnances spécifiques nominatives pour les antibiotiques à dispensation restreinte
- L'informatisation de la prescription (« recommandée depuis 1996 »; « il est souhaitable d'utiliser des **systèmes informatisés d'aide à la prescription** ayant pour objectif de générer des recommandations ou des alertes présentées au médecin lors de sa prescription, avec **l'objectif qu'il les prenne en considération** »)
- L'évaluation
- Les audits de pratiques avec retour d'information
- Formation universitaire (« à l'hôpital, l'importance de l'apprentissage par « compagnonnage » au lit du malade doit être rappelée »)
- Formation médicale continue

Méd Mal Infect 2002

Journal of Antimicrobial Chemotherapy (2008) **62**, 608–616
doi:10.1093/jac/dkn218
Advance Access publication 11 June 2008

JAC

Electronic antibiotic stewardship—reduced consumption of broad-spectrum antibiotics using a computerized antimicrobial approval system in a hospital setting

K. L. Buising[1,2]*†, K. A. Thursky[1,2]†, M. B. Robertson[3], J. F. Black[1,4], A. C. Street[1,2], M. J. Richards[1,2] and G. V. Brown[1,2,4]

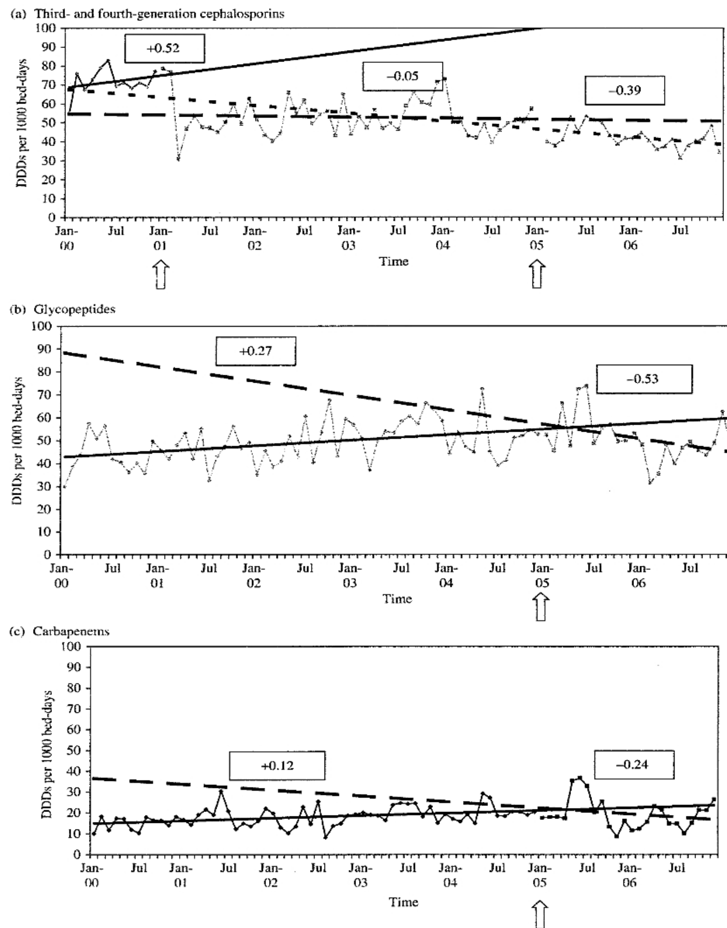


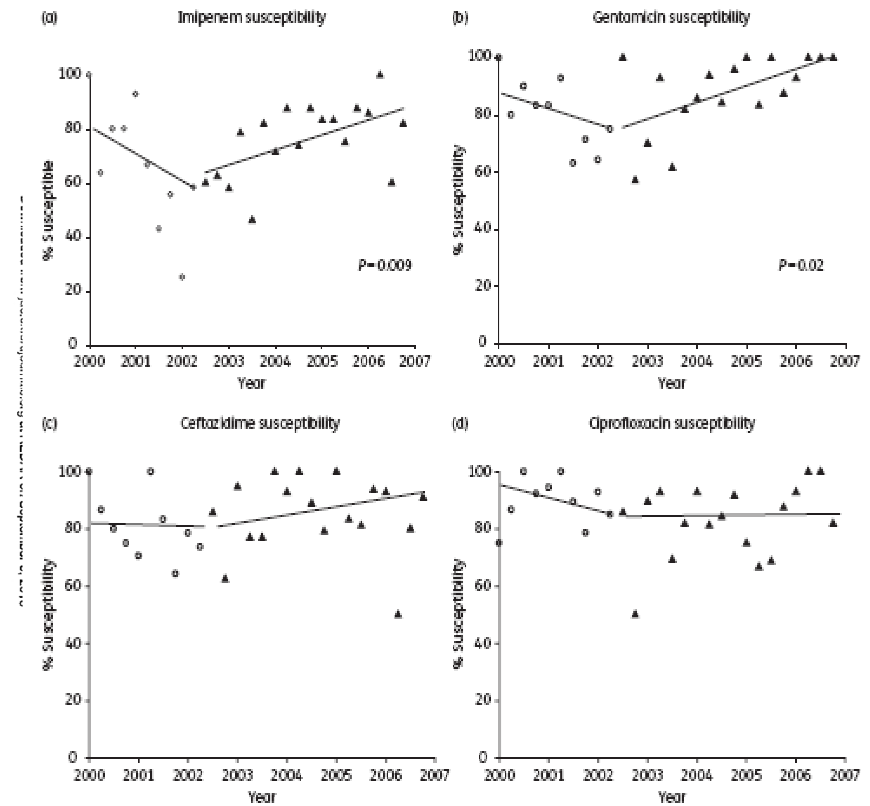
Figure 2. Consumption of restricted antibiotics reported as the number of DDDs/1000 patient bed-days per month. Trend lines established by linear regression before (continuous lines) and after (broken lines) deployment of a computerized approval system (in January 2005) are shown. Arrows indicate time of deployment of approval system. Note: For third-generation cephalosporins, pilot computerized approval programme deployed in January 2001 and permanent system deployed in January 2005. The figures in boxes represent the gradients of the trend lines in each time period assessed by linear regression.

J Antimicrob Chemother 2010; **65**: 1062–1069
doi:10.1093/jac/dkq058 Advance publication 9 March 2010

Journal of Antimicrobial Chemotherapy

Improved susceptibility of Gram-negative bacteria in an intensive care unit following implementation of a computerized antibiotic decision support system

M. K. Yong[1,2]*, K. L. Buising[1], A. C. Cheng[2,3] and K. A. Thursky[1]



re 1. Changes in ICU *Pseudomonas* susceptibility pre- and post-intervention.

Efficacité d'un programme informatisé d'aide à la prescription en réanimation

Table 4 Final adjusted model showing a reduction in the proportion of patients prescribed ceftriaxone, vancomycin, and carbapenems in the intervention group

	Ceftriaxone		Vancomycin		Carbapenems	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Intervention	0.58 (0.42–0.79)	0.001	0.67 (0.45–1.00)	0.05	0.61 (0.39–0.97)	0.04
Apache II score	0.98 (0.96–1.00)	0.20	1.08 (1.05–1.10)	<0.001	1.05 (1.02–1.08)	0.003
Intubation	1.16 (0.81–1.68)	0.41	0.65 (0.41–1.05)	0.08	0.69 (0.39–1.23)	0.21
Infection	15.36 (10.05–23.48)	<0.001	8.83 (4.52–17.23)	<0.001	7.71 (2.97–20.00)	<0.001
Pos microbiology	0.73 (0.46–1.16)	0.18	1.93 (1.19–3.13)	0.01	1.25 (0.73–2.14)	0.41
Readmission	0.82 (0.46–1.45)	0.49	3.04 (1.59–5.80)	0.001	2.32 (1.15–4.68)	0.02
Died in ICU	1.16 (0.70–1.91)	0.20	1.46 (0.83–2.55)	0.18	2.35 (1.30–4.27)	0.005
Log LOS	1.28 (1.04–1.58)	0.02	2.23 (1.73–2.88)	<0.001	2.50 (1.87–3.34)	<0.001
Medical patient	2.22 (1.62–3.06)	<0.001	0.91 (0.41–1.05)	0.63	0.79 (0.39–1.23)	0.57

95% CI, 95% confidence interval; log LOS, log-transformed length of stay; OR, odds ratio.

Table 5 Timeliness and adequacy of antibiotic therapy for all isolates

Antibiotic management	Pre-intervention [*N* (%)]	Intervention [*N* (%)]	OR (95% CI)	*P*-value
Untreated isolates	22/303 (7.3)	12/237 (5.1)	0.69 (0.35–1.37)	0.20
Delayed therapy	40/278 (14.4)	36/225 (16.0)	1.12 (0.73–1.68)	0.62
Initial susceptibility mismatch[1]	48/197 (24.4)	23/151 (15.2)	0.63 (0.39–0.98)	0.02
Directed susceptibility mismatch	41/240 (17.1)	30/185 (16.2)	0.94 (0.61–1.45)	0.90
Antibiotic spectrum reduced after susceptibilities available	14/185 (7.6)	24/155 (15.6)	2.20 (1.17–4.11)	0.01

Thursky KA. et al, Int J Qual Health Care 2006

A World Wide Web–Based Antimicrobial Stewardship Program in a Tertiary Care Pediatric Medical Center

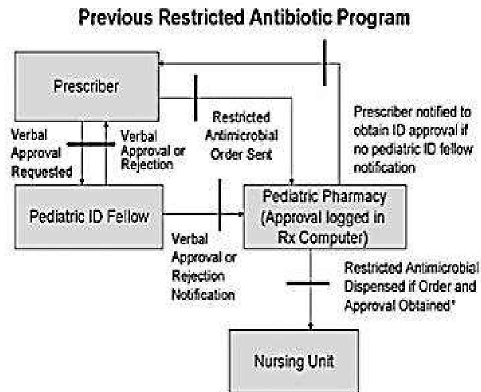
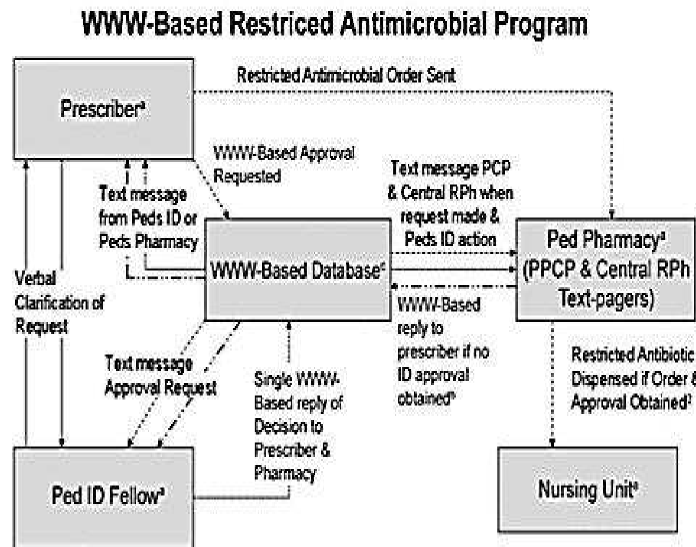


Figure 1. Schematic of the original antimicrobial restriction program at Johns Hopkins Children's Medical and Surgery Center. *Prescription of the first dose only is allowed between 11 P.M. and 8 A.M. or when the infectious diseases (ID) fellow cannot be contacted. Black bars indicate potential breaks in the system.



- ATB -11.6%
- Coût - $370,069
- Satisfaction 22% -> 68%
- Doses oubliées/retardées -21%, -32%
- Validation retardée -37%
- Appels téléphoniques -40%

Agwu AL. et al, Clin Infect Dis 2008

r Outils Maintenance Rapports Prescription labo

FOCH (FOCH) | REANIMATION POLYVALENTE

Monitoring

Tableau de bord

Traitements et prescriptions en cours d'antibiotiques controlés

marqués ATB dans Generix

Nombre de traitements = 18

Nombre de prescriptions = 20

Nombre de prescriptions signées par Pharmacie = 11

80% = jusqu'à la fin de l'hospitalisation

Le rapport ne tient pas compte des erreurs de prescriptions et traitements annulés et non distribués .

Le nom du prescripteur est celui du créateur de la prescription et non celui du dernier intervenant. Pour le détail consulter l'historique.

Patient	Date de naiss.	Localisation	Date prescription	Médicament	Prescripteur	Posologie	Arret prévu
			14/08/2014 11:20:00	CEFTAZIDIME 2 G PDRE POUR SOLUTION INJECTABLE -- 5039414		Lu: 2 gr. (18h) Me: 2 gr. (18h) Ve: 2 gr. (18h) [+DS]	
			14/08/2014 12:00:00	CIPROFLOXACINE 750 MG COMPRIME -- 5039463		750 mg 1 x par j. (12h)	

OmniPro | Gestion des lits | Monitoring

Randomized trial, antimicrobial prescribing for acute respiratory infections in primary care

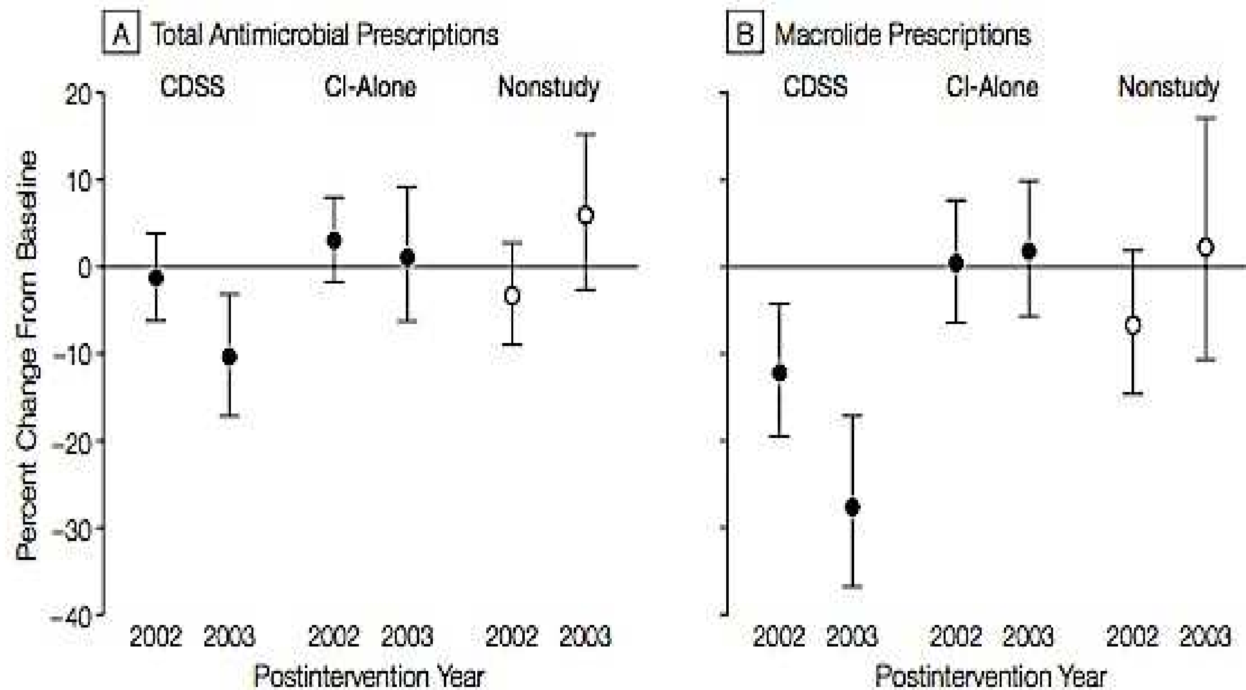


Figure 1. Relative Change in Prescribing Rates in Clinical Decision Support System (CDSS), Community Intervention Alone (CI-Alone), and Nonstudy Communities

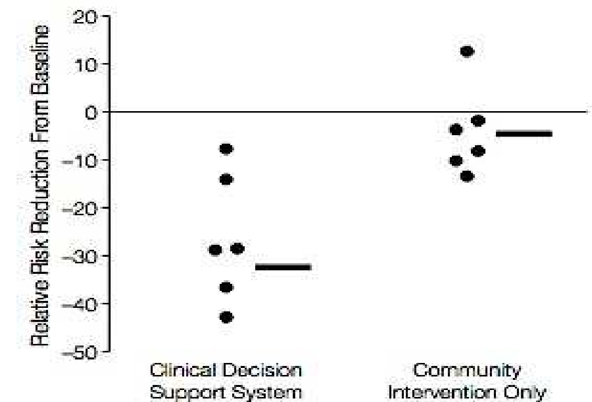


Figure 2. Relative Change in Prescribing Antimicrobial Agent for Visits in the "Never Indicated" Category

Relative change in probability of prescribing an antimicrobial agent for visits in the "never indicated" category during the postintervention period compared with the preintervention period, based on fitting a multilevel logistic regression model to the chart review data. Horizontal bars represent study group estimates and circles represent each community, calculated as the group estimate plus community-specific residual.

Samore MH. et al, JAMA 2005

ansm

Agence nationale de sécurité du médicament et des produits de santé

Rapport d'expertise

Caractérisation des antibiotiques considérés comme « critiques»

Diffusé en novembre 2013

Antibiotiques particulièrement générateurs de résistances bactériennes

- **association amoxicilline-acide clavulanique**

- **céphalosporines** : plus grande préoccupation pour les spécialités administrées par voie orale que par voie injectable; plus grande préoccupation pour les céphalosporines de troisième et quatrième générations ; préoccupation pour la ceftriaxone

- **fluoroquinolones**

Antibiotiques de dernier recours

Vis à vis des *cocci* à Gram positif
- **daptomycine**
- **linézolide**

Vis à vis des bactéries à Gram négatif
- **colistine injectable**
- **tigécycline**
- **pénèmes**
- **fosfomycine injectable**
- **phénicolés**
- ***témocilline (en perspective d'une réflexion sur une AMM nationale)***

Antibiotiques dont la prescription et/ou la dispensation doivent être contrôlées par des mesures spécifiques

- **association amoxicilline-acide clavulanique**
- **céphalosporines** : plus grande préoccupation pour les spécialités administrées par voie orale que par voie injectable; plus grande préoccupation pour les céphalosporines de troisième et quatrième générations ; préoccupation pour la ceftriaxone
- **fluoroquinolones**
- **daptomycine**
- **linézolide**
- **colistine injectable**
- **tigécycline**
- **pénèmes**
- **fosfomycine injectable**
- **phénicolés**
- ***témocilline (en perspective d'une réflexion sur une AMM nationale)***

Journal of Antimicrobial Chemotherapy Advance Access published October 24, 2013

J Antimicrob Chemother
doi:10.1093/jac/dkt403

Journal of Antimicrobial Chemotherapy

Fighting the spread of AmpC-hyperproducing Enterobacteriaceae: beneficial effect of replacing ceftriaxone with cefotaxime

P. Grohs[1*], S. Kernéis[1–5], B. Sabatier[3,6], M. Lavollay[1,4], E. Carbonnelle[1,4], H. Rostane[1], C. Souty[5], G. Meyer[3,4,7], L. Gutmann[1,4] and J. L. Mainardi[1–4]

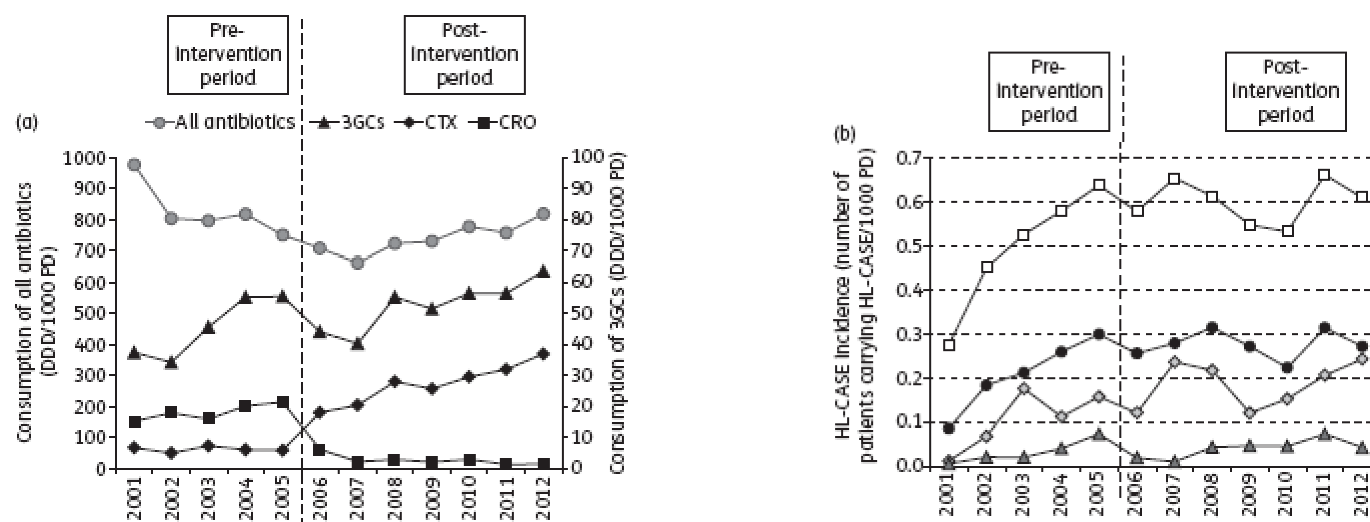


Figure 1. (a) Antibiotic consumption. CTX, cefotaxime; CRO, ceftriaxone. (b) HL-CASE incidence. Squares, Enterobacteriaceae harbouring inducible chromosomally encoded AmpC; circles, *E. cloacae*; diamonds, *E. coli*; triangles, Enterobacteriaceae without chromosomal AmpC (*Klebsiella pneumoniae*, *Proteus mirabilis* etc.). The vertical broken line corresponds to the date of replacement of ceftriaxone by cefotaxime.

Contrôle de la prescription des carbapénèmes

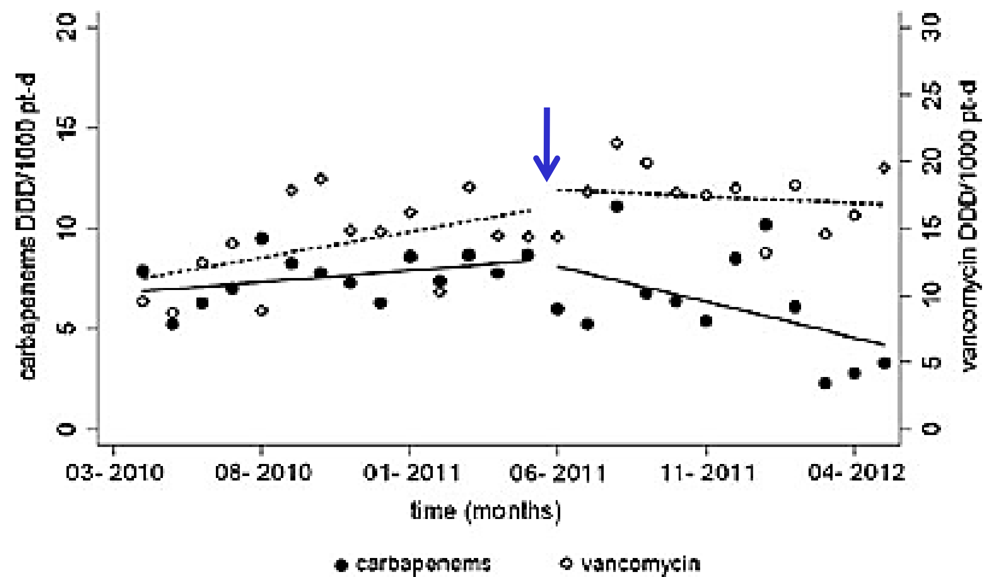


Fig. 1 Intervention effect on carbapenems and vancomycin consumptions. Carbapenems consumption is represented by *filled symbols* and vancomycin consumption is represented by *open symbols*. Consumption trends are represented by *lines*. The diffusion period was from May to July 2011. Only carbapenems consumption was affected by the intervention with a direct and sustained decreasing effect: (1) change in mean (−1.66 DDD/1,000 pt-d, p=0.048) corresponding to the global consumption change between the pre- and intervention periods; (2) change in level (−5.34 DDD/1,000 pt-d, p=0.049) corresponding to the consumption change at the start of the intervention; (3) change in slope (−2.66 DDD/1,000 pt-d, p=0.02) corresponding to the consumption change during the intervention period

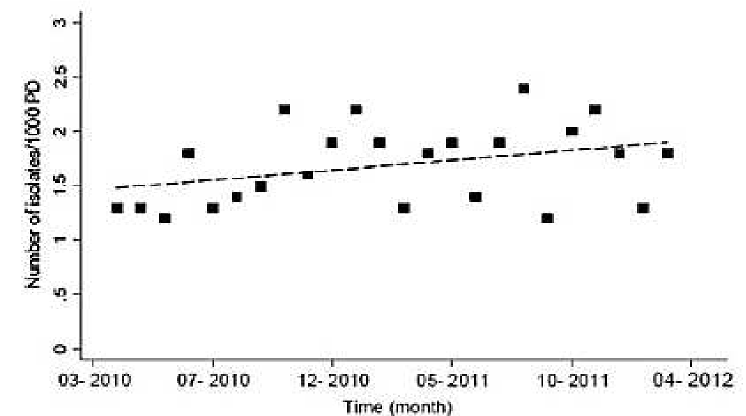


Fig. 2 ESBL-PE evolution among study. Trend (*dashed line*) to a linear increase in the monthly incidence of ESBL-PE (0.02/1,000 pt-d; p=0.093)

Delory T. et al, Eur J Clin Microb Infect Dis 2012

HENRI MONDOR hm
C.E.P.I.

Réévaluation des prescriptions de carbapénèmes

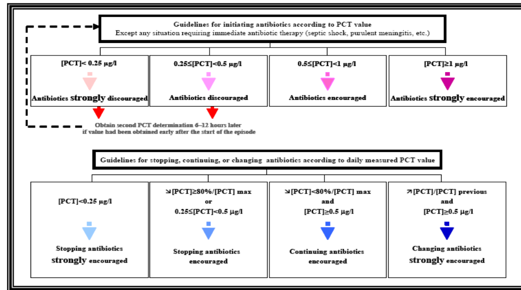
Réévaluation	Globale, nb (%)	Service, nb (%)	Référent, nb (%)
Désescalade*	176 (52.2)	63 (18.7)	113 (33.5)
Réduction durée	24 (7.1)	0 (0)	24 (7.1)
Relai per-os	20 (6.0)	15 (14.5)	5 (1.5)
Arrêt	51 (15.1)	32 (9.5)	19 (5.6)
Autre	7 (2.1)	0 (0)	7 (2.1)
Total	258 (76.6)	95 (28.2)	163 (48.4)

* céfoxitine, céfotaxime/ceftriaxone, céfépime, n=83 (47.2%); pip/taz, n= 48 (27.3%)

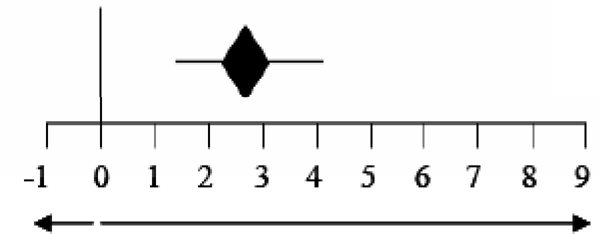
76.6% de modifications thérapeutiques, délai médian de 2 jours [1;4]

Delory T. et al, Eur J Clin Microb Infect Dis 2012

Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial)

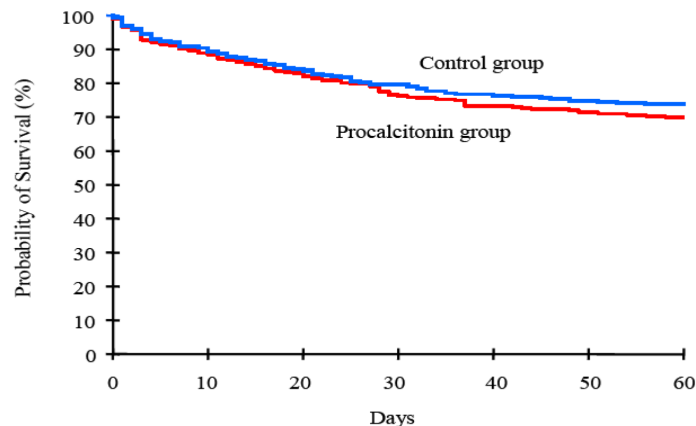


Baseline Characteristics	Control	Procalcitonin	Absolute difference, days (95% CI)
	Mean no. of antibiotic free-days/no. of patients		
Overall Population	11.6/314	14.3/307	



Less antibiotic exposure in control group

Less antibiotic exposure in procalcitonin group



No. at Risk							
Procalcitonin group	307	273	255	235	225	219	215
Control group	314	284	264	249	240	234	231

Bouadma L. et al, Lancet 2010

Procalcitonin-guided algorithm to reduce length of antibiotic therapy

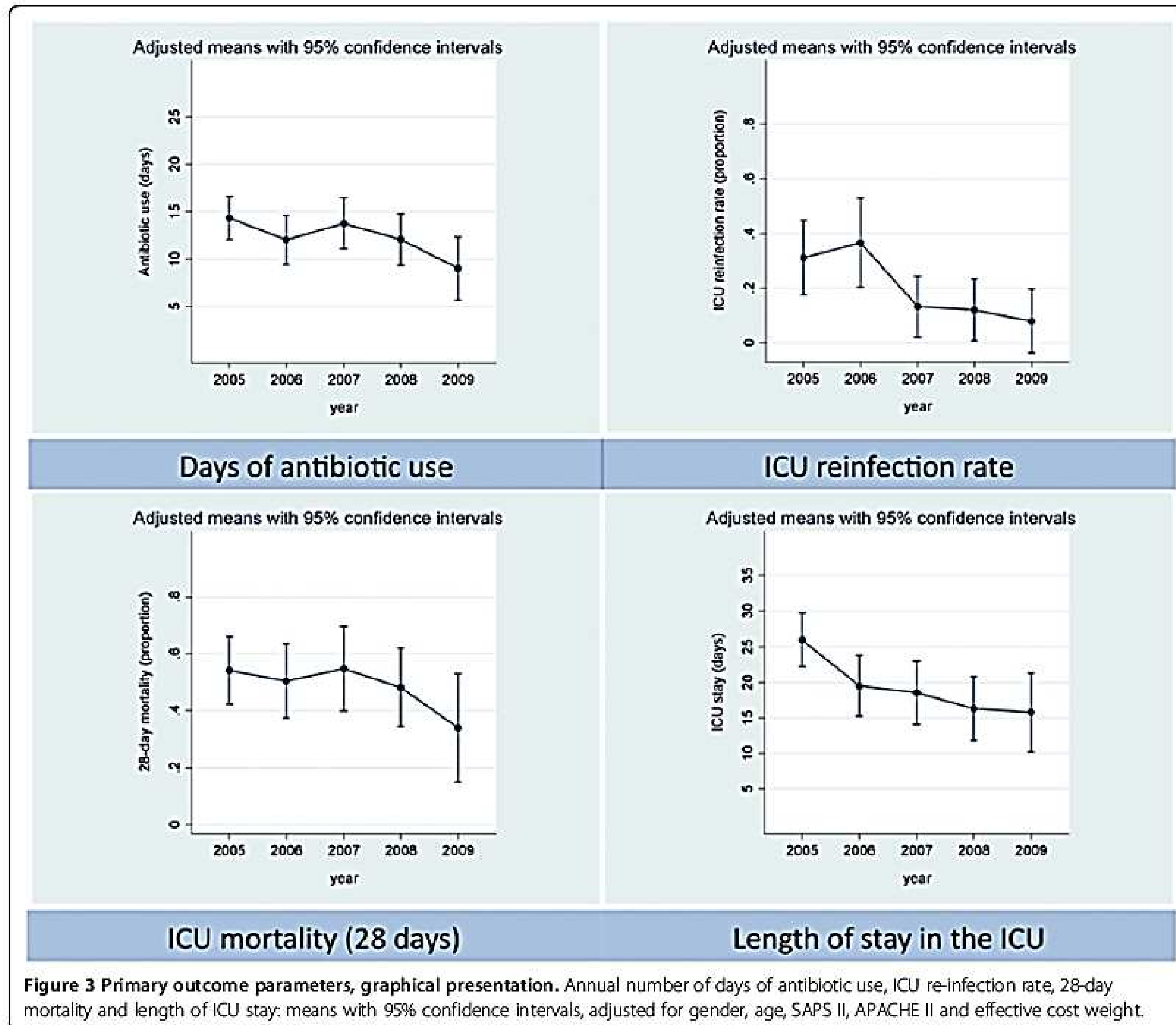


Figure 3 Primary outcome parameters, graphical presentation. Annual number of days of antibiotic use, ICU re-infection rate, 28-day mortality and length of ICU stay: means with 95% confidence intervals, adjusted for gender, age, SAPS II, APACHE II and effective cost weight.

Hohn A. et al,
BMC Infect Dis 2013

Impact of a novel antimicrobial stewardship tool on antibiotic use in nursing homes

	Intervention (baseline)	Intervention (RAMP)	Control (baseline)	Control (no RAMP)
N	825	838	803	778
Antibiotic consumption*	69.78	66.53	49.68	51.91
% change		**- 4.9** (-1;-8.6)		**+ 5.1** (0.2–10.2)

*DDD/1000 resident/day)

Table 3. Summary of compliance with individual 'good practice points' in RAMP

RAMP: Part A—Initiation of Treatment (n=372)		Yes (%)
A1	clinical signs and symptoms present or 'none at present' recorded	85
A2	whether resident examined by doctor, where and when documented	97
A3	initial diagnosis/suspected site of infection documented	93
A4	details of clinical specimens/swabs/urine dipstick or 'none taken' recorded	84
A5	check made that antibiotic supplied appropriate for	
	(a) clinical indication (type of infection suspected)	(a) 67
	(b) individual resident in terms of allergy status and medical history	(b) 97
A6	prompt initiation: time and date of administration of first dose recorded	97
RAMP: Part B—Review of Treatment (n=337)		**Yes (%)**
B1	review of clinical progress after 48–72 h treatment documented	78
B2	stop date for antibiotic or planned review date documented	77
B3	whether resident re-examined by doctor, where and when documented	64
B4	results of specimens/swabs or 'not available yet' or 'none taken' recorded	42
B5	outcome of antibiotic treatment documented	59

Fleet E. et al, J Antimicrob Chemother 2014

Reducing antimicrobial therapy for asymptomatic bacteriuria

« 'The majority of positive urine cultures from inpatients without an indwelling urinary catheter represent asymptomatic bacteriuria. If you strongly suspect that your patient has developed a urinary tract infection, please call the microbiology laboratory »

Table 2. Outcomes Before and After Implementation of Modified Urine Culture Reporting of Noncatheterized Medical and Surgical Inpatients

	Baseline		Intervention	
Outcome	Noncatheterized	Catheterized	Noncatheterized	Catheterized
Outcome measure				
ASB treatment rate	15/31 (48)	11/26 (42)	4/33 (12)	18/44 (41)
Process measures				
Total cultures reported	37/37 (100)	28/28 (100)	5/37 (14)	49/49 (100)
Labeling accuracy	35/37 (95)	25/28 (89)	37/37 (100)	41/49 (84)
Unintended consequences				
Calls to laboratory	0 (0)	0 (0)	5/37 (14)	1/49 (2)
Untreated UTI	1/37 (3)	1/28 (4)	0 (0)	0 (0)
Sepsis	0 (0)	1/28 (4)	0 (0)	1/49 (2)

Data are presented as No. (%).

Abbreviations: ASB, asymptomatic bacteriuria; UTI, urinary tract infection.

Treatment of ASB among noncatheterized inpatients decreased to 12% (95% CI, 5%–27%) for an absolute risk reduction of 36% (95% CI, 15%–57%; P = .002)

Leis JA, Clin Infect Dis 2014

Review of Rapid Diagnostic Tests Used by Antimicrobial Stewardship Programs

Table 3 Antimicrobial Stewardship Program Checklist for Rapid Diagnostic Tests

Preimplementation
- Identify most useful RDT based on hospital pathogen prevalence
  - Example: Number of *Staphylococcus aureus* bacteremias, number of coagulase-negative staphylococci, number of *Pseudomonas aeruginosa*, number of *Candida* species
- Identify hospital cost of infection
  - Example:
    - Utilize information warehouse personnel to pull cost by *ICD-9* code mortality data
    - Obtain time to ID specialist consult
    - Length of stay
    - 30-day readmission
- Time to effective therapy

Implementation
- Microbiologist-validated RDT instrument
- Determine if test is done in real time 24/7 or batch
- Communication of RDT results from microbiologist to physician and ASP pharmacist is established
- ASP pharmacist-physician educates medical staff
- ASP documents interventions and acceptance rate

Postimplementation
- Time to effective therapy
- Time to discontinuation or de-escalation
- Time to ID consult
- Documented negative blood culture prior to hospital discharge
- 30-day readmission
- Mortality

Abbreviations: ASP, antimicrobial stewardship program; *ICD-9*, *International Classification of Diseases, Ninth Revision*; ID, infectious diseases; RDT, rapid diagnostic test.

‘Rapid microbiologic technologies in combination with antimicrobial stewardship have demonstrated significant decreases in time to appropriate therapy and optimization of clinical and economic outcomes, including hospital length of stay, mortality, and healthcare costs’

Bauer KA, Clin Infect Dis 2014

Impact of rapid organism identification combined with antimicrobial stewardship team intervention

Table 3. Clinical and Treatment-Related Outcomes

Outcome	Total: Preintervention (n = 256)	Total: Intervention (n = 245)	*P* Value
Clinical outcomes			
30-day all-cause mortality	52 (20.3)	31 (12.7)	.021
Time to microbiological clearance, d	3.3 ± 4.8	3.3 ± 5.7	.928
Length of hospitalization, d[a]	14.2 ± 20.6	11.4 ± 12.9	.066
Length of ICU stay, d[a]	14.9 ± 24.2	8.3 ± 9.0	.014
Recurrence of same BSI	15 (5.9)	5 (2.0)	.038
30-day readmission with same BSI	9 (3.5)	4 (1.6)	.262
Treatment-related outcomes			
Time to effective therapy, h	30.1 ± 67.7	20.4 ± 20.7	.021
Time to optimal therapy, h	90.3 ± 75.4	47.3 ± 121.5	<.001

Data are No. (%) or mean ± standard deviation.

Abbreviations: BSI, bloodstream infection; ICU, intensive care unit.

[a] Length of hospitalization and ICU stay were defined as time from blood culture positivity to discharge.

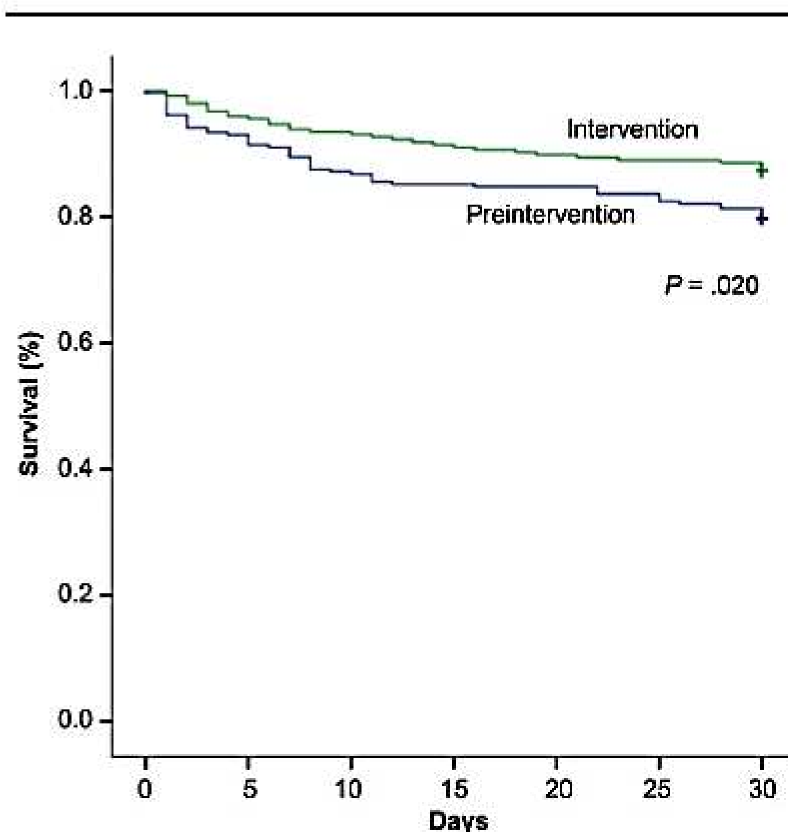
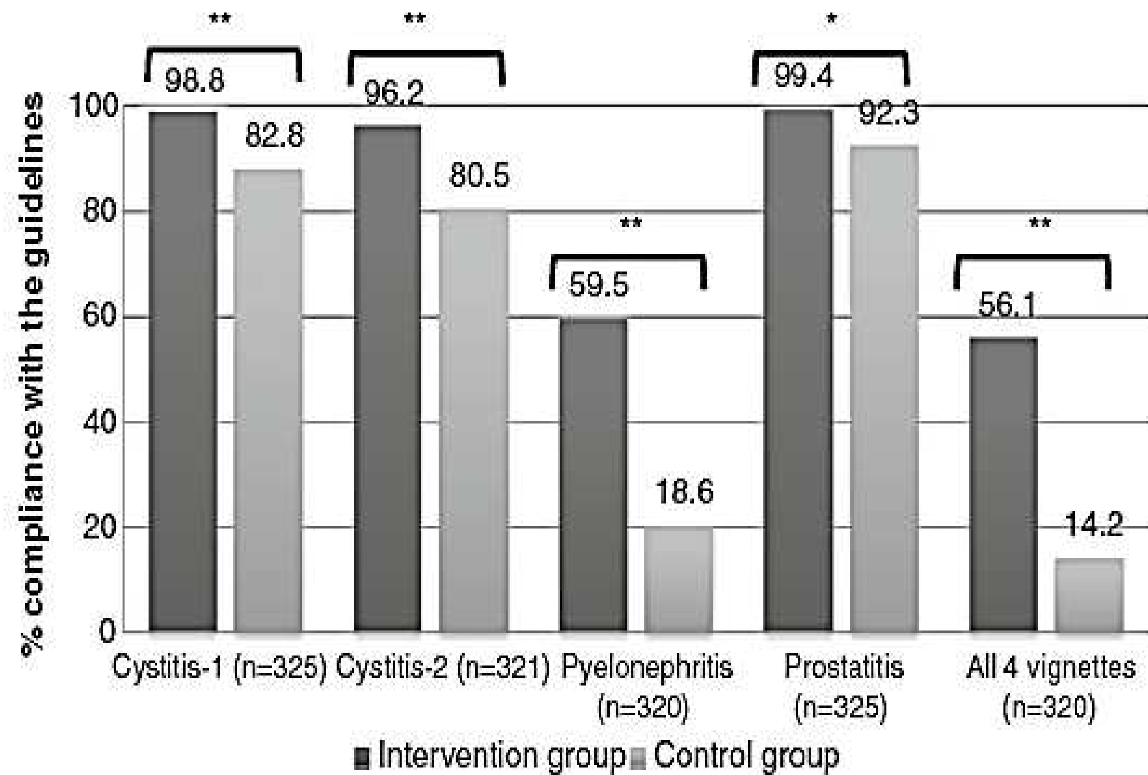


Figure 3. Kaplan-Meier survival analysis: overall survival in both study groups, censored for patients discharged prior to 30 days.

Huang AM. et al, Clin Infect Dis 2013

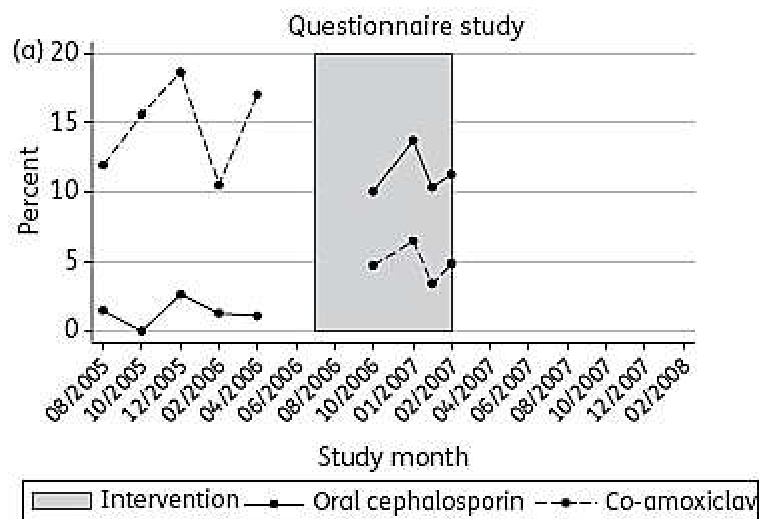
Selective reporting of susceptibility data improves the appropriateness of antibiotic prescriptions

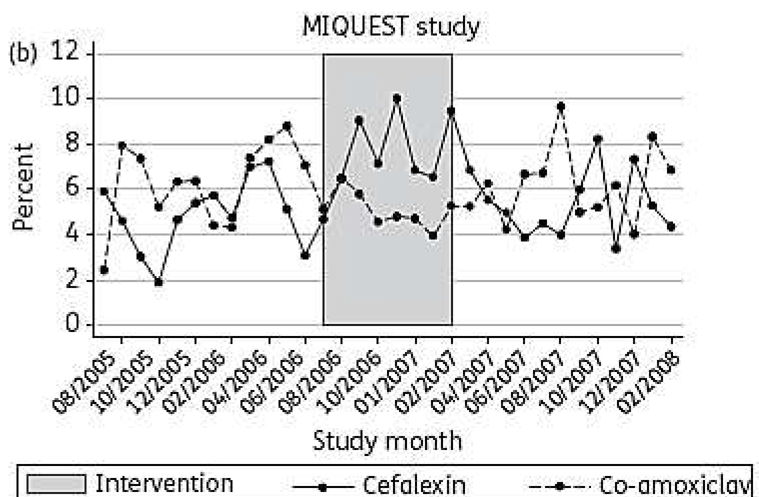
Fig. 1 Impact of selective reporting of antibiotic susceptibility data on the appropriateness of intended documented antibiotic prescriptions in the four vignettes. *p<0.01, **p< 0.001. All analyses were adjusted on the university (Dijon, Nice or Saint-Etienne)

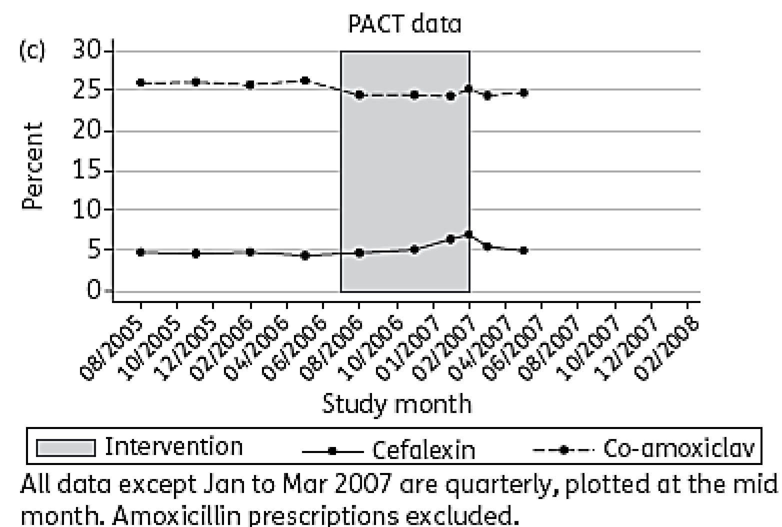


Coupat C. et al, Eur J Clin Microbiol Infect Dis 2013

Laboratory antibiotic susceptibility reporting and primary care prescribing in urinary tract infection







All data except Jan to Mar 2007 are quarterly, plotted at the mid month. Amoxicillin prescriptions excluded.

	Intervention, OR (95%CI)	**P**
Oral cephalosporins	9.875 (3.0-32.51)	< .001
Co-amoxiclav	0.304 (0.161-0.752)	< .001

McNulty C. et al, J Antimicrob Chemother 2011

Demonstrating the value of antimicrobial stewardship programs to hospital administrators

- Clinical outcome measures

Mortality, length of hospitalization, readmission rate

- Process measures

Amount of antimicrobial utilization

Time to effective therapy, duration of therapy

Incidence of *C. difficile* infection

- Economic measures

Total cost of care > antimicrobial acquisition cost

- Accreditation and quality indicators

Management of CAP

Prevention of healthcare-associated infections due to multidrug-resistant organisms

Nagel JL. et al, Clin Infect Dis 2014

Core Elements of Hospital Antibiotic Stewardship Programs (CDC)

Table 1. Core Elements of Hospital Antibiotic Stewardship Programs

Leadership commitment	Dedicating necessary human, financial, and information technology resources
Accountability	Appointing a single leader responsible for program outcomes and accountable to an executive-level or patient quality–focused hospital committee. Experience with successful programs shows that a physician or pharmacist leader is effective
Drug expertise	Appointing a single pharmacist leader responsible for working to improve antibiotic use
Action	Implementing at least 1 recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (ie, antibiotic "time-out" after 48 h)
Tracking	Monitoring process measures (eg, adherence to facility-specific guidelines, time to initiation or de-escalation), impact on patients (eg, *Clostridium difficile* infections, antibiotic-related adverse effects and toxicity), antibiotic use and resistance
Reporting	Regular reporting of the above information to doctors, nurses, and relevant staff
Education	Educating clinicians about disease state management, resistance, and optimal prescribing

Source: Centers for Disease Control and Prevention [4].

Pollack LA. et al, Clin Infect Dis 2014