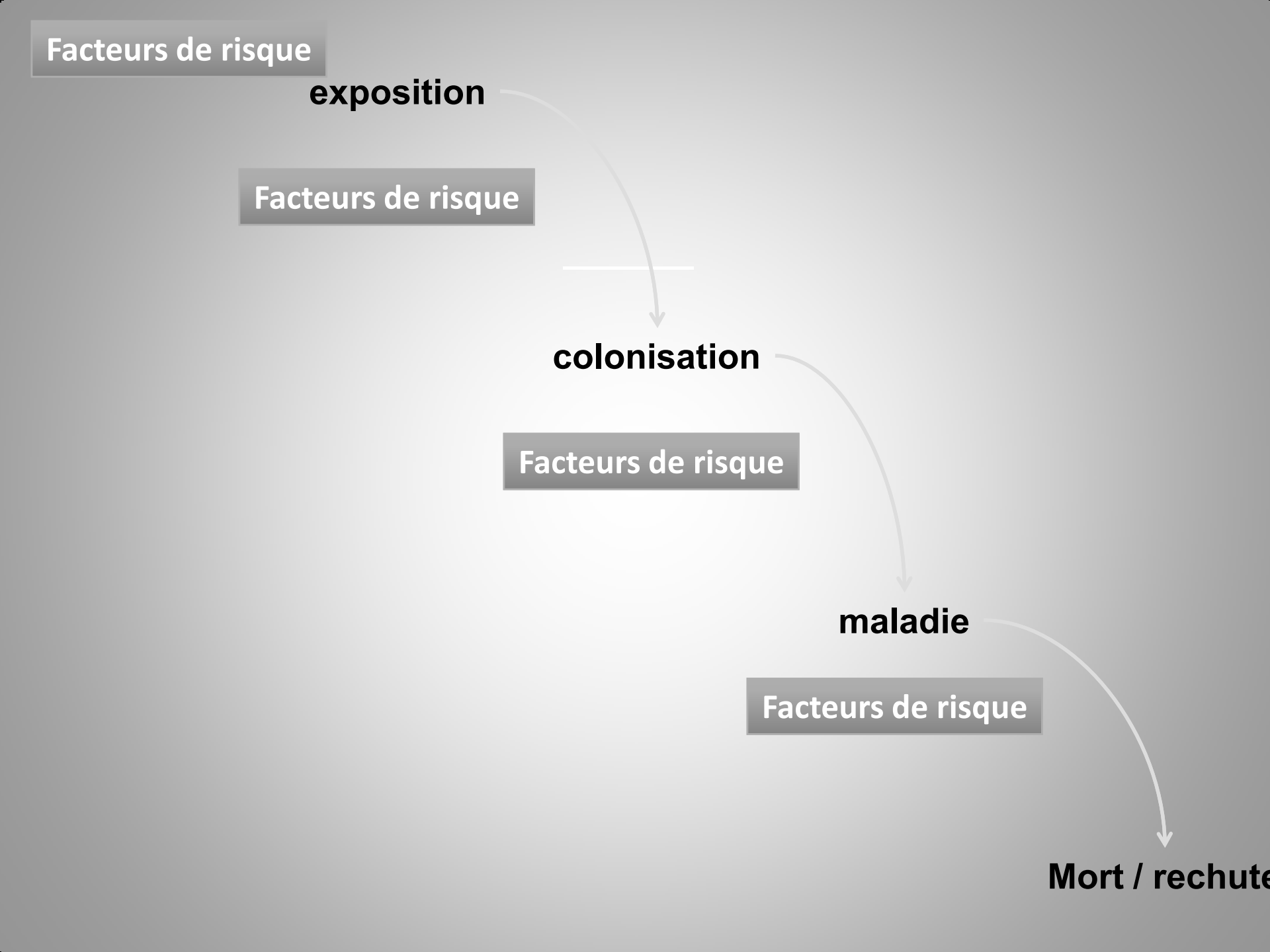
Clostridium difficile
facteurs de risque

JP Bru
CH Annecy


Facteurs de risque
exposition
Facteurs de risque
colonisation
Facteurs de risque
maladie
Facteurs de risque
Mort / rechute

Clostridium difficile – données historiques générales

Portage:

2 – 3 % de population communautaire

20 – 30 % patients hospitalisés

Colite

prévalences incidences non connue

Incidence 3.4 – 8.9 / 1000 admissions

facteurs de risque:

âge

hospitalisation

infection VIH

antibiothérapies

autres: IPP, sonde naso gastrique, laxatifs

Réponse au traitement 90%

Rechutes 10 – 15 %

Mortalité attribuable < 2 %

Bartlett NEJM 1978
Bartlett CID 1992
Kelly NEJM 1994
Wiström JAC 2001
Kine CID 2002

TABLE 2. Demographic and Clinical Characteristics of the 147 Patients With *Clostridium difficile*–Associated Diarrhea (CDAD)

Variable	Value
Age, y, mean ± SD (median)	58 ± 19 (59)
Sex	
Male	67 (45.6)
Female	80 (54.4)
Ward where hospitalized	
Medical unit	113 (76.9)
Surgical unit	9 (6.1)
Intensive care unit	25 (17.0)
Length of hospital stay, d, mean ± SD	31 ± 32
Risk factors for CDAD[a]	
Any risk factor	
⩾1 risk factors	136 (92.5)
0 risk factors	11 (7.5)
Specific risk factors	
Previous antibiotic treatment	123 (84.2)
Previous hospitalization	87 (59.2)
Chemotherapy	47 (32.0)
Nasogastric tube	24 (16.6)
Selective digestive decontamination	18 (12.2)
Abdominal surgery	15 (10.2)
$CD4^+$ counts <200 cells/mm^3	10 (6.8)

F Barbut Infect Control Hosp Epidemiol 2007; 28:131-139

Antibiotiques les quels sont les plus promoteurs et pourquoi

Autres facteurs de risque en particulier s’il n’y a pas eu d’antibiothérapie

Antibiotic-Associated Pseudomembranous Colitis Due to Toxin-Producing Clostridia

John G. Bartlett, M.D., TE Wen Chang, M.D., Marc Gurwith, M.D., Sherwood L. Gorbach, M.D., and Andrew B. Onderdonk, Ph.D.

N Engl J Med 1978; 298:531-534

Clostridium difficile physiopathologie des DACD

Importance de l'association antibiotique - colite à CD

	OR	RR	
		Mc Farlane (1)	Chang (2)
Exposition à antibiotique	2.86 – 6.92		4.22 (2.11-8.45 95% CI)
Clindamycine	2.12 – 42		
C3G	3.84 – 26	2.07 (1.06-6.62 95% CI)	
Pénicillines		3.62 (1.28-8.42 95% CI)	

C. Thomas J Antimicrob Chemoter 2003;51:1339-50
Revue systématique 49 publications

(1) - JID 1990;162:678-84
(2) - CID 2000;31:717-22

Clostridium difficile physiopathologie des DACD

Déséquilibre de la flore digestive (anaérobie probablement)

Facilite la colonisation par les spores de CD

Autorise la croissance de CD

s'accompagne de production et libération des exotoxines

Bartlett CID 2002

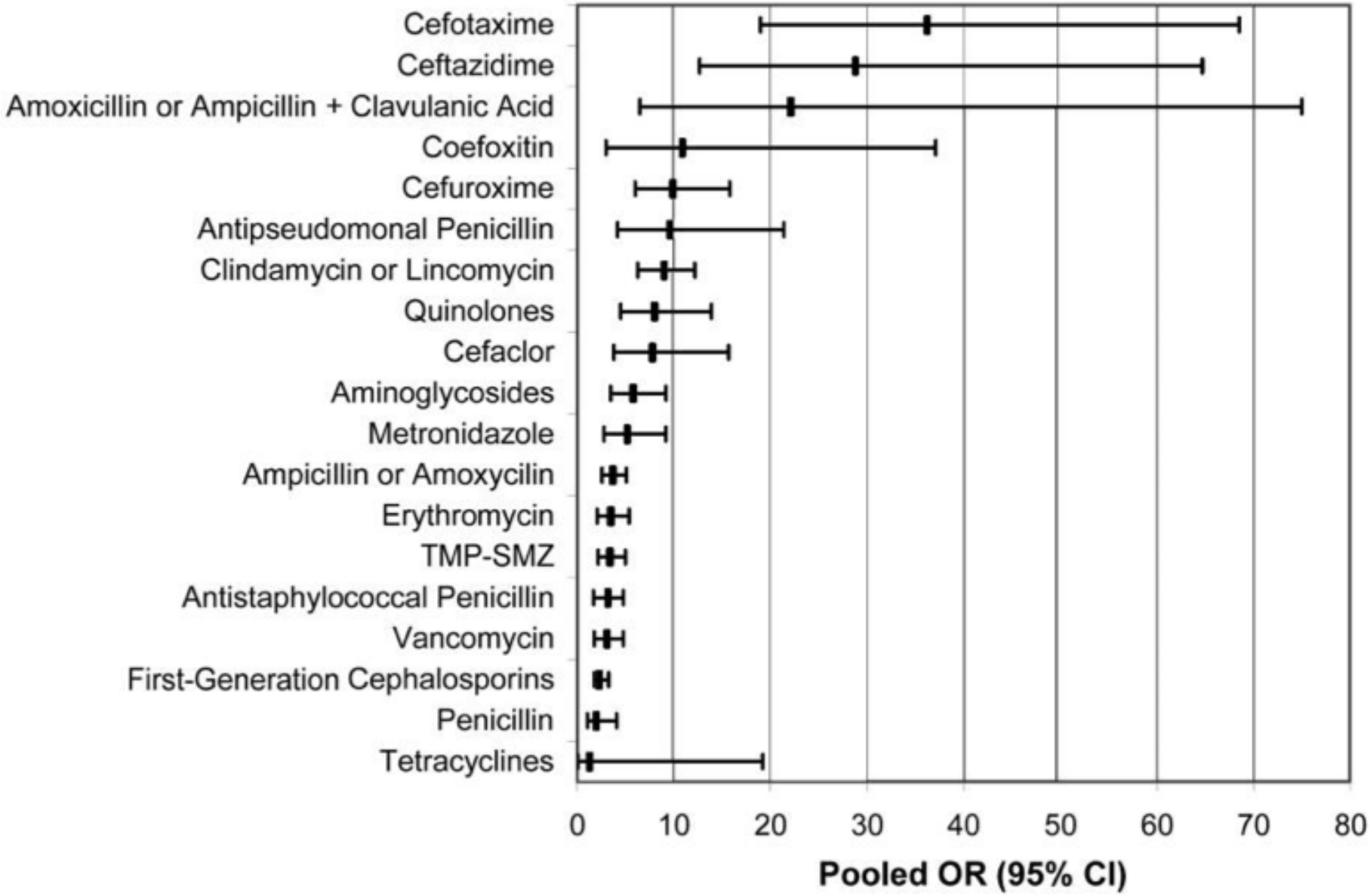
Hypothèse crédible mais qui mériterait confirmation

CD facteurs de risque considérations générales

La flore digestive constitue un important mécanisme d'inhibition de la colonisation par CD et d'autres pathogènes

L'antibiothérapie modifie la flore digestive en réduisant la diversité bactérienne

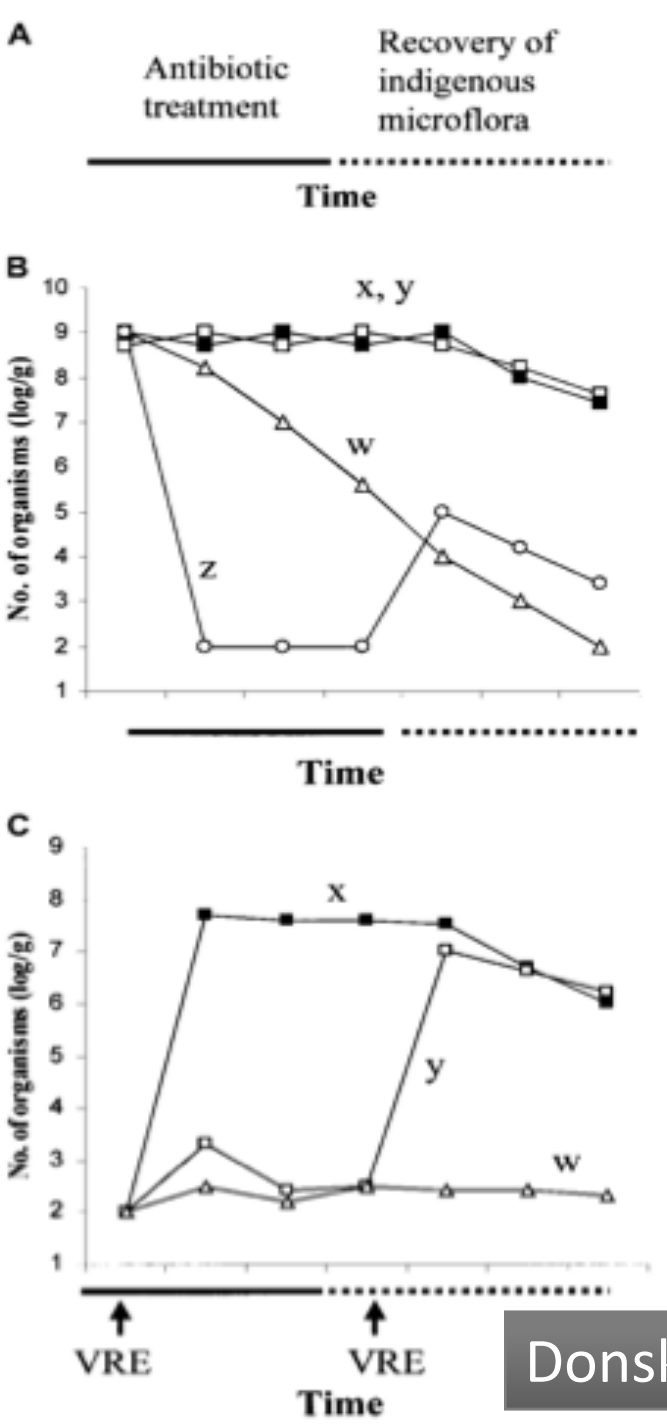
Donskey Clin Infect Dis 2004;39: 219–26.2.
Vollaard Antimicrob Agents Chemother 1994; 38:409–14.3.
Wilson Clin Infect Dis 1993; 16(Suppl 4):S214–8.4
Mai J Clin Microbiol 2006; 44:4550–2. 5
Young J Clin Microbiol 2004; 42:1203–6.
Gerding Clin Infect Dis 2004; 38:646–8.



Bignardi J Hosp Infect 1998;40:1-15

B, Effect of antibiotic treatment on vancomycin-resistant enterococci (VRE) previously established (the persistence model)

C, Effect of antibiotic treatment on establishment of colonization of VRE that was administered (the establishment model)



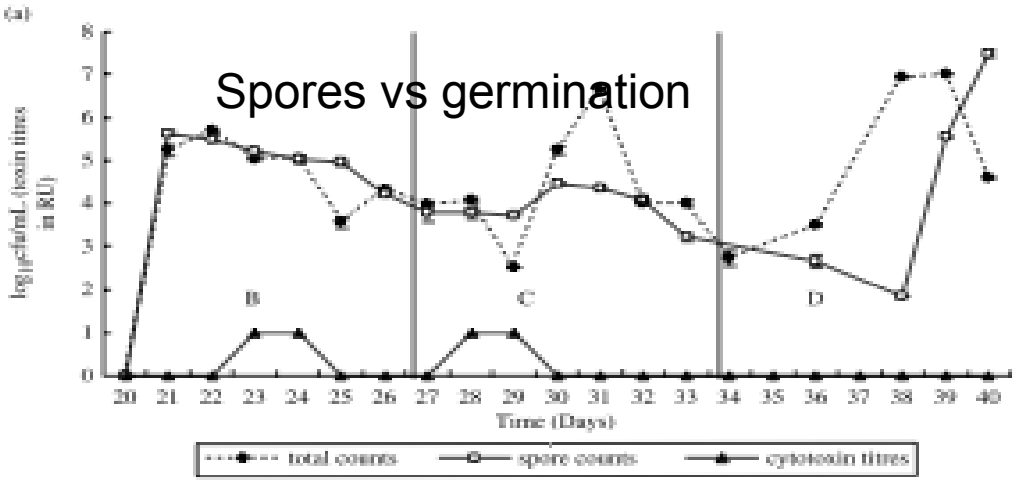
w, antibiotics that do not disrupt the anaerobic microflora (e.g., cefepime or aztreonam)

x, antibiotics that disrupt the anaerobic microflora and possess minimal antienterococcal activity (e.g., clindamycin or cefoxitin)

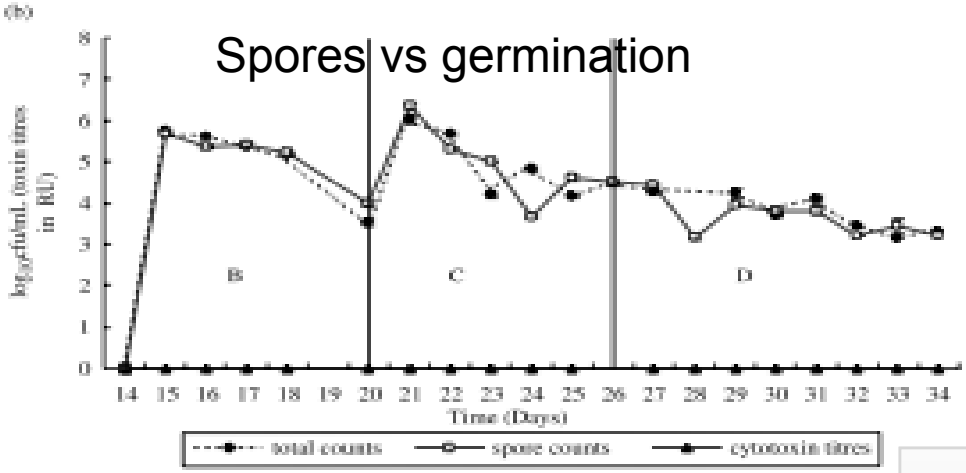
y, antibiotics that disrupt the anaerobic microflora and possess moderate antienterococcal activity (e.g., piperacillin-tazobactam)

z, antibiotics that disrupt the anaerobic microflora and possess potent activity against VRE (e.g., bacitracin).

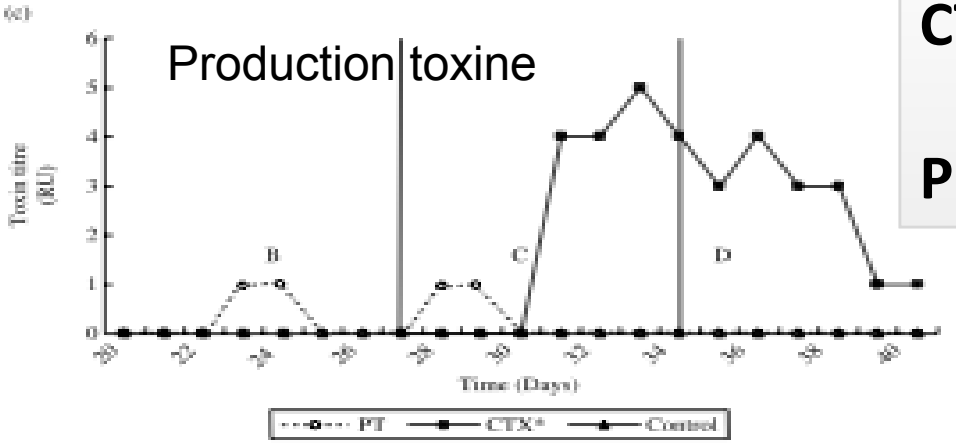
Donskey C I D 2004;39:219–26



Pipé + tazo



Pas d'antibiotique



CTX

Pipé+tazo

Baines
J A C (2005)
55, 974–982

Human gut model

Clostridium difficile – données historiques générales

Portage:

2 – 3 % de population communautaire

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Bartlett NEJM 1978
Bartlett CID 1992
Kelly NEJM 1994
Wiström JAC 2001
Kine CID 2002

Clostridium difficile nouvell

Augmentation de fréquence des cas

Épidémie à multiples foyers Am. nor

Mortalité anormalement élev

Récurrences plus fréquentes
chez les malades traités
par métronidazole

Quebec 2004 CD:
22.5 pour 1(
mortalité 6.

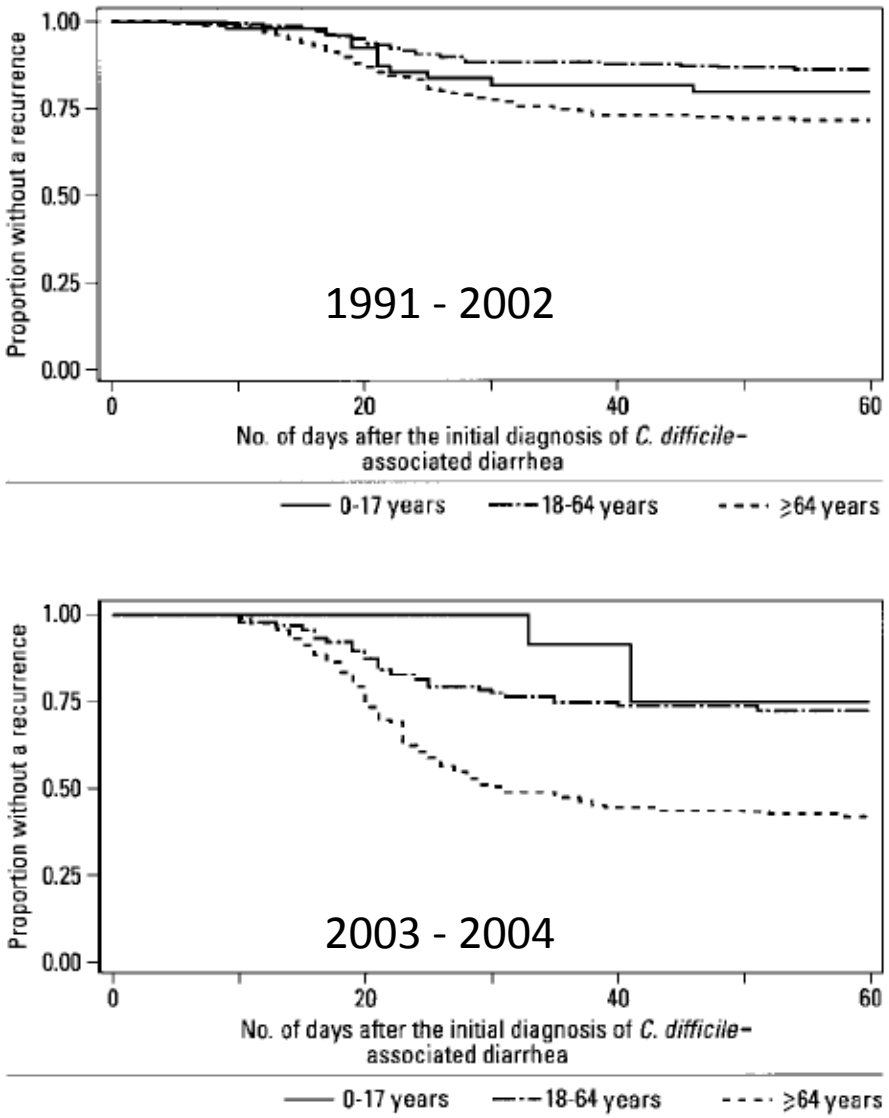


Figure 2. Kaplan-Meier plot of the 60-day probability of recurrence among patients with *Clostridium difficile*–associated diarrhea treated with only metronidazole in 1991–2002 *(top)* and 2003–2004 *(bottom)*, according to age group.

Table 3. Characteristics of Case Patients and Control Patients.*

Characteristic	Case Patients (N=237)	Controls (N=237)	P Value
Age — yr			0.48
Median	75	75	
Interquartile range	66–82	66–82	
Male sex — no. (%)	115 (48.5)	126 (53.2)	0.3
Charlson index†	2.6±1.9	2.6±2.0	0.66
Ward			0.82
Medicine	133 (56.1)	142 (59.9)	
Surgery	78 (32.9)	70 (29.5)	
Geriatrics	17 (7.2)	15 (6.3)	
Oncology	9 (3.8)	10 (4.2)	
Community hospital — no. (%)	68 (28.7)	67 (28.3)	0.9
Days at risk for *C. difficile*–associated diarrhea			0.02
Median	13	16	
Interquartile range	6–25	8–29	
No. of antibiotics received	1.9±1.1	1.3±1.3	<0.001
Any exposure to antibiotics — no. (%)	188 (79.3)	141 (59.5)	<0.001
Cephalosporins	115 (48.5)	65 (27.4)	<0.001
Clindamycin	19 (8.0)	6 (2.5)	0.007
Fluoroquinolones	128 (54.0)	75 (31.6)	<0.001
Chemotherapy — no. (%)	17 (7.2)	13 (5.5)	0.45
Proton-pump inhibitors — no. (%)	112 (47.3)	111 (46.8)	0.92
Histamine H_2–blockers — no. (%)	47 (19.8)	47 (19.8)	1.0
Enteral feeding — no. (%)	44 (18.6)	28 (11.8)	0.04

V Loo

N Engl J Med 2005; 353:2442-9.

Clostridium difficile rôle de la résistance: fluoroquinolones

Table 3. Multivariable model of risk factors for *Clostridium difficile*–associated diarrhea in cases (n=30) versus controls (n=60), controlling for days at risk

Risk factor	Odds ratio	95% confidence interval
Fluoroquinolones	12.7	2.6 to 61.6
Cephalosporins	0.4	0.1 to 1.5
Clindamycin	2.2	0.5 to 9.1

USA 4 hopitaux (Veterans Affairs Maryland)

M McCusker EID 2003

Clostridium difficile quels antibiotiques responsables

OR faibles	OR les plus élevés	
Pénicillines spectre étroit	Clindamycine	2 - 18
Vancomycine	C3G	5 – 36
Métronidazole	fluoroquinolones	2.2 – 9.13
Aminosides		
Macrolides		
Chimiothérapies anticancéreuses		
IPP		

Bignardi J Hosp Inf 1998
Johnson NEJM 99
Yip ICHE 2001
Starr age & aging 2003
Mc Cusker EID 2003
Thomas JAC 2003
Gaynes CID 2004
Pépin CID 2005
Loo NEJM 2005
Kazakova Ann Int Med 2006

Clostridium difficile épidémie actuelle

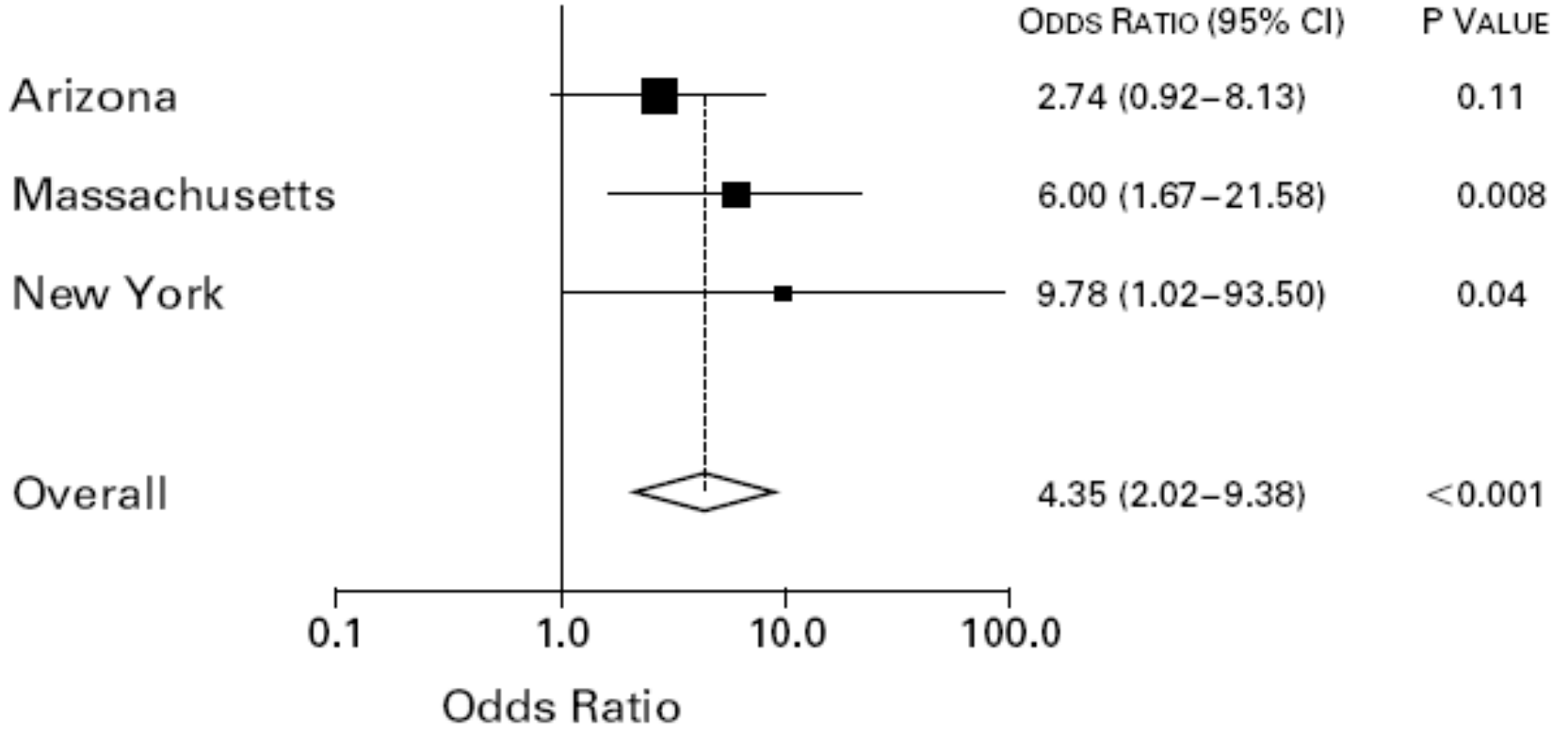
***Clostridium difficile* souche épidémique:**
ribotype 027 toxinotype III

⇨ Hyperproductrice de toxines A & B
(délétion tcdC)

⇨ **Haut niveau de résistance aux fluoroquinolones**

Clostridium difficile rôle de la résistance: clindamycine

TABLE 1. OUTBREAKS OF DIARRHEA ASSOCIATED WITH *CLOSTRIDIUM DIFFICILE*



Utilisation de clindamycine chez patients avec DACD: souche épidémique vs autres souches

S Johnson NEJM 1999

Clostridium difficile rôle de la résistance: clindamycine

TABLE 2. ANTIMICROBIAL-RESISTANCE PROFILES OF REPRESENTATIVE ISOLATES OF THE EPIDEMIC STRAIN OF *CLOSTRIDIUM DIFFICILE* AT EACH HOSPITAL AND CONTROL STRAINS.*

DRUG	EPIDEMIC STRAIN				CONTROL STRAIN		
	J9 (NEW YORK)	J7 (ARIZONA)	J9p2 (FLORIDA)	J9 (MASSACHUSETTS)	CLINDAMYCIN-SUSCEPTIBLE (K12p)	CLINDAMYCIN-SUSCEPTIBLE (Y4)	CLINDAMYCIN-RESISTANT (B1)
	minimal inhibitory concentration (micrograms per milliliter)						
Clindamycin	>256	>256	>256	>256	0.75	0.75	>256
Erythromycin	>256	>256	>256	>256	0.5	0.50	>256
Ciprofloxacin	>32	>32	>32	>32	>32	>32	>32
Ampicillin	0.75	0.75	0.75	0.75	3.0	1.0	1.5
Tetracycline	0.06	0.06	0.06	0.06	0.09	0.05	12

S Johnson NEJM 1999

Clostridium difficile rôle de la résistance: clindamycine

La résistance à la clindamycine

augmente le risque de DACD chez les malades traités par clindamycine

Participe au risque épidémique

S Johnson NEJM 1999

Table 4. Multivariate Model of the Risk of *Clostridium difficile*–Associated Diarrhea According to the Use of Antibiotics among Case Patients, as Compared with Matched Controls, January 11 through June 26, 2004.*

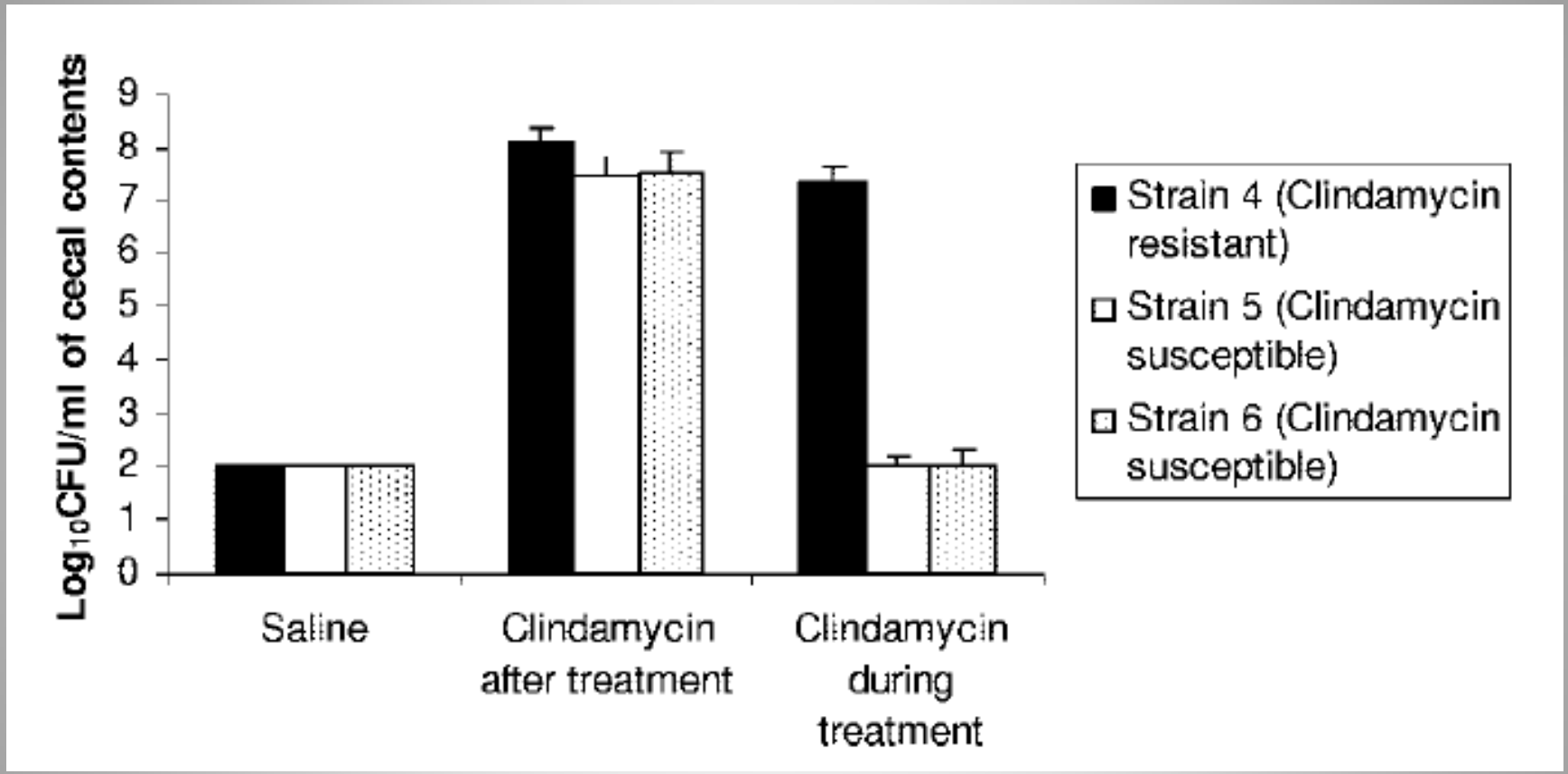
Antibiotic	Odds Ratio	95% Confidence Interval
Any cephalosporin	3.8	2.2–6.6
First-generation	2.4	1.2–4.6
Second-generation	6.0	2.1–17.5
Third-generation	3.0	1.4–6.8
Any fluoroquinolones	3.9	2.3–6.6
Ciprofloxacin	3.1	1.8–5.4
Gatifloxacin or moxifloxacin	3.4	1.5–7.7
Levofloxacin	0.6	0.2–1.9
Clindamycin	1.6	0.5–4.8
Aminoglycosides	0.7	0.3–1.9
Macrolides	1.3	0.6–2.9
Intravenous vancomycin	1.3	0.5–3.1
Penicillins combined with β-lactamase inhibitor	1.2	0.7–2.3
Penicillins	0.7	0.3–2.9
Carbapenems	1.4	0.3–6.3

Épidémie
DACD
Québec

souche 027
Clinda S

Loo NEJM 2005

C difficile. Effet de la clindamycine sur la croissance dans la flore fécale de souris selon la résistance de la souche



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 2007, p. 2674–2678

Clostridium difficile rôle de la résistance: fluoroquinolones

Molécule	OR
Clindamycine	4.8 (1.9 – 12)
Ceftriaxone	5.4 (1.8 – 15.8)
Lévofloxacine	2.0 (1.2 – 3.3)

Épidémie Pittsburg

Muto Inf Contr Hosp Inf 2005

Clostridium difficile épidémie actuelle

***Clostridium difficile* souche épidémique:**
ribotype 027 toxinotype III

⇨ Hyperproductrice de toxines A & B
(délétion tcdC)

⇨ Haut niveau de résistance aux fluoroquinolones

Clostridium difficile épidémie actuelle: rôle de la résistance aux fluoroquinolones

Table 2. Resistance of Current BI/NAP1 *Clostridium difficile* Isolates, Current Non-BI/NAP1 Isolates, and Historic BI/NAP1 Isolates to Clindamycin and Fluoroquinolones.*

Antimicrobial Agent	Current BI/NAP1 Isolates (N=24)	Current Non-BI/NAP1 Isolates (N=24)	P Value†	Historic BI/NAP1 Isolates (N=14)	P Value‡
	no. with intermediate resistance or resistant (%)§			*no. with intermediate resistance or resistant (%)*	
Clindamycin	19 (79)	19 (79)	1.0	10 (71)	0.7
Levofloxacin	24 (100)	23 (96)	1.0	14 (100)	1.0
Gatifloxacin	24 (100)	10 (42)	<0.001	0	<0.001
Moxifloxacin	24 (100)	10 (42)	<0.001	0	<0.001

USA 8 hôpitaux épidémie 2000 - 2003

C McDonald NEJM 2005

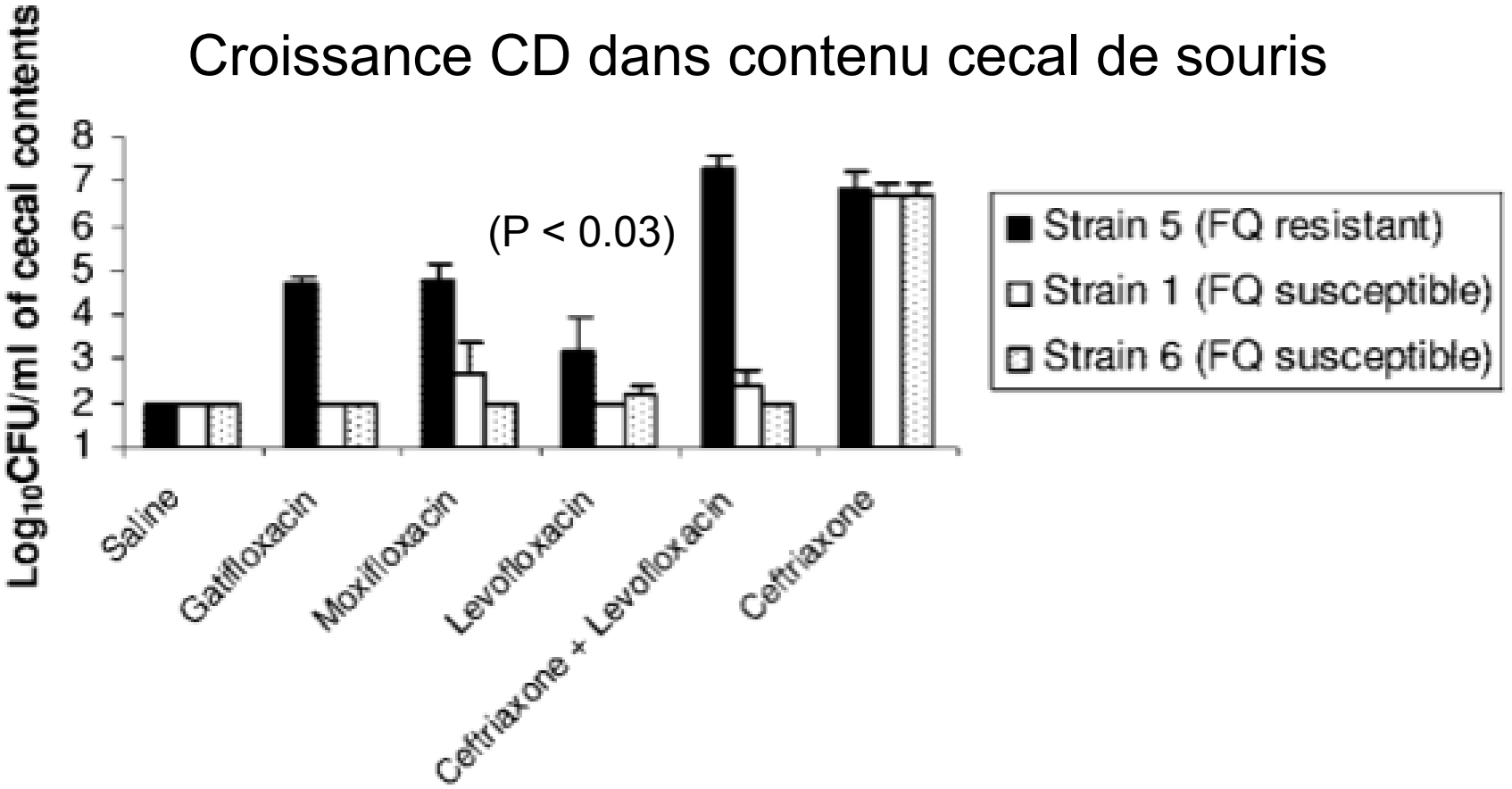
Clostridium difficile épidémie actuelle: rôle de la résistance aux fluoroquinolones

Antibiotic	NAP1 strains (174 isolates)			NAP2 strains (28 isolates)			Non-NAP1 non-NAP2 strains (46 isolates)		
	MIC_{50} (μg/ml)	MIC_{90} (μg/ml)	% Resistant	MIC_{50} (μg/ml)	MIC_{90} (μg/ml)	% Resistant	MIC_{50} (μg/ml)	MIC_{90} (μg/ml)	% Resistant
Clindamycin	2	4	0	>128	>128	88.8	4	>128	25
Clarithromycin	>128	>128	99.4	>128	>128	85.2	0.5	>128	25
Ceftriaxone	64	64	99.4	128	128	88.5	32	64	12.5
Gatifloxacin	128	>128	98.8	64	>128	88.5	4	64	12.5
Moxifloxacin	64	128	98.8	64	>128	88.5	4	64	12.5

Épidémie Québec

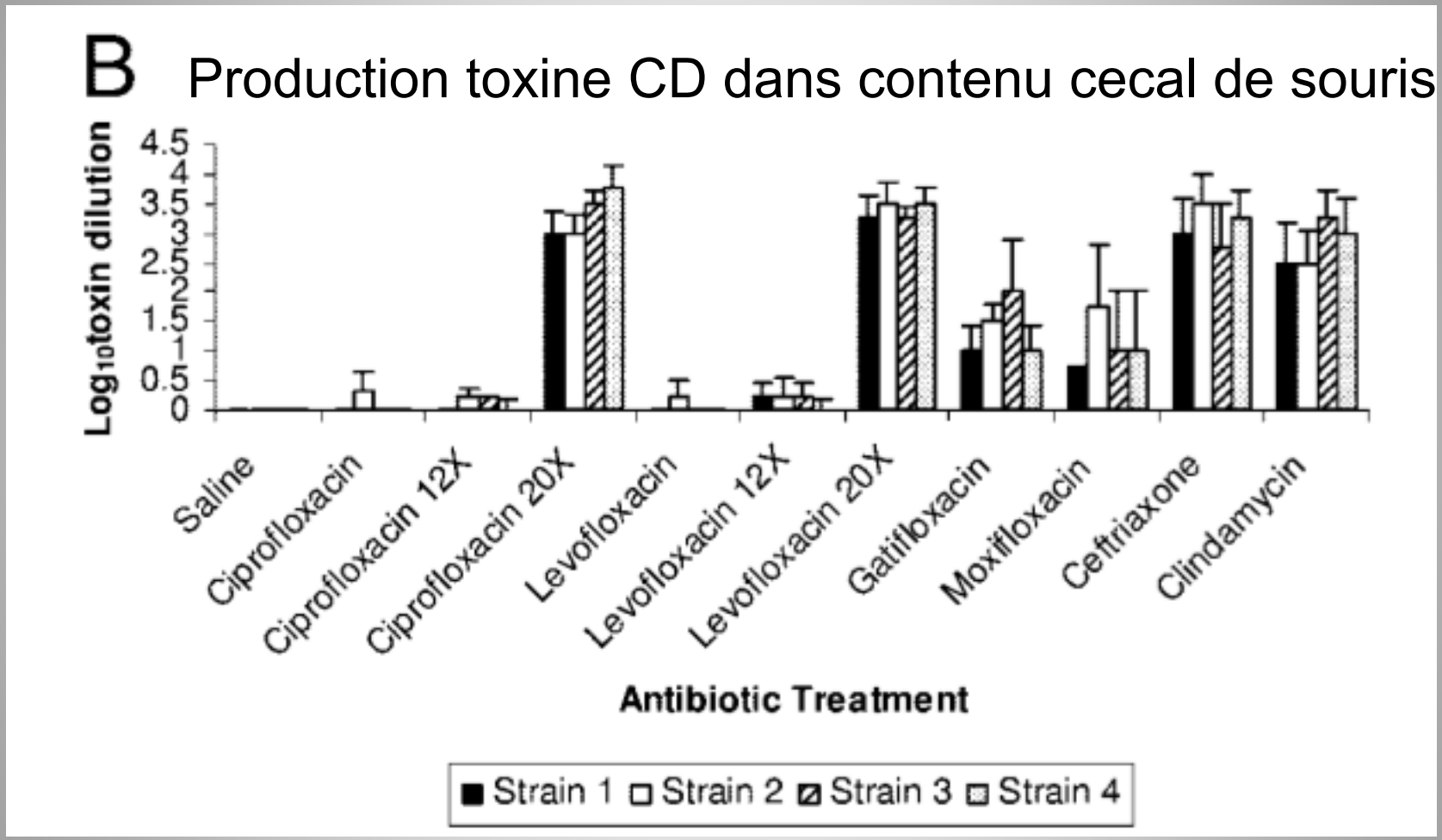
AM Bourgault AAC 2006

Clostridium difficile épidémie actuelle: rôle de la résistance aux fluoroquinolones



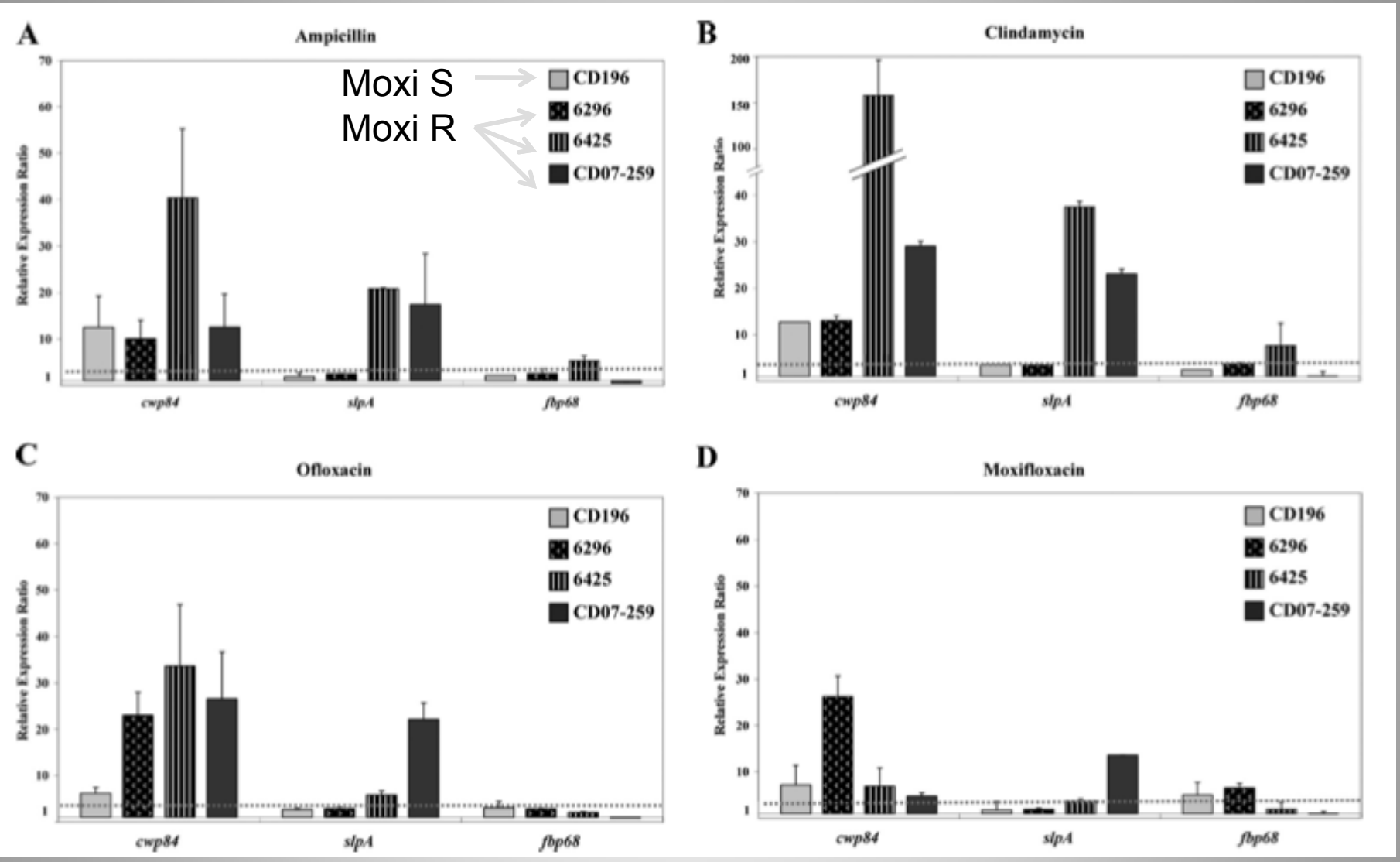
Hecht AAC, Aug. 2007, p. 2716–2719

Clostridium difficile épidémie actuelle: rôle de la résistance aux fluoroquinolones



Hecht AAC, Aug. 2007, p. 2716–2719

expression of C. difficile colonization factor-encoding genes in four NAP1/027 strain



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Dec. 2009, p. 5155–5162
Cécile Denève, Sylvie Bouttier,Bruno Dupuy, Frédéric Barbut, Anne Collignon, and Claire Janoir

Clostridium difficile épidémie actuelle: différences entre les fluoroquinolones ?

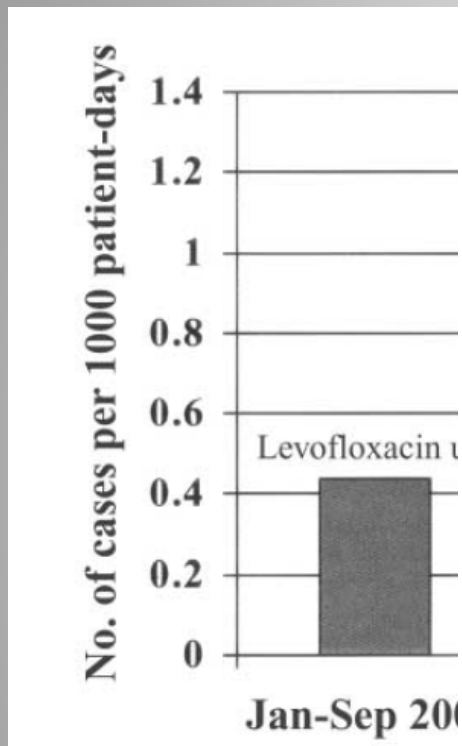


Figure 1. Rate of *Clostri* term care facility. *$P < .002$ period of gatifloxacin use.

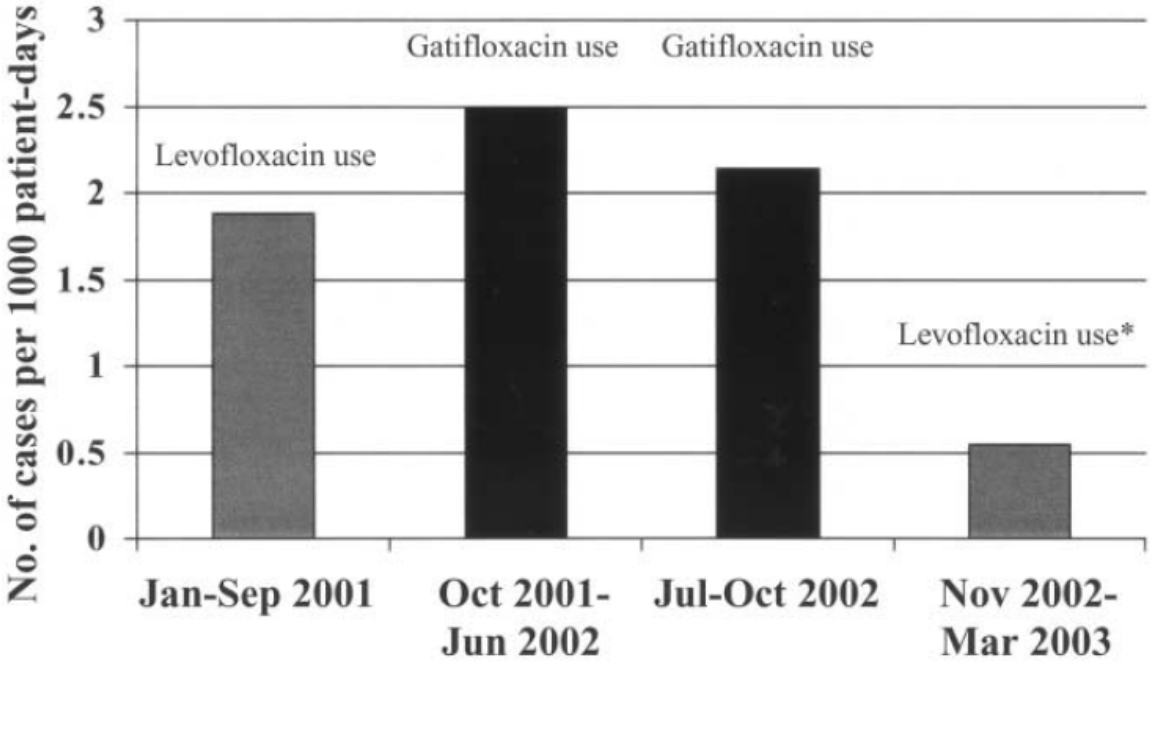


Figure 2. Rate of *Clostridium difficile*–associated diarrhea at an acute care hospital. $P < .002$ for either period of levofloxacin use versus the second period of gatifloxacin use (July through October 2002). No other rates differed significantly when compared with the adjacent period.

USA épidémie 2 structures de soins

R Gaynes CID 2004

Table 4. Multivariate Model of the Risk of *Clostridium difficile*–Associated Diarrhea According to the Use of Antibiotics among Case Patients, as Compared with Matched Controls, January 11 through June 26, 2004.*

Antibiotic	Odds Ratio	95% Confidence Interval
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Ciprofloxacin	3.1	1.8–5.4
Gatifloxacin or moxifloxacin	3.4	1.5–7.7
Levofloxacin	0.6	0.2–1.9
Clindamycin	1.6	0.5–4.8
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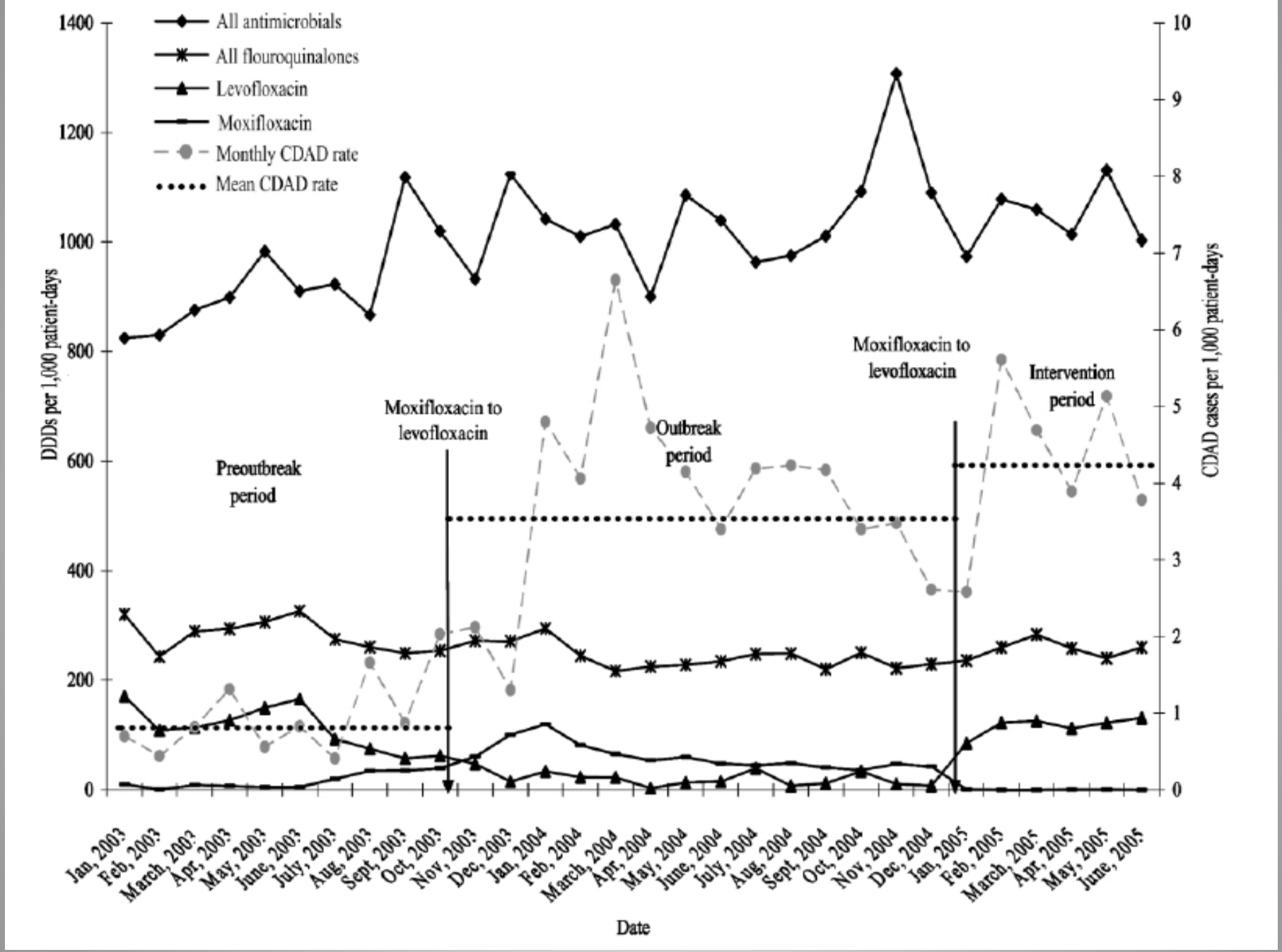
Épidémie
DACD
Québec

Loo NEJM 2005



USA (Pennsylvania) 1 hôpital

P Biller Infec Contr Hosp Inf 2007

Clostridium difficile épidémie actuelle: différences entre les fluoroquinolones ?

1 quelle réalité ?

2 si oui mécanisme ?

Conséquences différentes sur la flore digestive ?

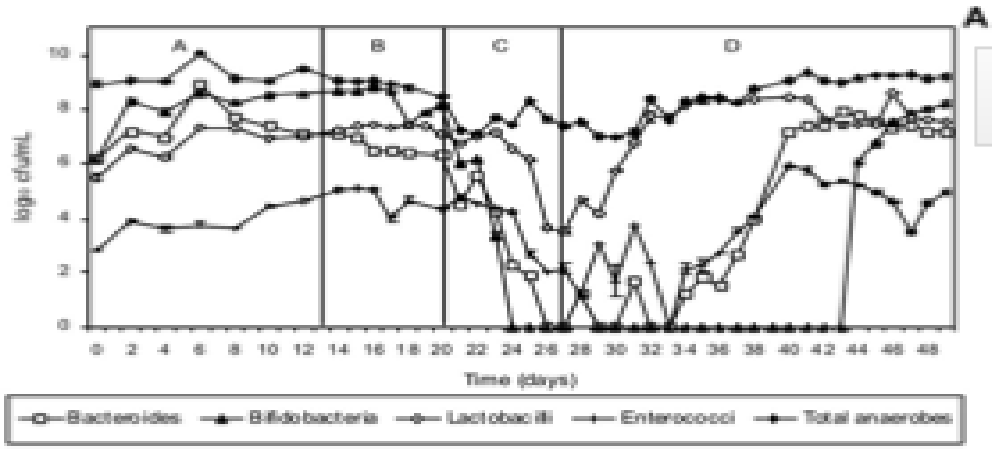
Fluoroquinolones activité in vitro anti anaérobie

Organism[a]	Levofloxacin		Gatifloxacin		Moxifloxacin		Gemifloxacin		References
	MIC_{50}, μg/mL	MIC_{90}, μg/mL	MIC_{50}, μg/mL	MIC_{90}, μg/mL	MIC_{50}, μg/mL	MIC_{90}, μg/mL	MIC_{50}, μg/mL	MIC_{90}, μg/mL	
Bacteroides species									[15, 20, 24–26]
Bacteroides fragilis	1.0	4.0	…	…	0.5	2.0	0.5	2.0	
Bacteroides thetaiotaomicron	4.0	16.0	…	…	1.0	4.0	1.0	16.0	
Bacteroides distasonis	4.0	16.0	…	…	0.5	8.0	8.0	16.0	
Bacteroides tectum	0.25	0.25	0.125	0.125	0.06	0.125	0.125	0.25	
Clostridium species									[15, 26]
Clostridium perfringens	0.25	1.0	…	…	0.5	0.5	0.06	0.06	
Clostridium clostridiiforme	8.0	16.0	…	…	8.0	8.0	0.5	0.5	
Fusobacterium nucleatum	0.5	0.5	0.25	0.5	0.125	0.25	0.125	0.25	[15, 18, 26]
Peptostreptococcus species									[18, 27]
Peptostreptococcus micros	0.5	0.5	0.25	0.25	0.25	0.5	0.125	0.125	
Peptostreptococcus magnus	0.25	0.5	0.125	0.25	0.125	0.125	0.06	0.06	
Porphyromonas saccharolytica	0.5	0.5	…	…	0.5	0.5	0.125	0.125	[15, 26]
Prevotella species									[15, 18, 20]
Prevotella melaninogenica	1.0	1.0	0.25	0.5	0.5	1.0	1.0	1.0	
Prevotella intermedia	0.25	0.5	0.125	0.25	0.25	0.5	0.5	0.5	

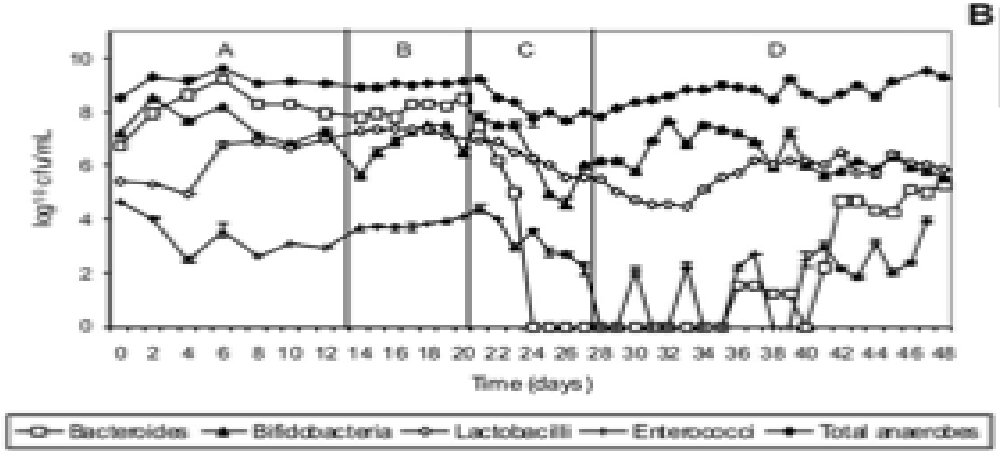
NOTE. MICs were determined at the R. M. Alden Research Laboratory (Santa Monica, CA).

[a] At least 10 strains were tested for each organism.

Stein CID 2006



ciprofloxacine



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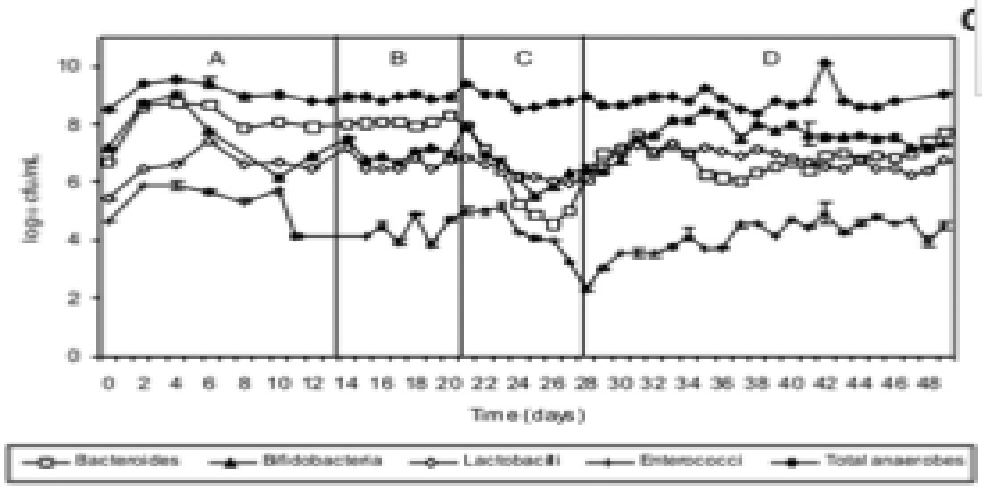

lévofloxacine

K Saxton
Human Gut Model

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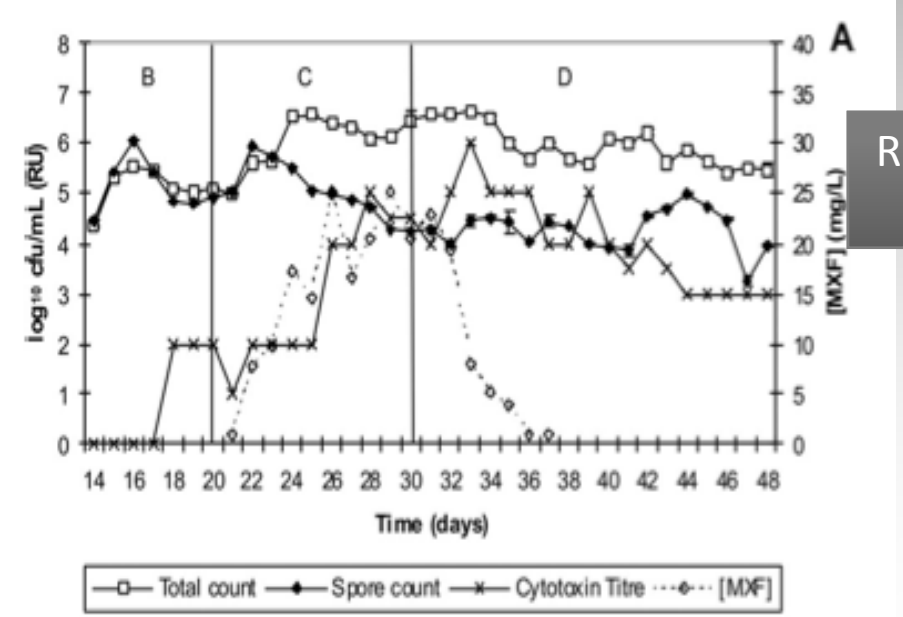
p. 412–420



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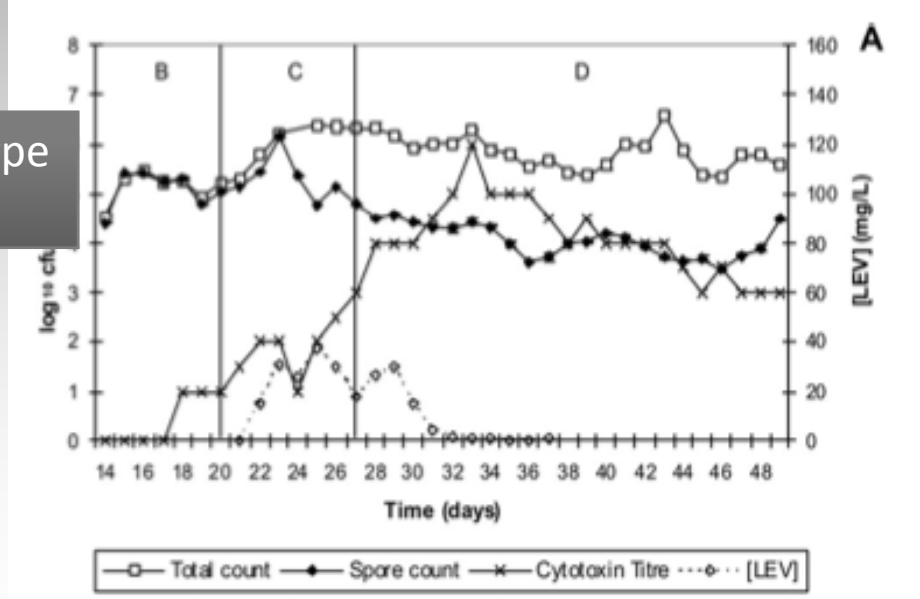

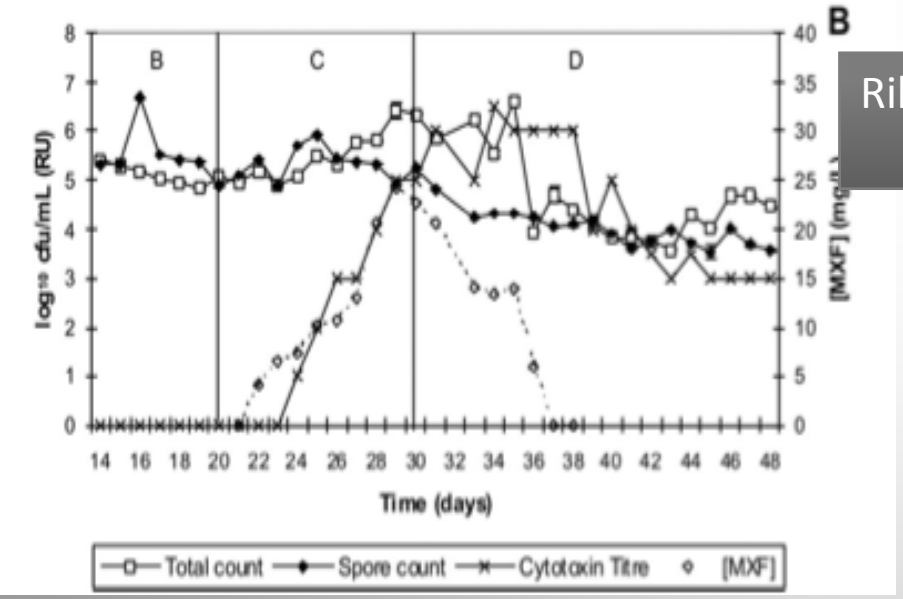

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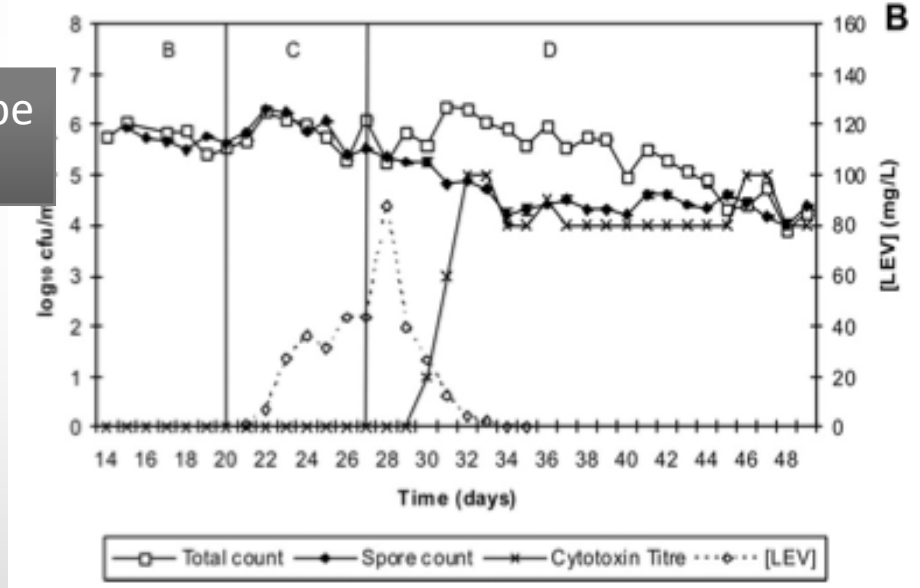


moxifloxacine

lévofloxacine

K Saxton AAC Feb. 2009 p. 412–420

Lai et al. [53]		
Ciprofloxacin	92 cases, 78 controls	2.29 (1.13–166)
McCusker et al. [14]		
Clindamycin	9 cases, 7 controls	Not significant
Levofloxacin, ciprofloxacin, and/or gatifloxacin[b]	22 cases, 15 controls	12.7 (2.6–61.6)
Muto et al. [12]		
Clindamycin	32 cases, 13 controls	4.8 (1.9–12.0)
Ceftriaxone	21 cases, 8 controls	5.4 (1.8–15.8)
Levofloxacin	120 cases, 83 controls	2.0 (1.2–3.3)
Any proton-pump inhibitor	78 cases, 54 controls	2.4 (1.3–4.4)
Any histamine H_2 blocker	159 cases, 141 controls	2.0 (1.1–3.5)
Pepin et al. [13][c]		
Fluoroquinolones		
Overall	1708	3.4 (2.6–4.5)
Ciprofloxacin	1153	3.74 (2.8–4.9)
Levofloxacin	368	2.52 (1.6–3.7)
Levofloxacin and ciprofloxacin	127	4.55 (2.9–7.1)
Gatifloxacin[d]	22	6.10 (2.2–16.7)
Moxifloxacin[d]	27	Not significant
Cephalosporins		
First generation	661	1.8 (1.3–2.5)
Second generation	1001	1.9 (1.4–2.5)
Third generation	581	1.6 (1.2–2.1)
Clindamycin	147	1.8 (1.1–3.0)
Any β-lactam/β-lactamase inhibitor	355	1.9 (1.4–2.6)
Loo et al. [11]		
Any cephalosporin	115 cases, 65 controls	3.8 (2.2–6.6)
Any fluoroquinolone	128 cases, 75 controls	3.9 (2.3–6.6)
Ciprofloxacin	No data	3.1 (1.8–5.4)
Gatifloxacin or moxifloxacin	No data	3.4 (1.5–7.7)
Levofloxacin[d]	No data	Not significant

Clostridium difficile épidémie actuelle et consommation fluoroquinolones

référence	Consommation fluoroquinolones		
	Avant épidémie	Pendant épidémie	
Kazakova AIM 2006	185.5 DDD/1000pts-j	200.9 DDD/1000pts-j	P<.001
Muto ICHE 2005	217 DDD/1000pts-j	275 DDD/1000pts-j	P<.001
Pépin CID 2004		25 % des pts hospitalisés ont reçu des fluoroquinolones	

Clostridium difficile facteurs de risque durée antibiothérapie

Table 3. Adjusted hazard ratios of developing *Clostridium difficile*–associated diarrhea (CDAD), according to the duration of use of each class of antibiotics.

	Adjusted hazards ratio (95% CI),[a] by duration of therapy		
Antibiotic class	1–3 days	4–6 days	⩾7 days
Fluoroquinolones	2.42 (1.62–3.62)	2.99 (2.06–4.35)	4.33 (3.21–5.84)
First-generation cephalosporins	1.07 (0.66–1.75)	2.61 (1.28–5.31)	3.14 (1.98–4.98)
Cefuroxime and oral second-generation cephalosporins	1.20 (0.73–1.98)	1.80 (1.17–2.76)	1.80 (1.20–2.69)
Cefoxitin	3.41 (2.07–5.60)	2.58 (0.36–18.63)	2.14 (0.29–15.54)
Third-generation cephalosporins	1.41 (0.94–2.10)	1.53 (0.93–2.53)	1.75 (1.08–2.83)
Macrolides	1.38 (0.80–2.40)	1.62 (0.88–2.97)	2.09 (1.12–3.90)
Clindamycin	1.15 (0.47–2.83)	2.35 (0.86–6.43)	2.38 (1.15–4.93)
Intravenous β-lactam/β-lactamase inhibitors	1.75 (0.96–3.18)	1.98 (1.13–3.50)	1.82 (1.15–2.88)

Épidémie Québec

Pépin CID 2005

Clostridium difficile facteurs de risque durée antibiothérapie

TABLE 1. Incidence of *C. difficile* and cytotoxin after injection of a single dose of different antibiotics

Antibiotic	No. of patients (%)			
	Total	Evaluable	Total colonized	Total toxin positive
Cefazolin	14	14	2 (14.3)	2 (14.3)
Cefoxitin	14	12	1 (8.3)	1 (8.3)
Cefotetan	21	20	4 (20.0)	4 (20.0)
Cefoperazone	17	16	7 (43.7)	4 (25.0)
Ceftriaxone	12	12	3 (25.0)	3 (25.0)
All cephalosporins	78	74	17 (23.0)	14 (18.9)
Mezlocillin	30	30	1 (3.3)	1 (3.3)
All antibiotics	108	104	18 (17.3)	15 (14.4)
Controls	15	15	0	0

G Privitera AAC 1991 35:208-10

Clostridium difficile facteurs de risque durée antibiothérapie

Ertapenem versus Cefotetan Prophylaxis in Elective Colorectal Surgery

Kamal M.F. Itani, M.D., Samuel E. Wilson, M.D., Samir S. Awad, M.D.,
Erin H. Jensen, M.S., Tyler S. Finn, B.A., and Murray A. Abramson, M.D., M.P.H.

N Engl J Med 2006;355:2640-51

the overall incidence of Clostridium difficile infection was 1.7% in the ertapenem group and 0.6% in the cefotetan group (P=0.22).

Épidémie CD 027 Quebec

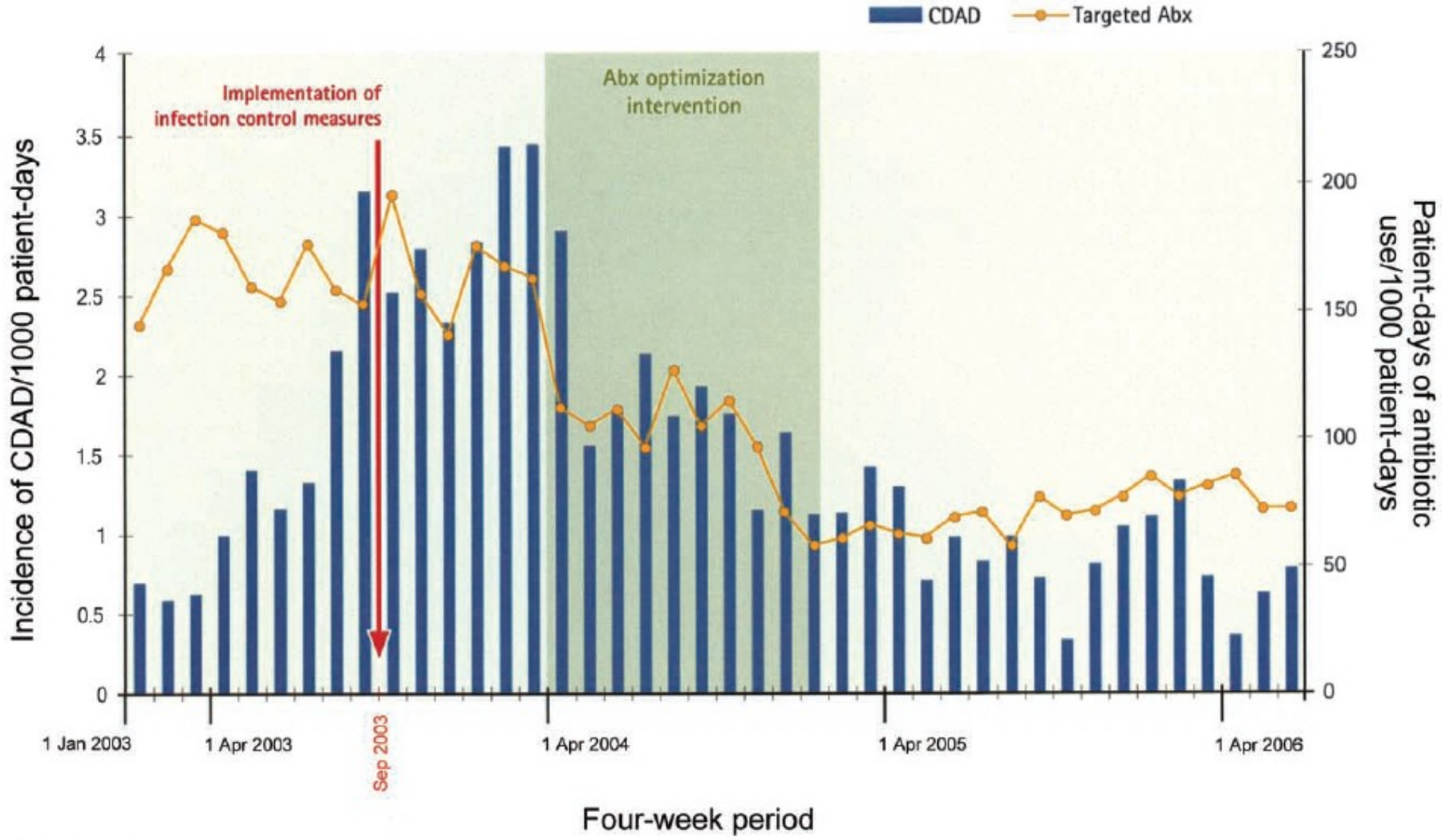


Figure 2. Targeted antibiotic (Abx) consumption and nosocomial *Clostridium difficile*–associated disease (CDAD) incidence per 1000 patient-days of hospitalization.

Épidémie CD 027 Quebec

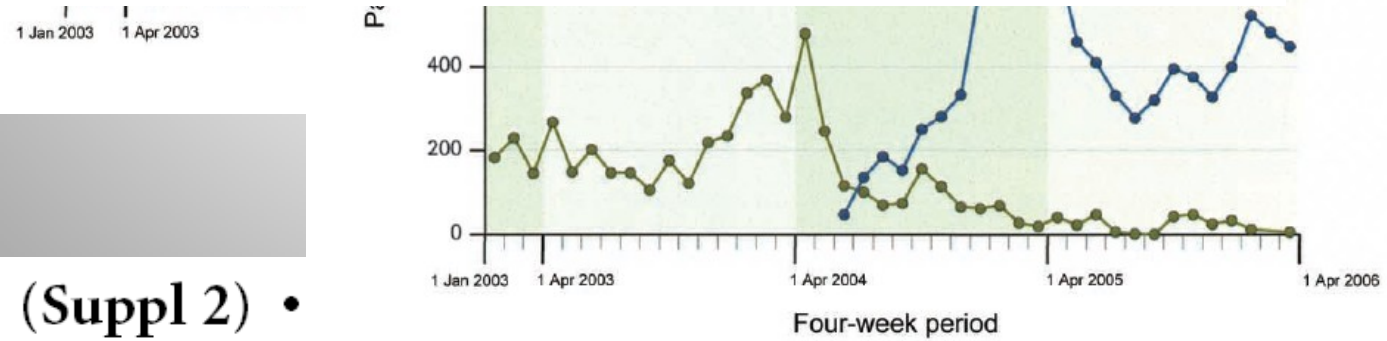
Table 1. Use of specific antibiotics, 2003–2006.

Antibiotic	2003–2004[a]	2004–2005	2005–2006	Change between 2003–2004 and 2005–2006, %
Cephalosporins				
First-generation	47.0	35.9	37.1	−21
Second-generation	32.8	8.0	2.4	−93
Third-generation	19.4	6.7	4.1	−79
Clindamycin	10.6	3.3	1.8	−87
Macrolides	8.6	3.3	1.9	−78
Ciprofloxacin	87.5	63.6	62.4	−29
Respiratory fluoroquinolones[b]	15.6	33.5	28.0	+79
Piperacillin/tazobactam	19.6	29.4	42.0	+114

NOTE. Data are patient-days of use per 1000 patient-days of hospitalization, unless otherwise indicated.

[a] Includes 3 additional fiscal periods (January–March 2003), for a total of 16 periods.

[b] Moxifloxacin was introduced in June 2004.



Épidémie CD 027 Quebec

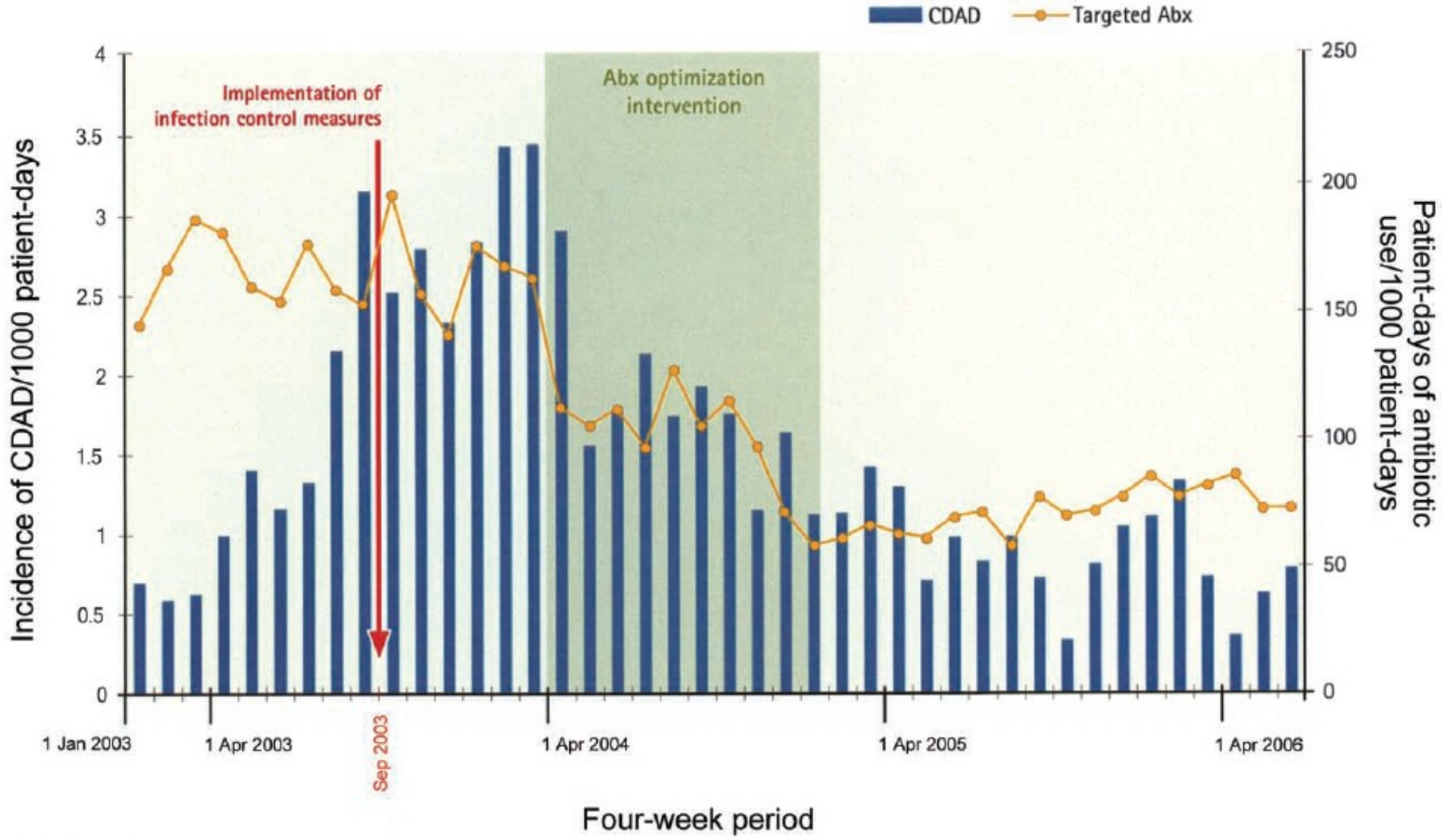


Figure 2. Targeted antibiotic (Abx) consumption and nosocomial *Clostridium difficile*–associated disease (CDAD) incidence per 1000 patient-days of hospitalization.

CD facteurs de risque : traitements antiacides

Table 2. Multivariable Analysis for Factors Associated With Nosocomial *Clostridium difficile* Infection[a]

Factor	Odds Ratio (95% Confidence Interval)	*P* Value
Acid suppression		
No acid suppression therapy	1 [Reference]	
H_2RA only	1.53 (1.12-2.10)	.008
Daily PPI	1.74 (1.39-2.18)	<.001
PPI more frequently than daily	2.36 (1.79-3.11)	<.001
Age, per year	1.01 (1.01-1.01)	<.001
No antibiotics therapy	1 [Reference]	
Low-risk antibiotics	1.82 (1.17-2.82)	.008
High-risk antibiotics	3.37 (2.64-4.31)	<.001
Weight loss	2.29 (1.57-3.36)	<.001
Chronic heart failure	1.31 (1.06-1.62)	.01
Renal failure	1.57 (1.29-1.91)	<.001
Fluid and electrolyte disorders	1.49 (1.25-1.77)	<.001
Coagulation disorder	1.76 (1.30-2.40)	<.001
Malignancy	1.57 (1.29-1.91)	<.001

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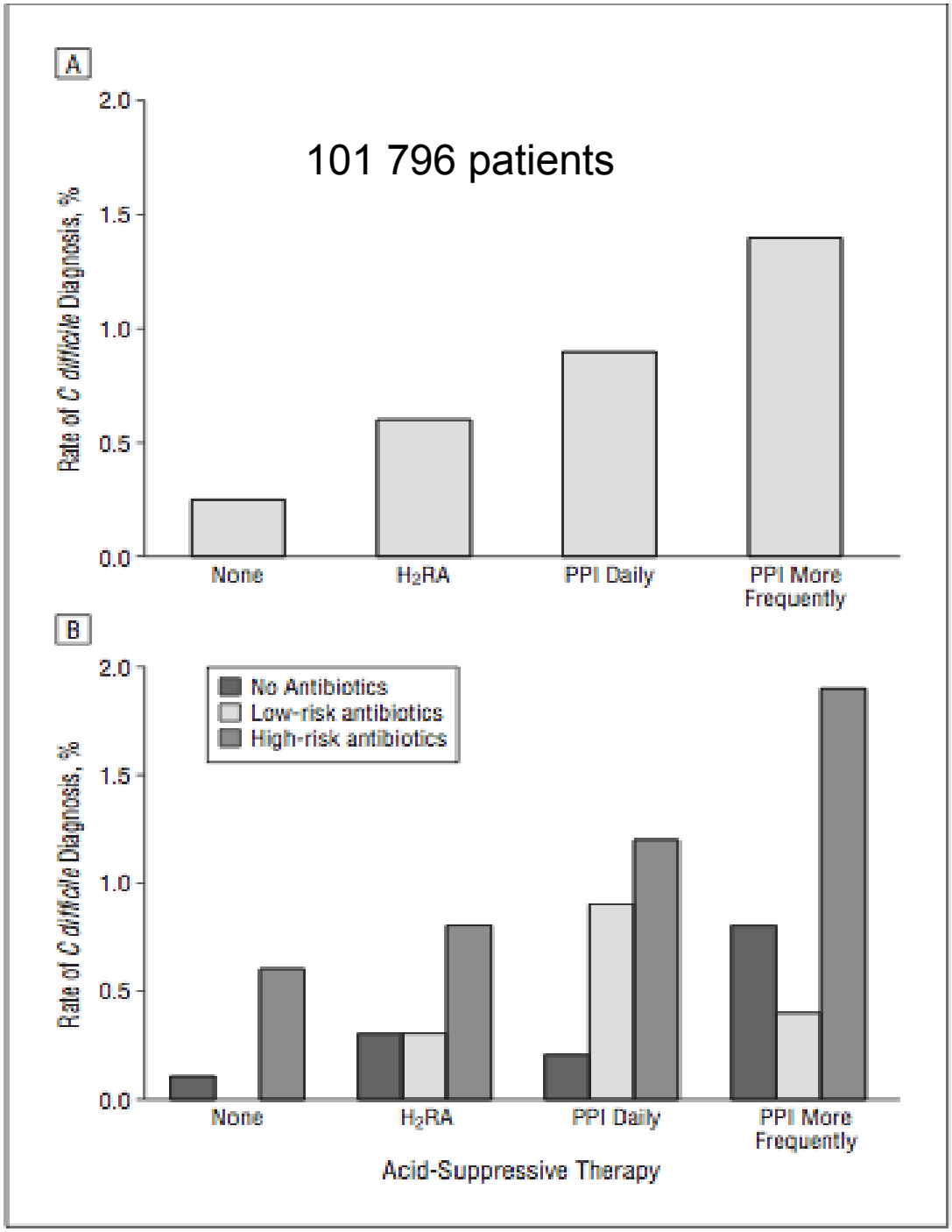

Howell

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Table 3. Characteristics of Case Patients and Control Patients.*

Characteristic	Case Patients (N=237)	Controls (N=237)	P Value
Age — yr			0.48
Median	75	75	
Interquartile range	66–82	66–82	
Male sex — no. (%)	115 (48.5)	126 (53.2)	0.3
Charlson index†	2.6±1.9	2.6±2.0	0.66
Ward			0.82
Medicine	133 (56.1)	142 (59.9)	
Surgery	78 (32.9)	70 (29.5)	
Geriatrics	17 (7.2)	15 (6.3)	
Oncology	9 (3.8)	10 (4.2)	
Community hospital — no. (%)	68 (28.7)	67 (28.3)	0.9
Days at risk for *C. difficile*–associated diarrhea			0.02
Median	13	16	
Interquartile range	6–25	8–29	
No. of antibiotics received	1.9±1.1	1.3±1.3	<0.001
Any exposure to antibiotics — no. (%)	188 (79.3)	141 (59.5)	<0.001
Cephalosporins	115 (48.5)	65 (27.4)	<0.001
Clindamycin	19 (8.0)	6 (2.5)	0.007
Fluoroquinolones	128 (54.0)	75 (31.6)	<0.001
Chemotherapy — no. (%)	17 (7.2)	13 (5.5)	0.45
Proton-pump inhibitors — no. (%)	112 (47.3)	111 (46.8)	0.92
Histamine H_2–blockers — no. (%)	47 (19.8)	47 (19.8)	1.0
Enteral feeding — no. (%)	44 (18.6)	28 (11.8)	0.04

V Loo

N Engl J Med 2005; 353:2442-9.

CD facteurs de risque : traitements anti acides

Table 2. Association between outpatient proton pump inhibitor (PPI) use and hospitalization for *Clostridium difficile*–associated disease (CDAD).

Timing of most recent PPI exposure[a]	No. (%) of patients with exposure		OR (95% CI)	
	Case patients (n = 1389)	Control subjects (n = 12,303)	Unadjusted	Adjusted
≤90 days	306 (22.0)	2254 (18.3)	1.2 (1.1–1.4)	0.9 (0.8–1.1)
91–180 days	30 (2.2)	331 (2.7)	0.8 (0.5–1.2)	0.7 (0.5–1.0)
181–365 days	37 (2.7)	317 (2.6)	1.1 (0.8–1.5)	0.9 (0.6–1.3)

[a] Includes lansoprazole, omeprazole, pantoprazole, and rabeprazole.

Lowe Clinical Infectious Diseases2006;43:1272–6

facteurs de risque d'infection à clostridium difficile

L'antibiothérapie est le facteur de risque principal

Les antibiotiques sont variablement promoteurs d'infection à CD

Le double mécanisme déséquilibre de flore – résistance est le paramètre prépondérant

- il convient le mieux pour expliquer les constats cliniques globaux dont les disparités entre les classes d'antibiotiques

D'autres mécanismes existent – promotion de facteurs favorisant la colonisation - promotion de germination – promotion de production de toxine

- ils interviennent probablement dans les disparités intra classe

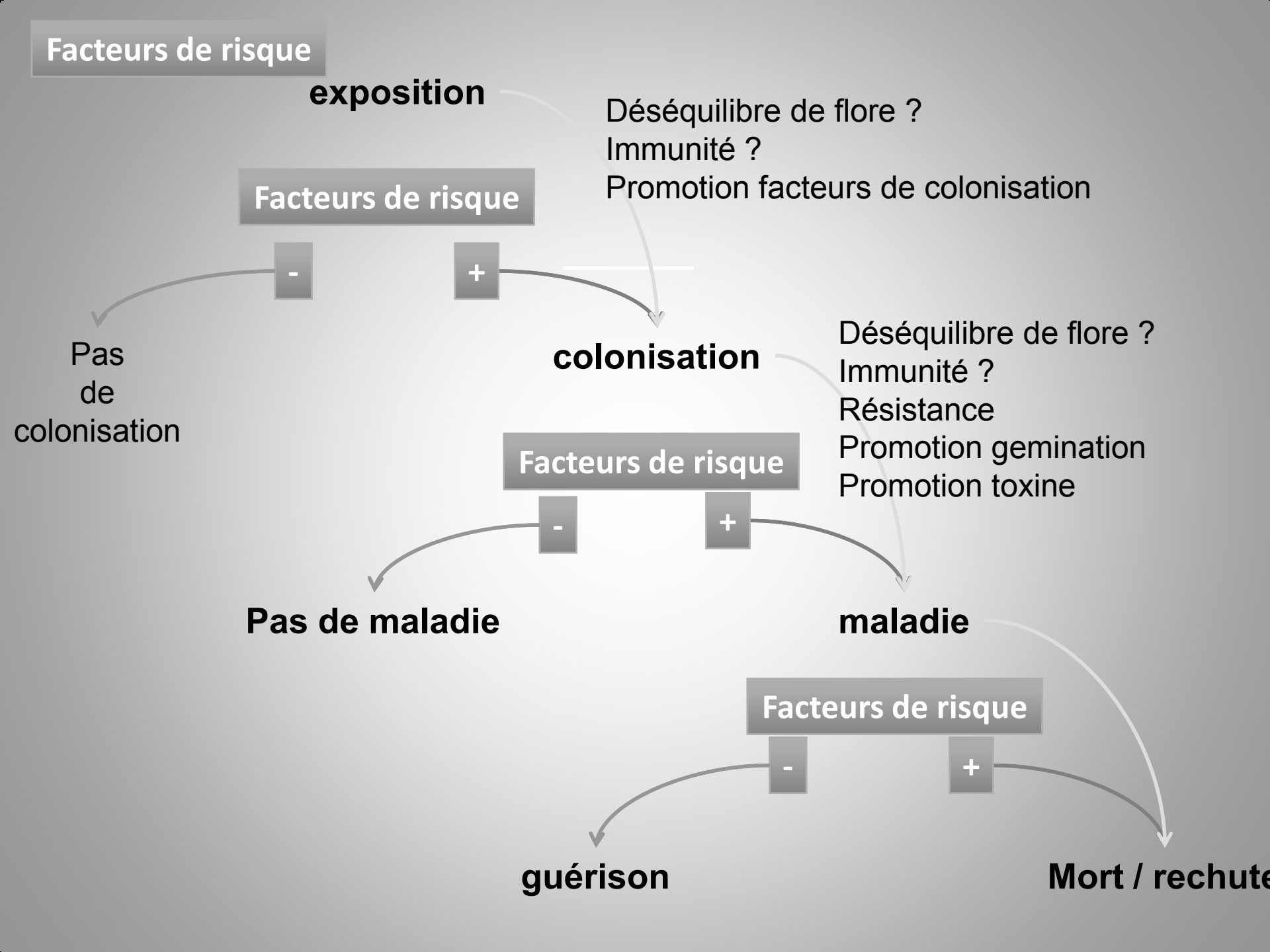
La leçon d'écologie de CD027

Désordre d'une flore

+ émergence d'une souche résistante

+ augmentation importante de l'utilisation d'une famille d'antibiotiques

+ transmission nosocomiale


Facteurs de risque
exposition
Déséquilibre de flore ?
Immunité ?
Promotion facteurs de colonisation
Facteurs de risque
-
+
Pas de colonisation
colonisation
Déséquilibre de flore ?
Immunité ?
Résistance
Promotion gemination
Promotion toxine
Facteurs de risque
-
+
Pas de maladie
maladie
Facteurs de risque
-
+
guérison
Mort / rechute

Diarrhées Associées à *C.difficile*

modèle très pur de conséquences écologiques de l'usage des antibiotiques