The Challenge of Implementing Molecular Diagnostics for Infection Control

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Disclosures

* Salary and benefits from Cepheid, a molecular diagnostics company

Rapid Diagnostics for Infection Control: Issues for Consideration

* How often does the laboratory ask you (Infection Preventionist) what tests you need?
* Would most Infection Preventionists know what molecular diagnostics or surveillance tests are available?
  * In many cases, yes!
* In fact, Infection Preventionists have had a major influence over test selection in several hospitals.
* Infection Prevention can be a key ally that helps the laboratory acquire the new technology they need.

Title: Discontinuation of Contact Precautions for Methicillin-Resistant *Staphylococcus aureus* (MRSA): A Randomized Controlled Trial Comparing Passive and Active Screening with Culture and Polymerase Chain Reaction (CID 2013)

Erica S. Shenoy, MD, PhD, JiYeon Kim, MD, MPH, Eric S. Rosenberg, MD, Jessica A. Cotter, MPH, Hang Lee, PhD, Rochelle P. Walensky, MD, MPH* and David C. Hooper, MD*

Goal: Get MRSA-negative patients out of costly isolation rooms

Table 3. Single First PCR Test Performance Compared to Three Sequential CA in Intervention Arm Population.

	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive Predictive Value % (95% CI)	Negative Predictive Value % (95% CI)
All subjects, series of 3 swabs completed (N=191)	93.9 (85.4 to 97.6)	92.0 (85.9 to 95.6)	86.1 (75.9 to 93.1)	96.6 (91.6 to 99.1)

NPV of 1 negative PCR test available in <2 hours = 3 negative cultures where results took 5 days

Clin Infect Dis. 2013 Jul;57(2):176-84

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Estimated Effect on Unnecessary Contact Precaution Days Avoided and Costs Saved Justified Bringing PCR into the Lab

Strategy	Passive cultures	Active surveillance cultures	PCR screening
Discontinuation rates of contact precautions	6.6%	26.2%	63.8%
Fewer contact precaution days	104	418	1841
Cost savings	$86,950	$349,472	$1,539,180

Clin Infect Dis. 2013 Jul;57(2):176-84

Novel Applications of Rapid Diagnostics: Air and Water

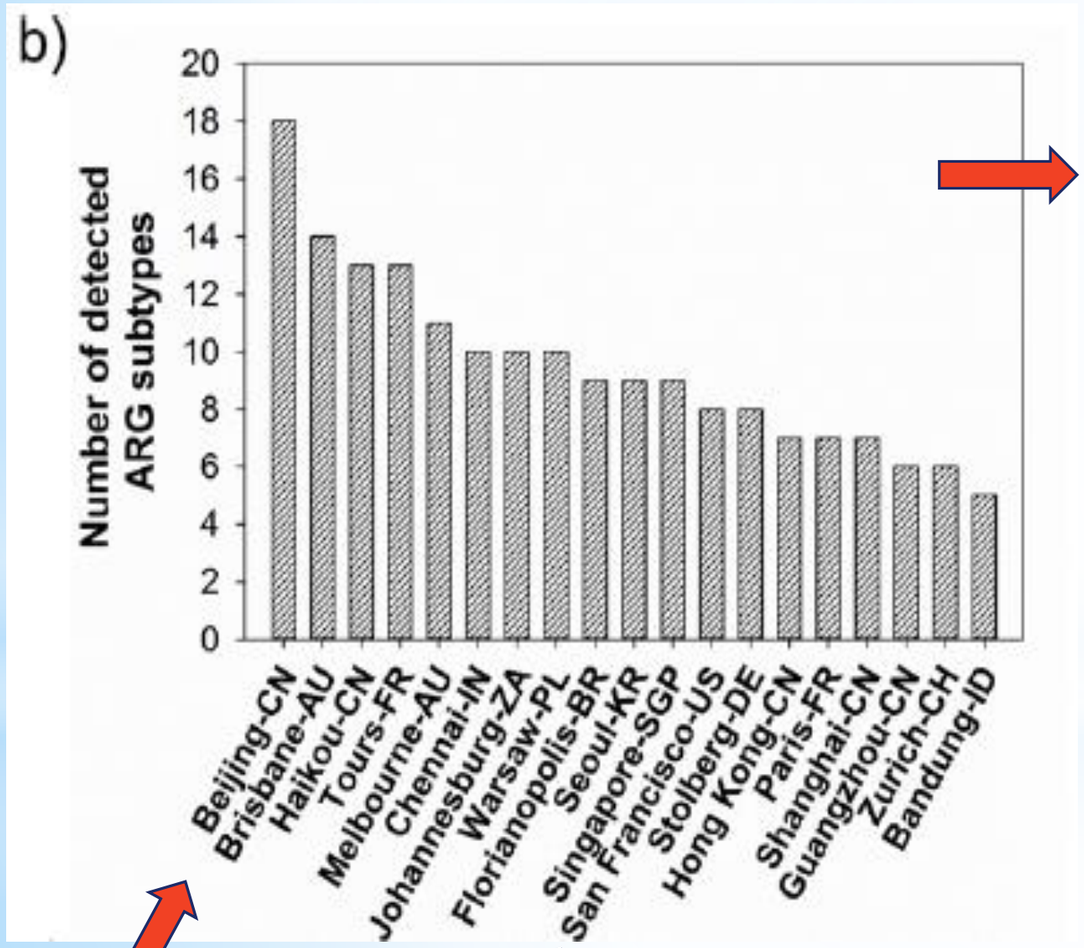
You may think of this…

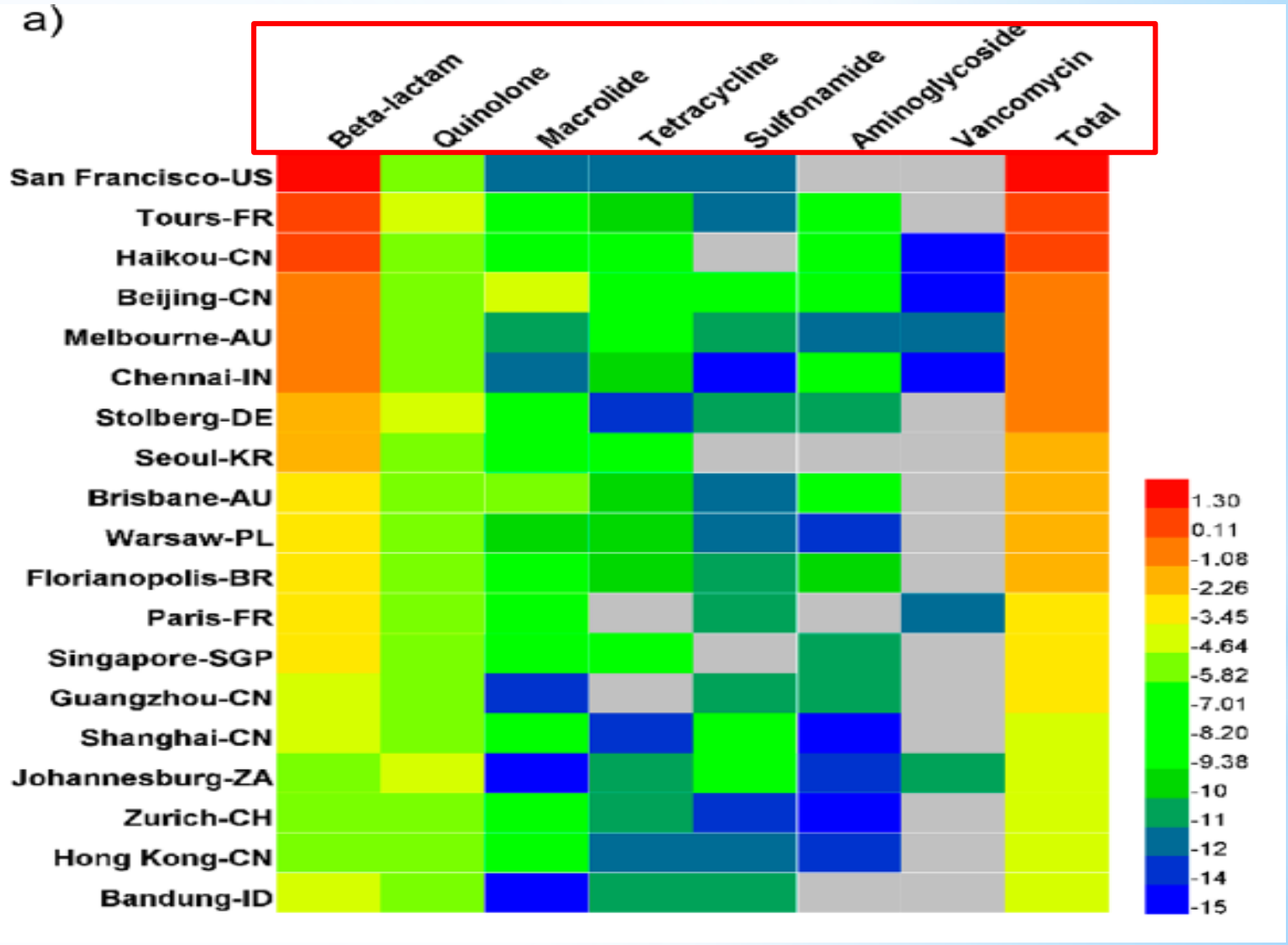
But for Infection control consider this…

Global Survey of Antibiotic Resistance Genes in Air

Jing Li,[†] Junji Cao,[‡] Yong-guan Zhu,[§] Qing-lin Chen,[§] Fangxia Shen,[∥] Yan Wu,[⊥] Siyu Xu,[#] Hanqing Fan,[▽] Guillaume Da,[○] Ru-jin Huang,[‡] Jing Wang,[◆,¶] Alma Lorelei de Jesus,[∞] Lidia Morawska,[∞] Chak K. Chan,[⊗] Jordan Peccia,[⊙] and Maosheng Yao*[,†]

Environ. Sci. Technol. *(on line 2018)*





Identification of 76 novel B1 metallo-β-lactamases through large-scale screening of genomic and metagenomic data

Fanny Berglund[1,2], Nachiket P. Marathe[2,3], Tobias Österlund[1,2], Johan Bengtsson-Palme[2,3], Stathis Kotsakis[2,3], Carl-Fredrik Flach[2,3], D G Joakim Larsson[2,3] and Erik Kristiansson[1,2*]

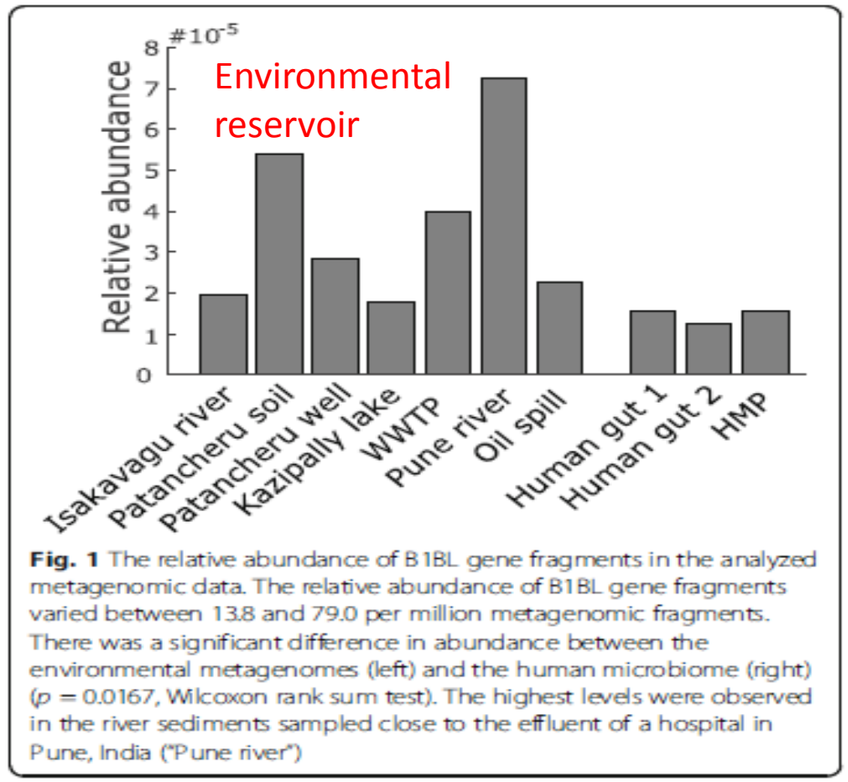


Fig. 1 The relative abundance of B1BL gene fragments in the analyzed metagenomic data. The relative abundance of B1BL gene fragments varied between 13.8 and 79.0 per million metagenomic fragments. There was a significant difference in abundance between the environmental metagenomes (left) and the human microbiome (right) ($p = 0.0167$, Wilcoxon rank sum test). The highest levels were observed in the river sediments sampled close to the effluent of a hospital in Pune, India ("Pune river")

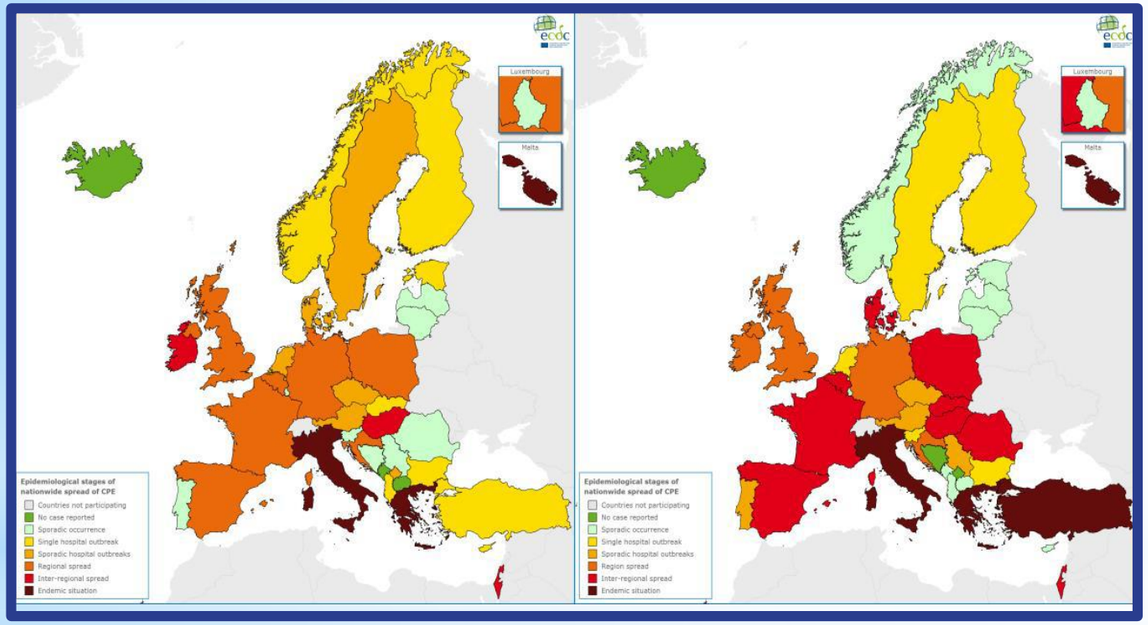
"This study (in India) more than doubles the number of known B1 metallo-β-lactamases. The findings have further elucidated the diversity and evolutionary history of this important class of antibiotic resistance genes and prepare us for some of the challenges that may be faced in clinics in the future."

Reservoirs of antimicrobial resistance genes are growing

Berglund *et al. Microbiome* (2017) 5:134
DOI 10.1186/s40168-017-0353-8

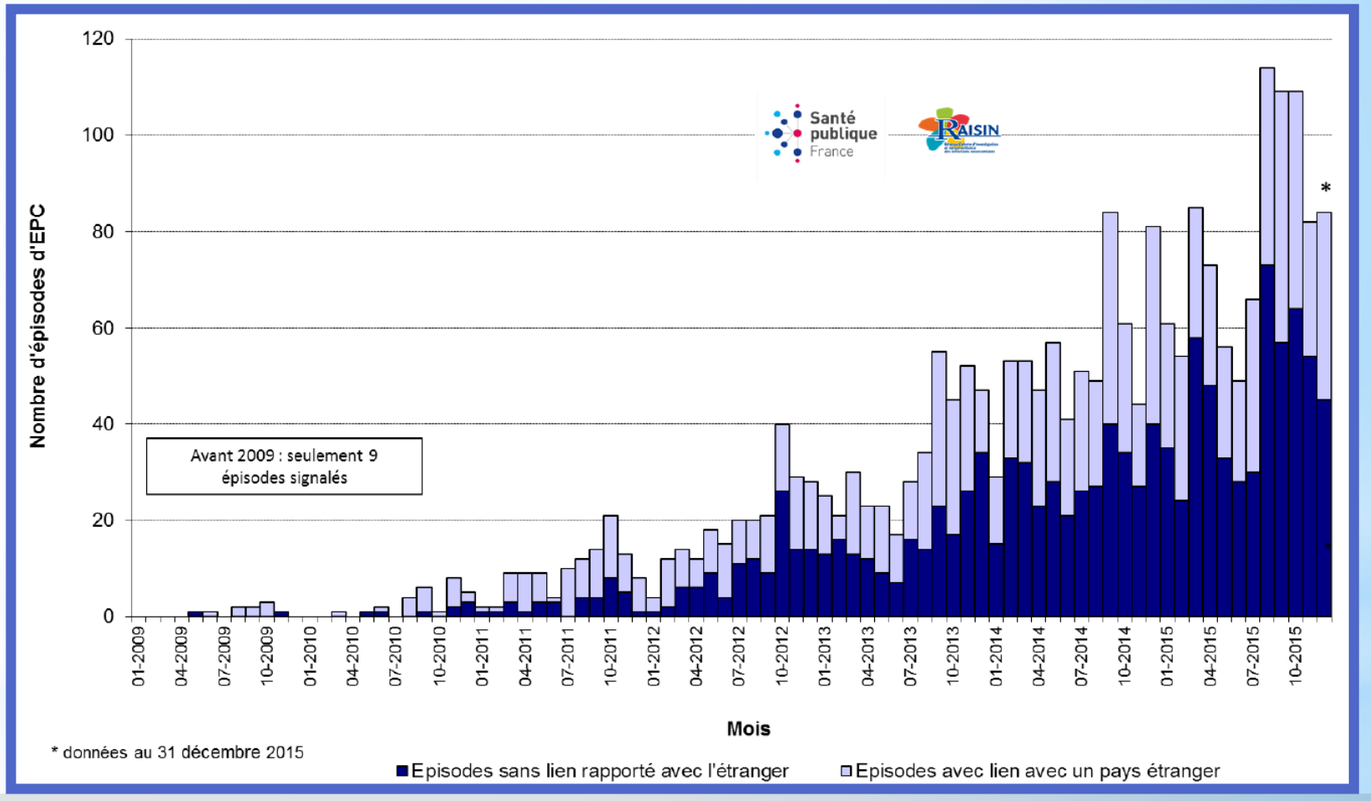
Carbapenemase-Producing Organisms are Spreading and the Problem is Getting Worse

Occurrence of CPE using an epidemiological scale of nationwide spread in 38 European countries



2013 2015

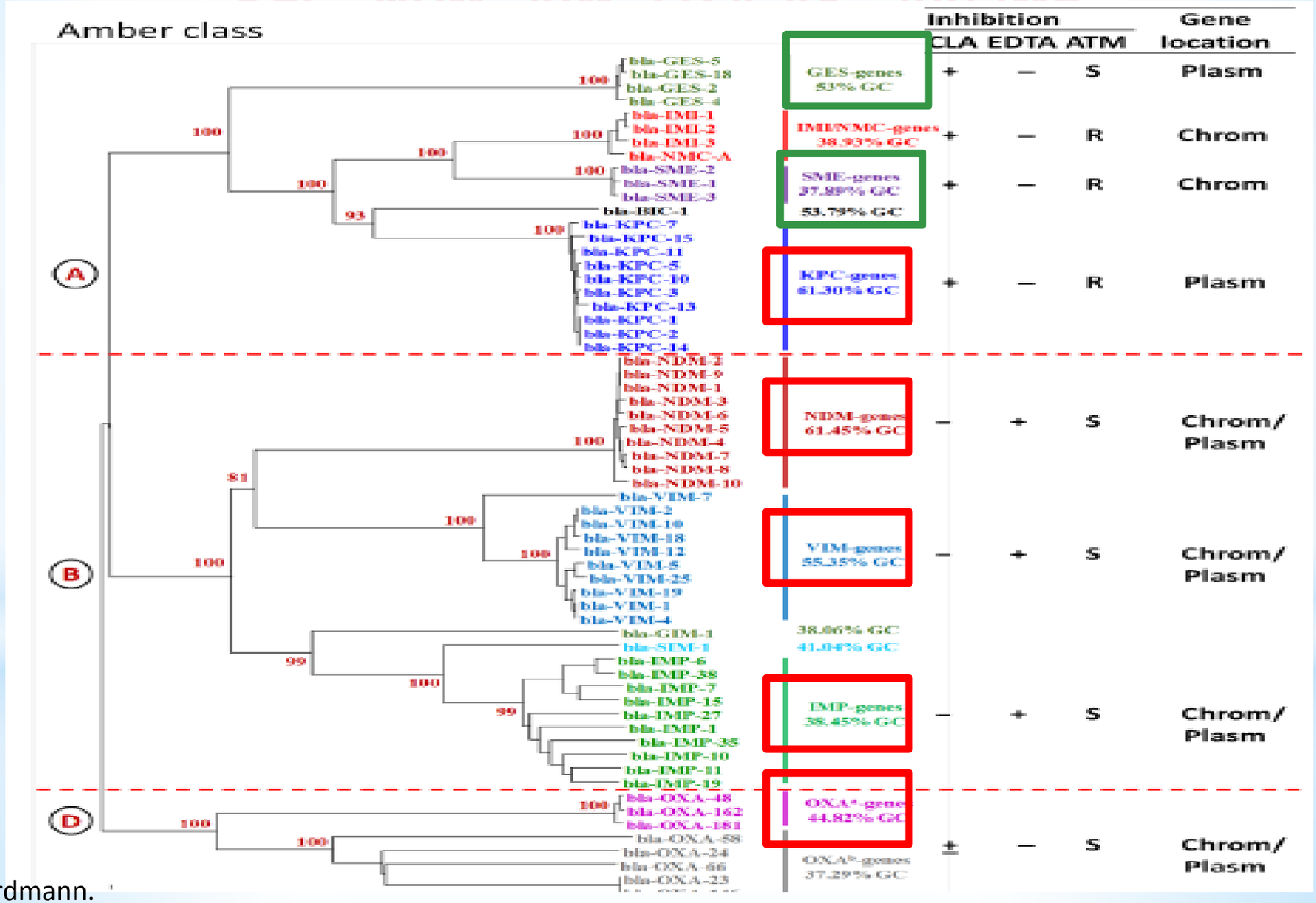
Numbers of CPE cases in France between January 2004 and December 2015, with and without a link to a foreign country (N=2026)



ECDC Evidence Brief Nov. 2015; Update on the spread of carbapenemase-producing *Enterobacteriaceae* in Europe

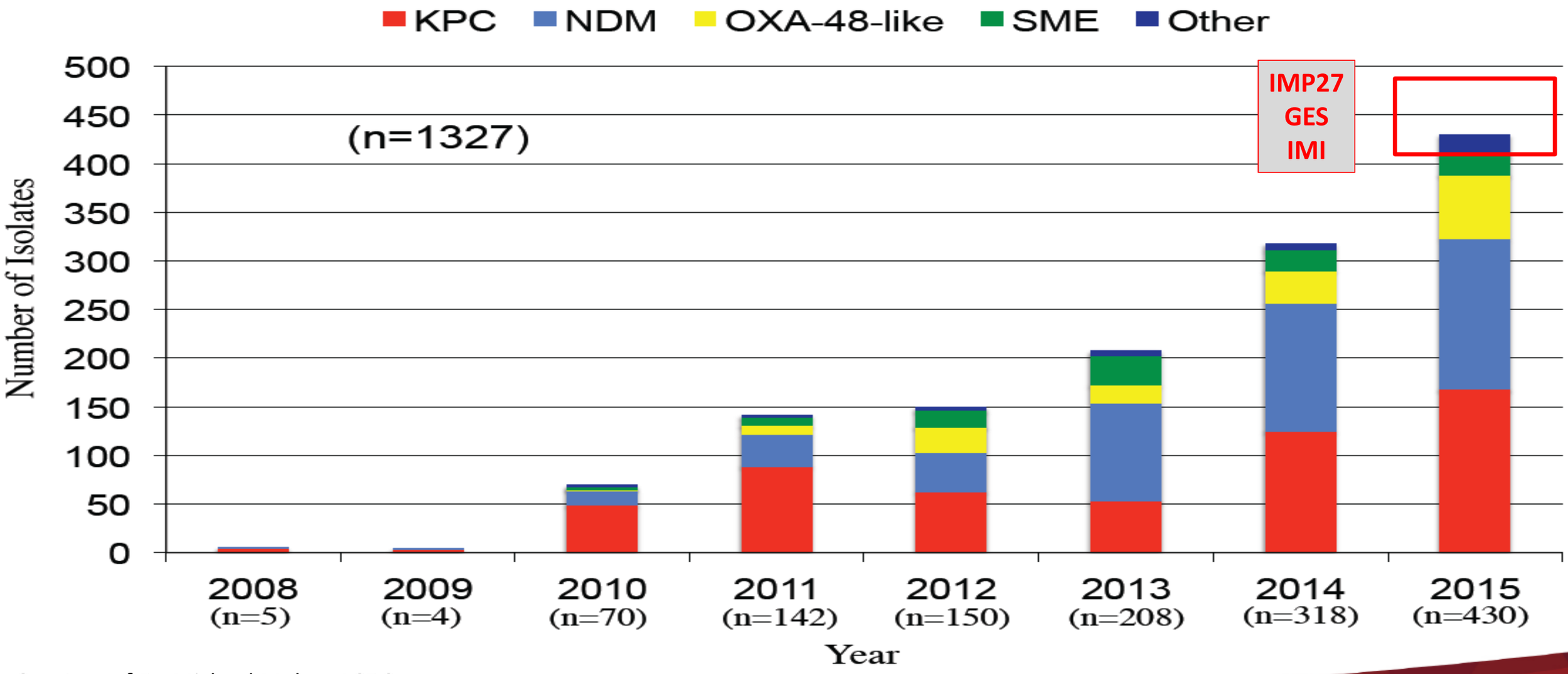
V. Pontiés et al. Épisodes impliquant des EPC en France – Bilan épidémiologique national au 31 décembre 2015 - Santé Publique

The “BIG 5” Carbapenemases
KPC, NDM, VIM, OXA-48, and IMP



Slide courtesy of P. Nordmann.

CPE in Canada: CPHLN Data



Courtesy of Dr. Michael Mulvey LCDC

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 64
August 4, 2015

Vital Signs: Estimated Effects of a Coordinated Approach for Action to Reduce Antibiotic-Resistant Infections in Health Care Facilities — United States

FIGURE 1. Comparison between the projected number of annual health care–associated infections from selected antibiotic-resistant bacteria* and *Clostridium difficile* with no intervention and the projected number with an aggressive national intervention — United States, 2014–2019†

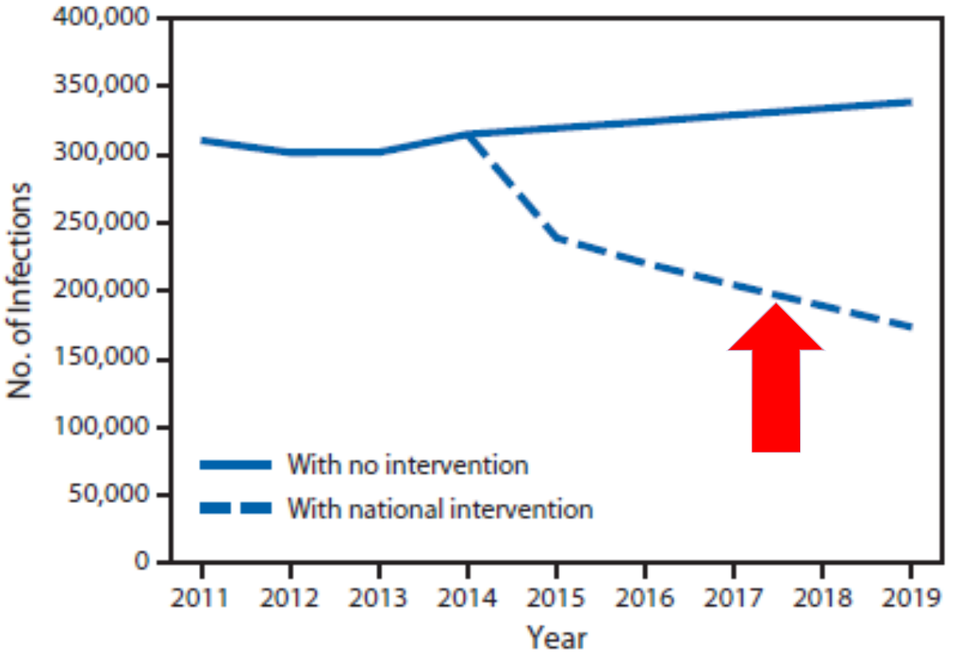
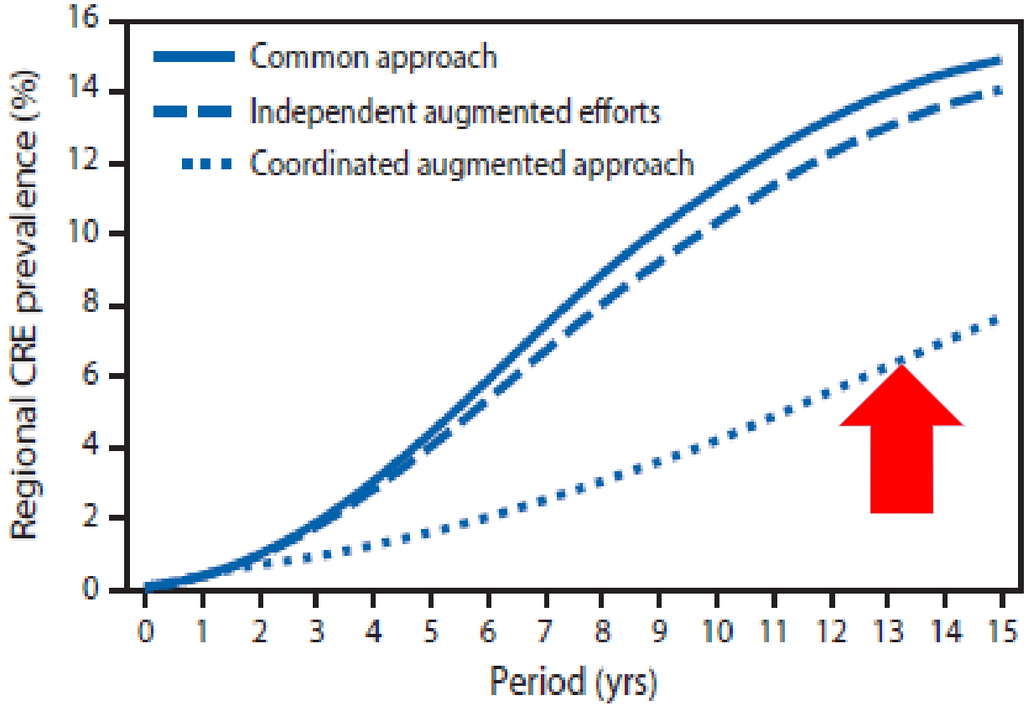
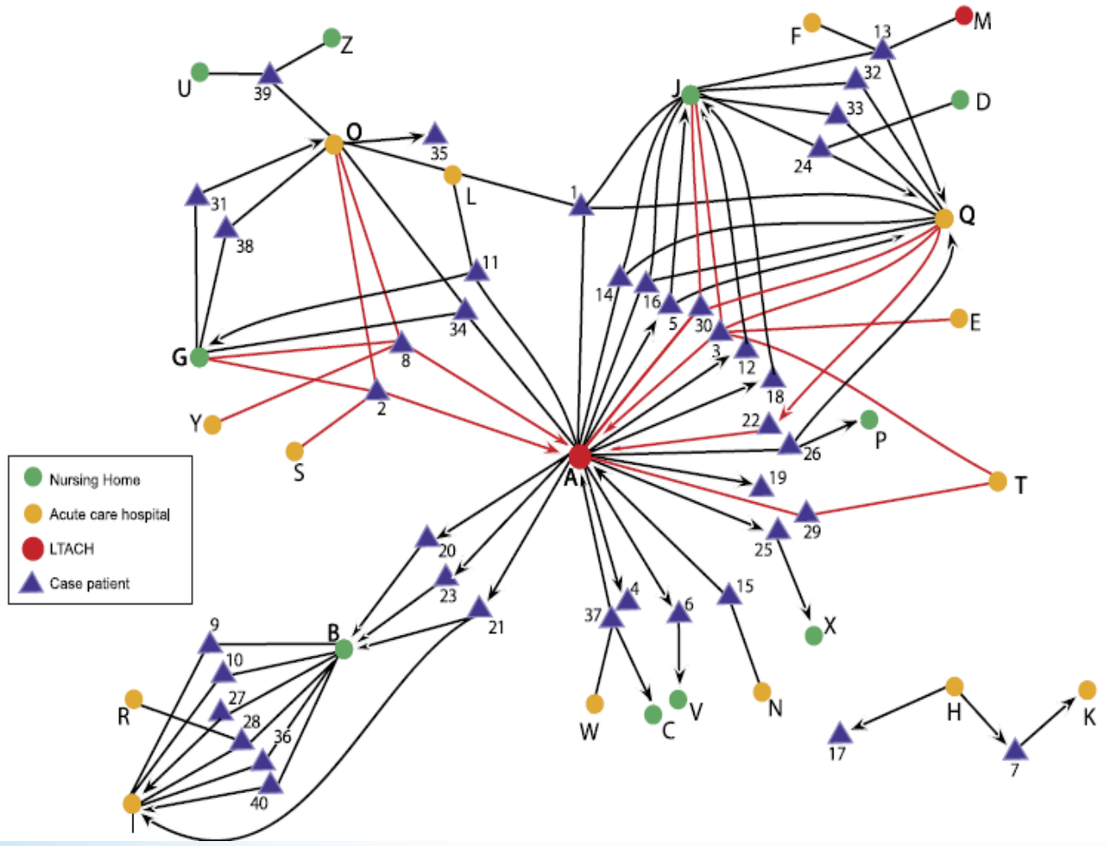


FIGURE 3. Projected countywide prevalence of carbapenem-resistant *Enterobacteriaceae* (CRE) over a 15-year period under three different intervention scenarios — 102-facility model, Orange County, California*



Emergence and Rapid Regional Spread of *Klebsiella pneumoniae* Carbapenemase–Producing *Enterobacteriaceae*

Sarah Y. Won,[1,2] L. Silvia Munoz-Price,[3] Karen Lolans,[4] Bala Hota,[4,5] Robert A. Weinstein,[4,5] and Mary K. Hayden[4] for the Centers for Disease Control and Prevention Epicenter Program



Chicago area hospital and long term care facilities

Conclusions.” We observed extensive transfer of KPC-positive patients throughout the exposure network of 14 acute care hospitals, 2 LTACHs, and 10 nursing homes. Although few cases were identified at most institutions, many facilities were affected. Successful control of KPC-producing Enterobacteriaceae will require a coordinated, regional effort among acute and long-term health care facilities and public health departments. “

Clinical Infectious Diseases 2011;53(6):532–540

The relative importance of large problems far away versus small problems closer to home: insights into limiting the spread of antimicrobial resistance in England

Hospitals receive only a small proportion (1.8%) of CPE-colonized patients from hospitals outside of their own region. Most spread of CPE was from patients moving from hospital to hospital within their region

Wide Variety Of CPE Types From 2008 – 2014

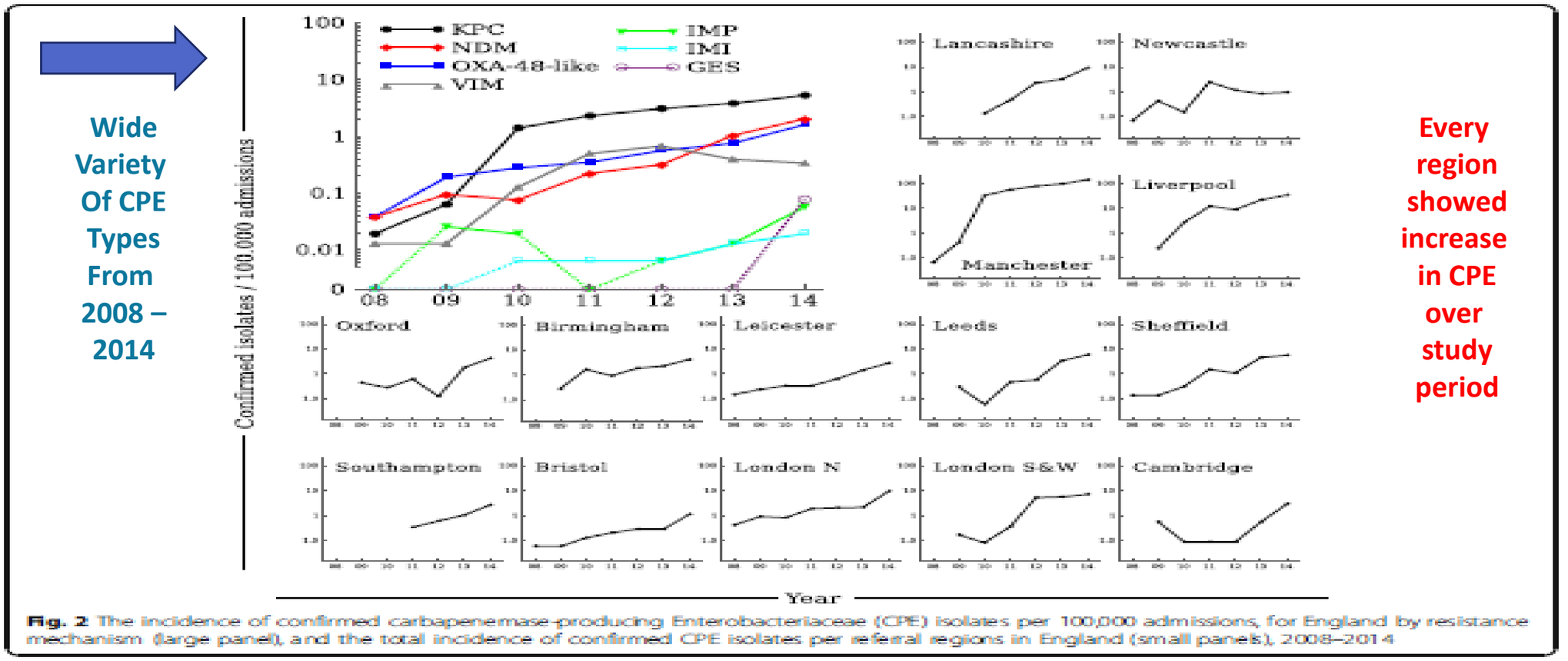


Fig. 2 The incidence of confirmed carbapenemase-producing Enterobacteriaceae (CPE) isolates per 100,000 admissions, for England by resistance mechanism (large panel), and the total incidence of confirmed CPE isolates per referral regions in England (small panels), 2008–2014

Every region showed increase in CPE over study period

Donker *et al. BMC Medicine* (2017) 15:86
DOI 10.1186/s12916-017-0844-2

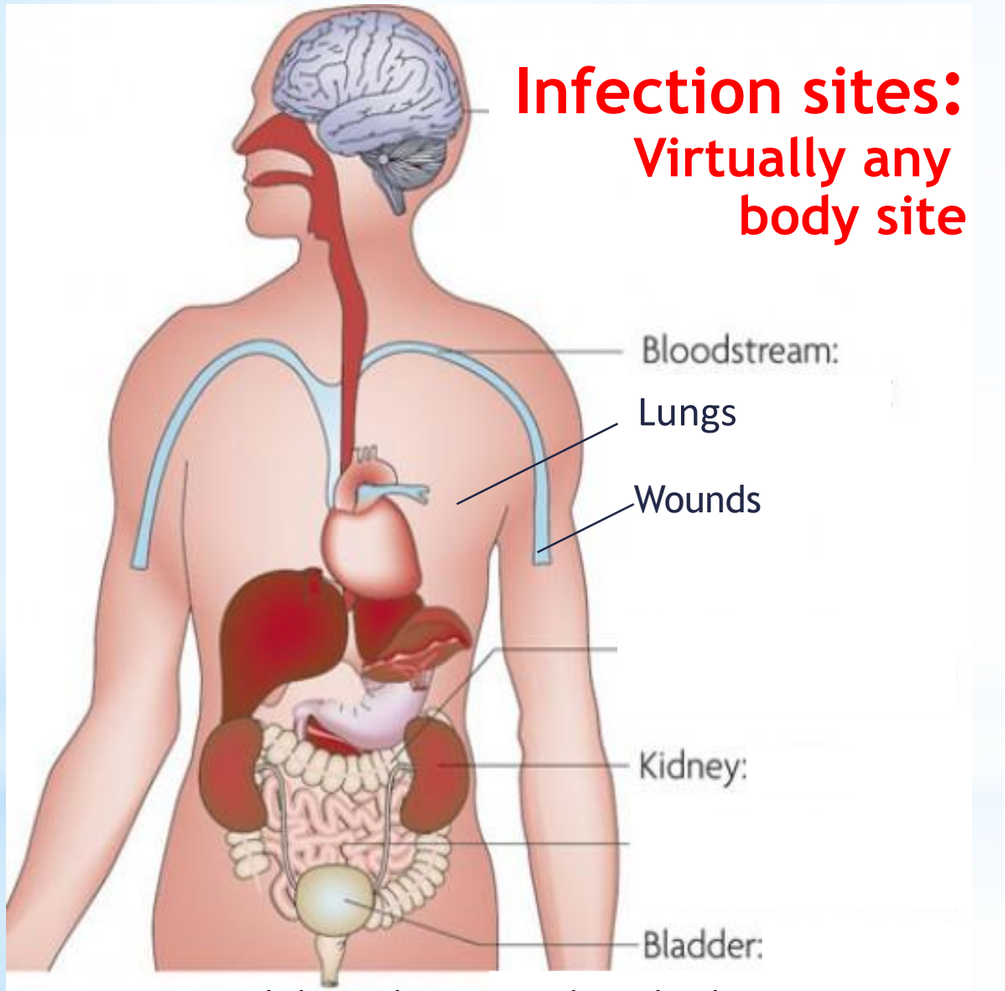
Carbapenem-Resistant *Enterobacteriaceae*: A Strategic Roadmap for Infection Control

N. Deborah Friedman, MBBS, FRACP, MD, MPH;[1] Yehuda Carmeli, MD, MPH;[2,3,4] Aaron Lea Walton, MD, FRACP, FRCPA;[1] Mitchell James Schwaber, MD, MPH[3,4]

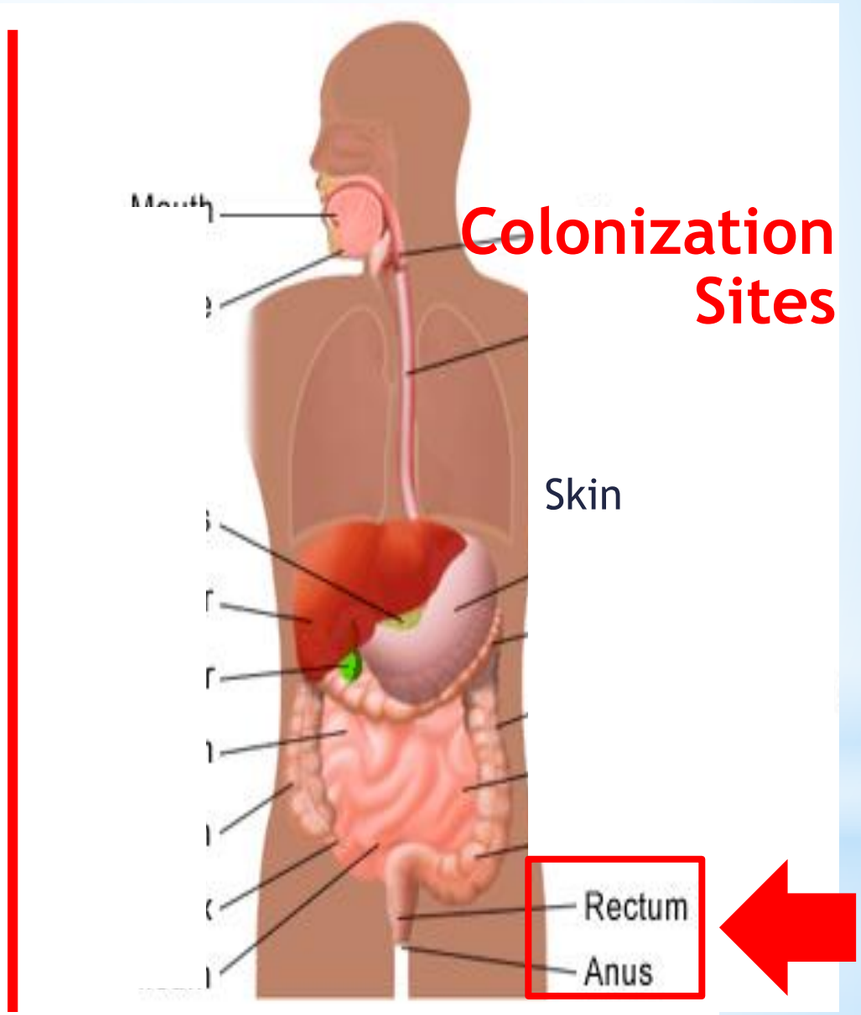
The incidence of carbapenem-resistant *Enterobacteriaceae* (CRE) has increased worldwide with great regional variability. Infections caused by these organisms are associated with crude mortality rates of up to 70%. The spread of CRE in healthcare settings is both an important medical problem and a major global public health threat. All countries are at risk of falling victim to the emergence of CRE; therefore, a preparedness plan is required to avoid the catastrophic natural course of this epidemic. Proactive and adequate preventive measures locally, regionally, and nationally are required to contain the spread of these bacteria. The keys to success in preventing the establishment of CRE endemicity in a region are early detection through targeted laboratory protocols and containment of spread through comprehensive infection control measures. This guideline provides a strategic roadmap for infection control measures based on the best available evidence and expert opinion, to enable preparation of a multifaceted preparedness plan to abort epidemics of CRE.

Infect Control Hosp Epidemiol 2017;38:580–594

Carbapenem-resistant Enterobacteriaceae: Causes infections but also colonization



Detected through routine clinical cultures



Only detected through surveillance testing

Intestinal Carriage of Carbapenemase-Producing Organisms: Current Status of Surveillance Methods

Clin Microbiol Rev 29:1-27.

Roberto Viau,[a] Karen M. Frank,[b] Michael R. Jacobs,[c] Brigid Wilson,[d] Keith Kaye,[e] Curtis J. Donskey,[f,g,h] Federico Perez,[f,h] Andrea Endimiani,[i] Robert A. Bonomo[a,f,h,j]

* **Challenges to Screening for Gastrointestinal Carriage**
* Time to detection:
  * PCR-based methods = **≥48 minutes**
  * Culture-based methods = **48-72 hours** (culture plus susceptibility testing, which may require a day to get a pure culture from chromogenic agar)
* Detecting organism with low carbapenem MICs
  * Not all carbapenem resistance genes are expressed at high MIC levels; this can be species related (low MIC in *Citrobacter* but high MIC in *K. pneumoniae*)
  * PCR-based methods have the advantage here
* Detecting low numbers of organisms
  * Organism may have high carbapenem MICs, but there may be low numbers of organisms present in a rectal swab. Without broth enrichment these may be missed
  * PCR has greater sensitivity than un-enriched cultures; similar to broth enriched culture
* PCR amplification methods: expensive and new mechanisms will escape detection

PCR Can Facilitate Infection Control Activities and Stewardship

	Day 1	Day 2	Day 3	Day 4
Rectal swabs for traditional culture method on chromagar	Perform culture on chromagar (18-20 hr)	Presumptive positive; subculture isolate (18-20 hr)	Perform susceptibility test for resistance (18-20 hr)	Susceptibility test results confirm CRE
Rectal Swabs for PCR testing	 **PCR results In 48 Min**			

Opportunity for early Interventions to prevent spread of CPE

Determine mechanism of carbapenem resistance from pure colonies for therapeutic strategies and CPE resistance gene typing

CE IVD In Vitro Diagnostic Medical Device

Not all tests available in all countries

Prospective study of the feasibility of point-of-care testing strategy for carbapenem-resistant organism detection

Rahul Pannala[1], Bruce Baldwin[1], Vijay Aluru[1], Thomas E. Grys[2], Jordan Holmes[1], Laurence J. Miller[1], M. Edwyn Harrison[1], Cuong C. Nguyen[1], Fred C. Tenover[3], David Persing[3], Douglas O. Faigel[1]

Endoscopy International Open 2018; 06: E58–E63

Conclusions The more comprehensive POC CRO testing of patients in the endoscopy suite is feasible and results are available in <1 hour. This strategy may enable rapid risk stratification of duodenoscope exposure to CRO and potentially improve operational efficiency and decrease costs.

► **Table 2** Feasibility parameters of the point-of-care (POC) assay (Xpert CARBA-R CRO assay, Cepheid, Sunnyvale, CA, United States).

Assay characteristics (n = 201)	
Specimen collection and handling time, median (IQR), min	3 (3 – 6)
Ease of use[1]	**97%**
▪ Very easy, n (%)	107 (54)
▪ Easy, n (%)	86 (43)
Run time, median (IQR), min	55 (53 – 55)

This is on-label testing done by nurses

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Not all tests available in all countries

Direct Detection of Carbapenem-Resistant Organisms from Environmental Samples Using the GeneXpert Molecular Diagnostic System

mSphere 3:e00113-18.

K. A. Perry,[a] J. B. Daniels,[a] S. C. Reddy,[a] A. J. Kallen,[a] A. L. Halpin,[a] J. K. Rasheed,[a] J. A. Noble-Wang[a]

		Culture	PCR
Formula sink drain	*Enterobacter asburiae, Klebsiella pneumoniae*	Negative	KPC+
Room A sink p-trap	*Citrobacter freundii, Pseudomonas aeruginosa*	Negative	Negative
Room A sink p-trap	*Achromobacter xylosoxidans, Citrobacter freundii, Stenotrophomonas maltophilia*	Negative	KPC+
Room A sink p-trap	*Citrobacter freundii, Pseudomonas aeruginosa*	Negative	Negative
Room A toilet swab	NA	None	KPC+
Room B toilet swab	NA	None	KPC+
Room C sink drain	VIM+ *Citrobacter amalonaticus*	VIM+	Negative

IMPORTANCE Use of the Carba-R assay for detection of carbapenem-resistant Gram-negative organisms (CROs) can provide data for implementation of a rapid infection control response to minimize the spread of CROs in the health care setting.

Off-label use: Not approved for environmental samples

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Clostidium difficile and your Microbiome –Think Life on the Beach

Normal Gut Flora

Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

L. Clifford McDonald,[1] Dale N. Gerding,[2] Stuart Johnson,[2,3] Johan S. Bakken,[4] Karen C. Carroll,[5] Susan E. Coffin,[6] Erik R. Dubberke,[7] Kevin W. Garey,[8] Carolyn V. Gould,[1] Ciaran Kelly,[9] Vivian Loo,[10] Julia Shaklee Sammons,[6] Thomas J. Sandora,[11] and Mark H. Wilcox[12]

Clinical Infectious Diseases, Volume 66, Issue 7, 19 March 2018, Pages e1–e48

If you control for colonization and laxative use, a NAAT alone or an algorithm can be used

European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic gu

Clinical Microbiology and Infection 22 (2016) 563–581

difficile infection

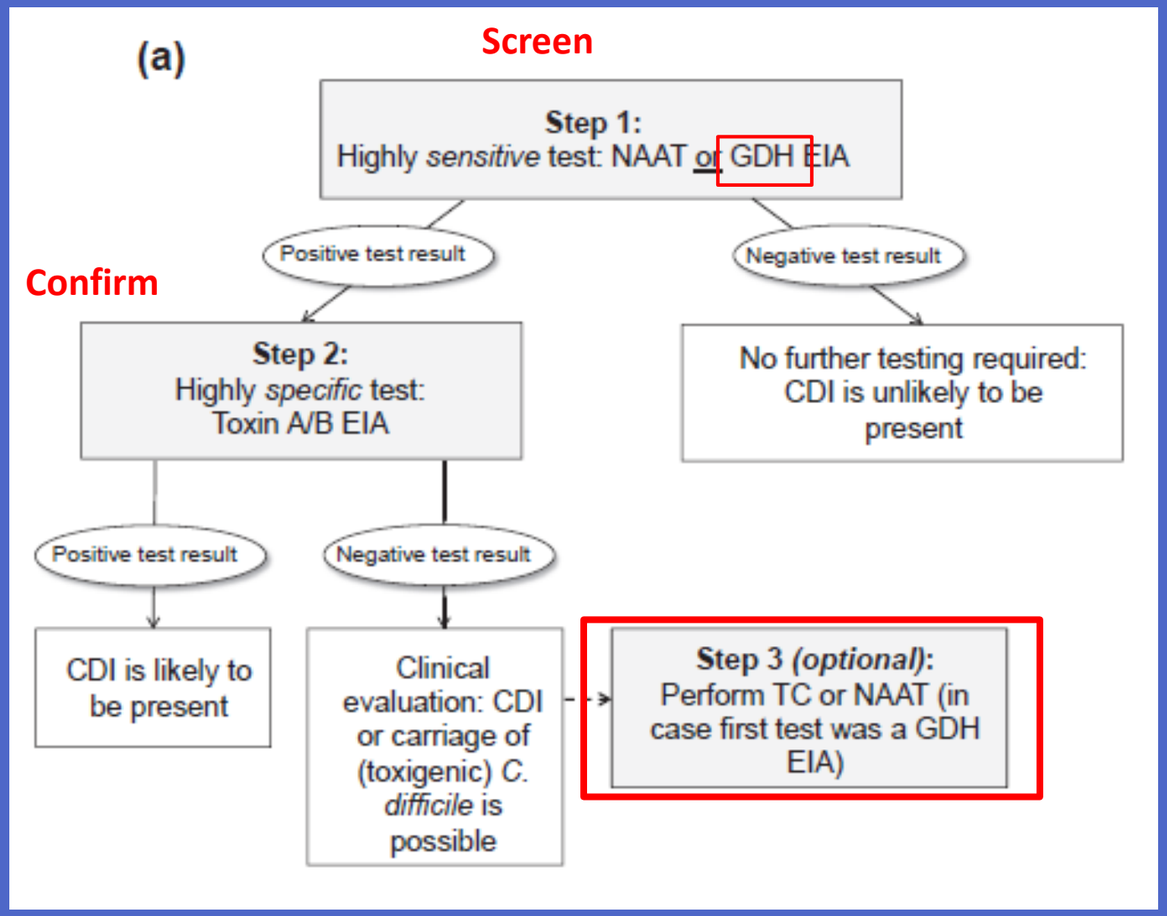
M.J.T. Crobach [1], T. Planche [4], C. Eckert [5], F. Barbut [5], E.M. Terveer [1], O.M. Dekkers [2, 3], M.H. Wilcox [6], E.J. Kuijper [1, *]

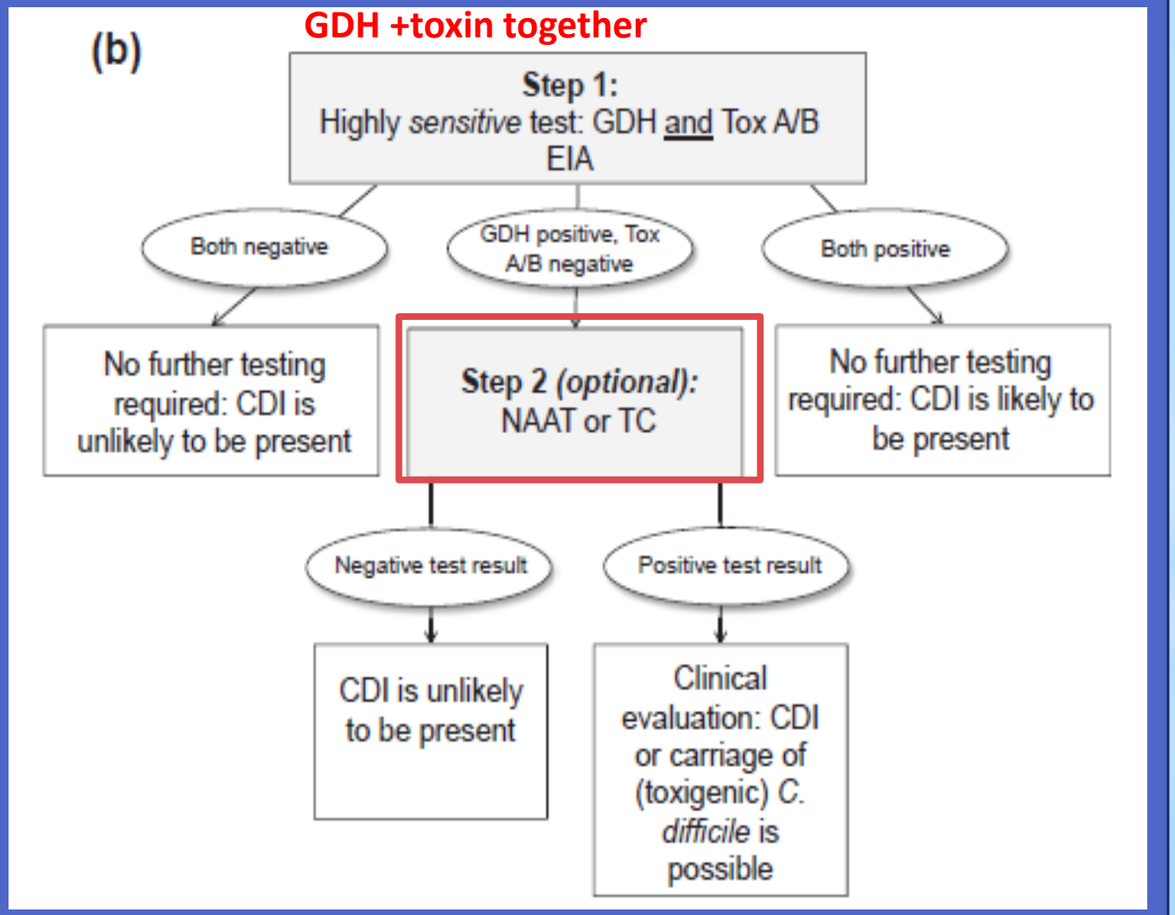
Toxin A/B testing required

European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection

M.J.T. Crobach [1], T. Planche [4], C. Eckert [5], F. Barbut [5], E.M. Terveer [1], O.M. Dekkers [2, 3], M.H. Wilcox [6], E.J. Kuijper [1, *]

Clinical Microbiology and Infection 22 (2016) 563–581





Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

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Clinical Infectious Diseases, Volume 66, Issue 7, 19 March 2018, Pages e1–e48

Formed stool tested with NAAT may indicate colonization

Clinicians and laboratory personnel agree at the institutional level to not submit stool specimens on patients receiving laxatives and to submit stool specimens only from patients with unexplained and new onset ≥ 3 unformed stools in 24 h for testing for CDI.

No

Stool toxin test* as part of a multiple step algorithm (i.e. GDH plus toxin; GDH plus toxin, arbitrated by NAAT; or NAAT plus toxin) rather than a nucleic acid amplification test (NAAT) alone.

1.) Meets clinical definition of CDI
2.) Patient not on laxatives
3.) Stool is not formed

Yes

NAAT alone OR stool toxin test* as part of a multiple step algorithm (i.e. GDH plus toxin; GDH plus toxin, arbitrated by NAAT; or NAAT plus toxin) rather than a toxin test alone.

*Approved stool EIA toxin tests vary widely in sensitivity. Laboratories should choose a toxin test with sensitivity in the upper range of sensitivity as reported in the literature [146–149, 156].

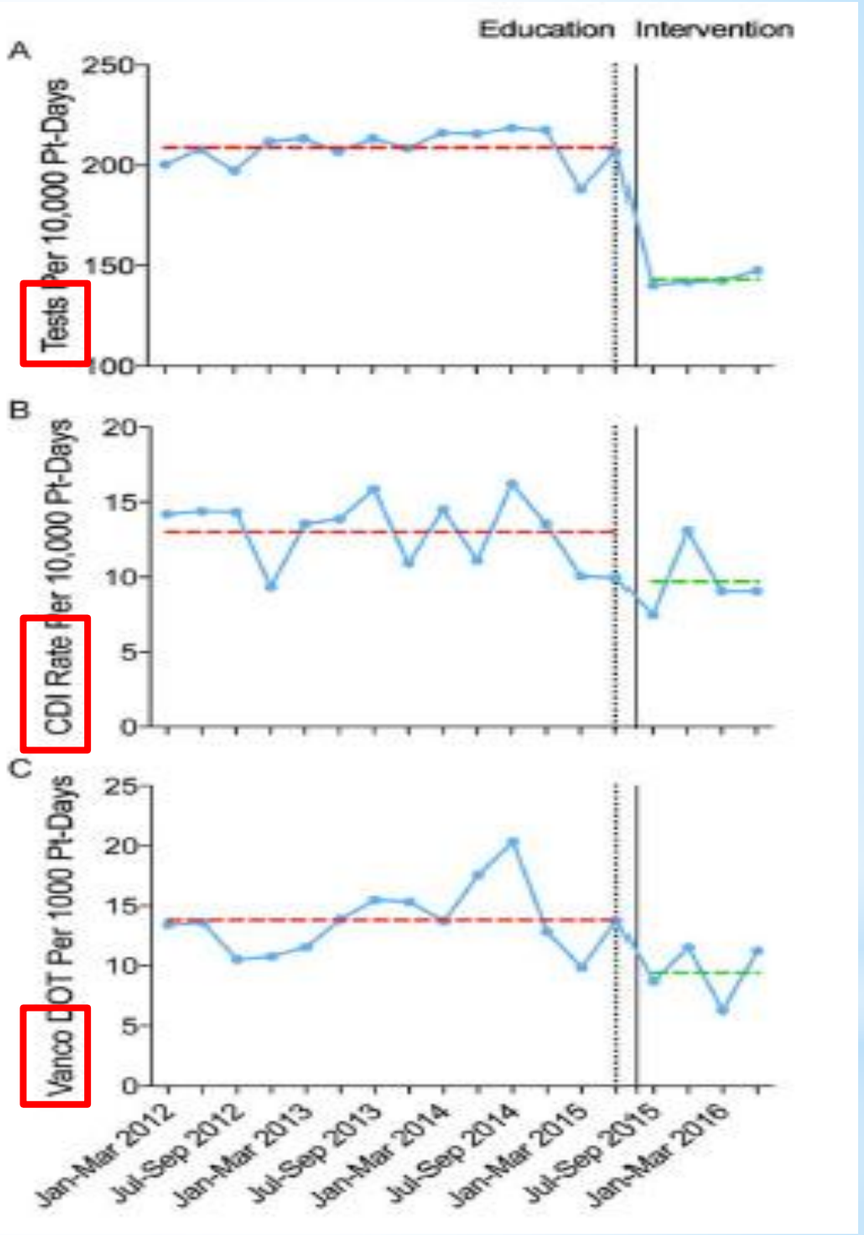
Real-Time Electronic Tracking of Diarrheal Episodes and Laxative Therapy Enables Verification of *Clostridium difficile* Clinical Testing Criteria and Reduction of *Clostridium difficile* Infection Rates

Cynthia Y. Truong,[a] Saurabh Gombar,[a] Richard Wilson,[b] Gopalakrishnan Sundararajan,[b] Natasa Tekic,[b] Marisa Holubar,[c,d,e] John Shepard,[d] Alexandra Madison,[d] Lucy Tompkins,[c,d] Neil Shah,[a] Stan Deresinski,[c,e] Lee F. Schroeder,[f] Niaz Banaei[a,c,g]

TABLE 2 Clinical outcomes in patients with canceled *C. difficile* orders

Clinical outcome	% of patients with indicated outcome (no. of patients with indicated outcome/total no. of patients), 95% CI[a]: Canceled orders (n = 375)	Accepted orders, *C. difficile* negative (n = 869)	P value
Diarrhea in 7 days	63.2 (237/375), 58.3–68.1	73.7 (640/869), 70.7–76.6	<0.001
WBC rise to >15,000 cells/ml in 7 days	12.5 (27/216), 8.1–16.9	13.1 (73/557), 10.3–15.9	0.91
ICU admission in 7 days	13.1 (49/375), 9.7–16.5	10.5 (91/869), 8.4–12.5	0.20
30-day all-cause mortality	10.3 (34/329), 7.0–13.6	8.3 (65/783), 6.4–10.2	0.30

[a]Canceled-order data represent canceled orders for patients without diarrhea or with laxative intake. Accepted-order data represent accepted orders for patients with diarrhea and no laxative intake.



Checking to make sure patient has diarrhea and did not get a laxative in the prior 48 hours reduces the number of tests run dramatically, lowers the CDI rate, and decreases vancomycin use

CE IVD In Vitro Diagnostic Medical Device

Not all tests available in all countries

Key Issues About Testing Formed Stool

* None of the *C. difficile* tests, including PCR, GDH, and toxin assays, can reliably differentiate colonization from infection if formed stools are tested.
* However, anyone with toxigenic *C. difficile*, including asymptomatic carriers, needs to be in contact precautions because they can spread disease.

C. difficile Summary

* NAAT as a stand alone test *is acceptable* in the new IDSA-SHEA guidelines as long as the hospital has policies in place to insure that only patients with clinical CDI are tested, they are not on laxatives, and formed stools are not tested in the laboratory.
* ESCMID guideline stresses the importance of algorithm testing to take advantage of the sensitivity of NAAT or GDH, coupled with the specificity of toxin testing
* Algorithms that start with GDH may benefit from NAAT testing for GDH-positive/toxin-negative specimens
* Data suggest that placing colonized patients in contact precautions can help control spread of *C. difficile* in a hospital.
* We are still learning about CDI. In terms of testing, isolating, and treating – one size does not fit all.

Rapid Molecular Detection of Tuberculosis and Rifampin Resistance

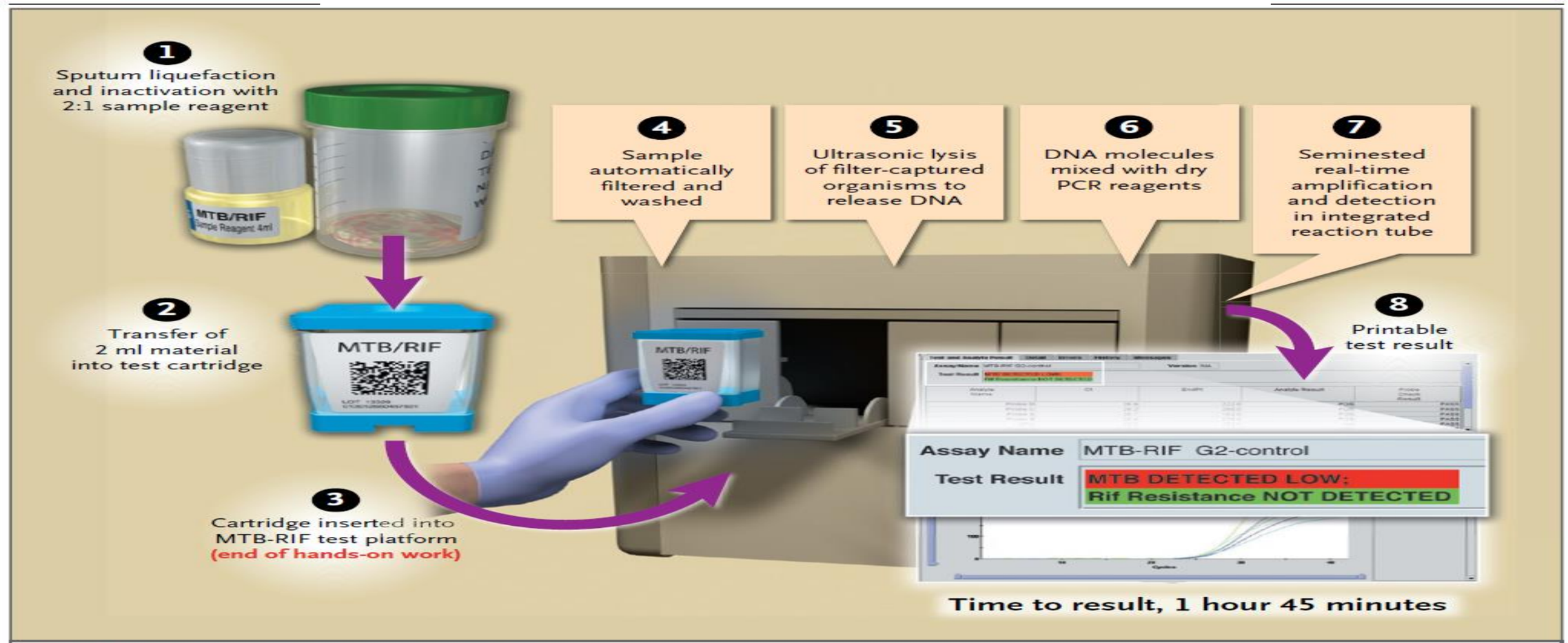


Figure 2. Assay Procedure for the MTB/RIF Test.

TB and rifampin resistance results in 110 minutes direct from specimen

From:Boehme, *et.al.* NEJM 363:1005. Sept. 9, 2010

CE IVD In Vitro Diagnostic Medical Device

Not all tests available in all countries

Impact of GeneXpert MTB/RIF on Patients and Tuberculosis Programs in a Low-Burden Setting

A Hypothetical Trial

J. Lucian Davis[1,2], L. Masae Kawamura[3], Lelia H. Chaisson[1], Jennifer Grinsdale[3], Jihane Benhammou[4], Christine Ho[5], Anna Babst[6], Houmpheng Banouvong[3], John Z. Metcalfe[1,2], Mark Pandori[6], Philip C. Hopewell[1,2], and Adithya Cattamanchi[1,2]

Doctor judgment vs PCR	TB (n=13)	Not TB (n=143)
Received empiric TB Rx		**47→3 Over-treatments** **Over-Rx Days: 2280→136** **PCR+ 1** **PCR- 45**
No Empiric TB Rx		**96→140 Early rule-outs** Added Specificity = +31%

Rapid Molecular Testing for TB to Guide Respiratory Isolation in the U.S.: A Cost-Benefit Analysis

Alexander J. Millman[3,5], David W. Dowdy[6], Cecily R. Miller[4], Robert Brownell[3], John Z. Metcalfe[1,2,3], Adithya Cattamanchi[1,2,3], J. Lucian Davis[1,2,3]*

PLOS ONE | www.plosone.org 1 November 2013 | Volume 8 | Issue 11 | e79669

Results: Among a hypothetical cohort of 234 individuals undergoing evaluation for presumed active TB annually, 6.4% had culture-positive TB. Compared to smear microscopy, Xpert reduced isolation bed utilization from an average of 2.7 to 1.4 days per patient, leading to a 48% reduction in total annual isolation bed usage from 632 to 328 bed-days. Xpert saved an average of $2,278 (95% uncertainty range $1582–4570) per admission, or $533,520 per year, compared with smear microscopy.

Conclusions: Molecular testing for TB could provide substantial savings to hospitals in high-income countries by reducing respiratory isolation usage and overall length of stay.

CE IVD In Vitro Diagnostic Medical Device

Not all tests available in all countries

JAMA Internal Medicine | Original Investigation

Association of Rapid Molecular Testing With Duration of Respiratory Isolation for Patients With Possible Tuberculosis in a US Hospital

JAMA Intern Med. 2018;178(10):1380-1388. d

Table 2. Length of Hospital Stay and Time Intervals in the Diagnostic Evaluation Process for Patients With Negative Results on Rapid Testing for Pulmonary Tuberculosis

Time Period	Median (IQR) Preimplementation (n = 223)	Postimplementation (n = 250)	*P* Value
Hospital admission to hospital discharge, days[a]	6.0 (3.8-10.9)	4.9 (2.9-8.9)	.003
Hospital admission to sputum collection, hours	19.1 (10.3-40.3)	18.0 (9.2-41.8)	.62
Sputum collection to final negative result reporting, hours	39.1 (35.6-42.9)	22.4 (13.7-30.6)	<.001
Sputum collection to first result reporting, hours	18.4 (15.5-23.6)	4.6 (3.4-6.9)	<.001
Sputum collection to sputum receipt in laboratory, hours	1.5 (0.5-2.5)	1.1 (0.5-2.0)	.02
Sputum receipt in laboratory to first result reporting, hours	16.0 (13.6-22.3)	2.9 (2.5-4.5)	<.001
Final negative result reporting to hospital discharge, hours[a]	66.5 (26.6-160.3)	49.6 (21.5-139.8)	.08
Isolation admission to isolation discharge, days[b]	2.9 (2.0-3.7)	2.5 (1.7-3.4)	.001

CE IVD In Vitro Diagnostic Medical Device

Not all tests available in all countries

New Xpert® MTB/RIF Ultra

	Both assays	
System	GeneXpert (6-color)	
Sample type	Sputum, induced sputum, sediment	
Sample Incubation	15 min inactivation with Sample Reagent	
	Xpert MTB/RIF	Xpert MTB/RIF Ultra
Target(s)	*rpoB*	*rpoB*, IS*1081* & IS*6110*
Reaction Tube	25 µL	50 µL
Detection Method	Hemi-Nested PCR	Fully Nested PCR + Melt analysis
Turn around Time	110 minutes	~80 minutes

* CE-IVD. In Vitro Diagnostic Medical Device. Product may not be available in all countries

Ref: 301-5987, Rev. D May 2017 Xpert MTB/RIF Ultra product insert; 301-0191, Rev. D, November 2014, MTB/RIF product insert

Added Value of Xpert MTB/RIF Ultra for Diagnosis of Pulmonary Tuberculosis in a Low-Prevalence Setting

Onya Opota,[a] Fathiah Zakham,[a*] Jesica Mazza-Stalder,[b] Laurent Nicod,[b] Gilbert Greub,[a,c] Katia Jaton[a]

February 2019 Volume 57 Issue 2 e01717-18 Journal of Clinical Microbiology

TABLE 1 Comparative performance of smear microscopy, Xpert MTB/RIF, and Xpert Ultra using culture as the gold standard (n = 196 specimens)

Test	*M. tuberculosis* detection			
	% sensitivity (95% CI)			% specificity (95% CI)
	All culture-positive specimens (n = 47)	Smear-positive/ culture-positive specimens (n = 23)	Smear-negative/ culture positive specimens (n = 24)	All culture-negative specimens (n = 149)
Smear microscopy	48.94 (35.28–62.76) 23/47			100 (97.49–100) 149/149
Xpert MTB/RIF	82.98 (69.86–91.11) 39/47	100 (85.69–100) 23/23	66.67 (46.71–82.03) 16/24	97.32 (93.30–98.95) 145/149
Xpert Ultra	95.74 (85.75–99.24) 45/47	100 (85.69–100) 23/23	91.67 (74.15–98.52) 22/24	96.64 (92.39–98.56) 144/149

CE IVD In Vitro Diagnostic Medical Device

Not all tests available in all countries

One Key Antidote for Controlling Resistance: Antimicrobial Stewardship Programs

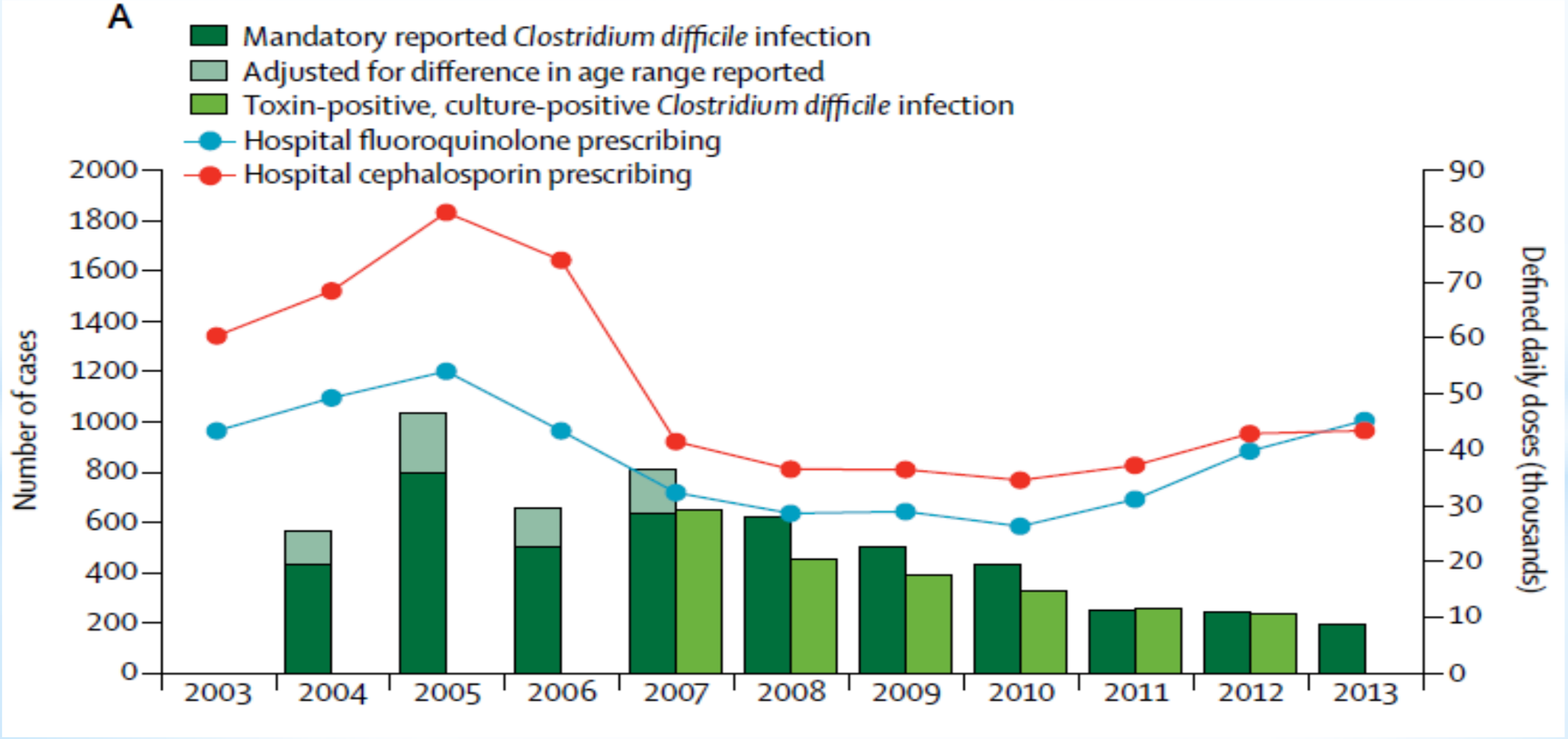
* "Antimicrobial stewardship is a coordinated program that promotes the appropriate use of antimicrobial agents, improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms."
* Stewardship programs stress choosing the right drug, at the right dosage, for the right duration. Antimicrobial stewardship is not just antibacterial drugs, but antivirals, antifungals, and antiparasitic agents

http://www.apic.org/Professional-Practice/Practice-Resources/Antimicrobial-Stewardship

Effects of control interventions on *Clostridium difficile* infection in England: an observational study

Lancet Infect Dis 2017; 17: 411–21

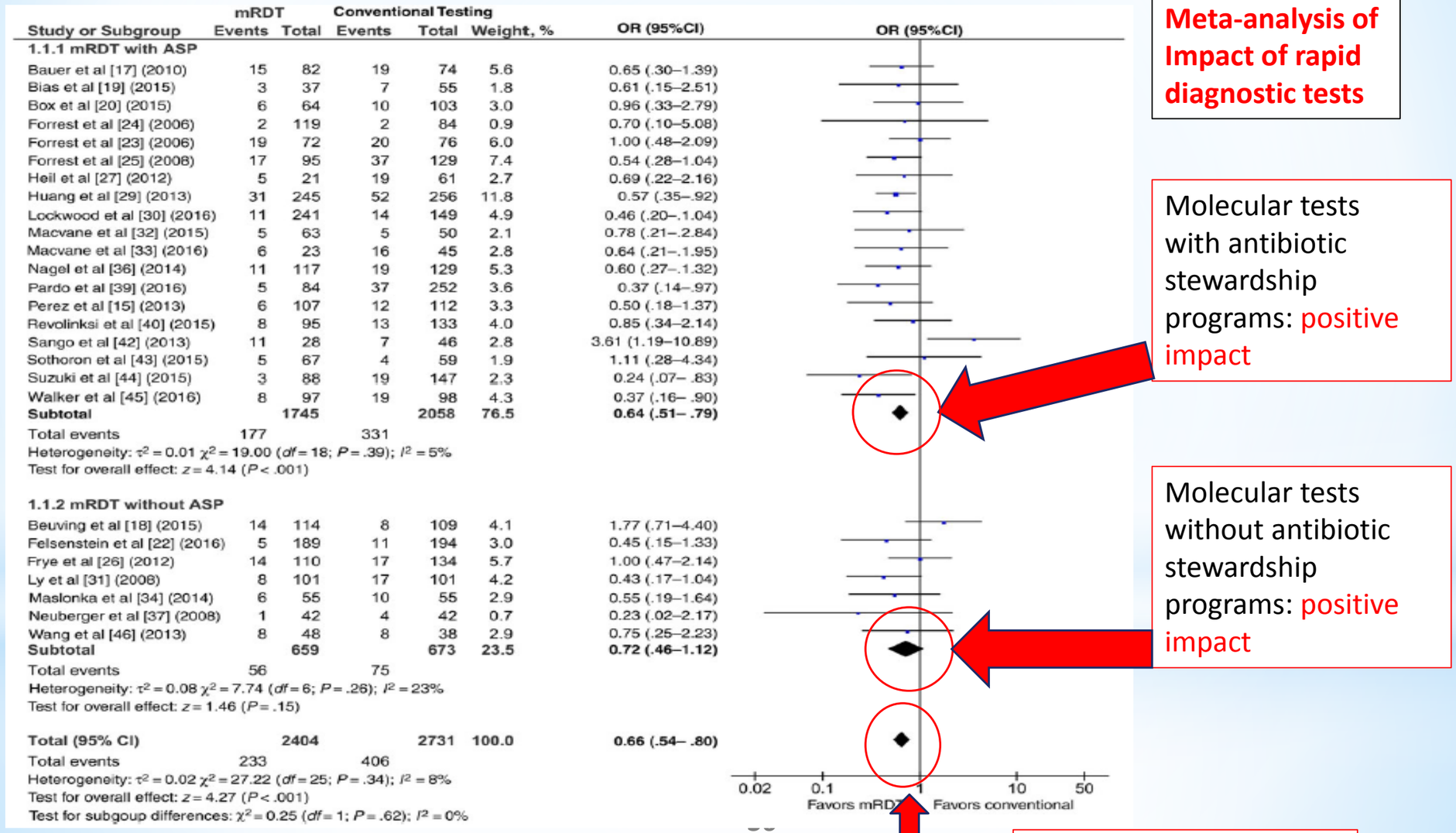
Interpretation Restricting fluoroquinolone prescribing appears to explain the decline in incidence of *C difficile* infections, above other measures, in Oxfordshire and Leeds, England. Antimicrobial stewardship should be a central component of *C difficile* infection control programmes.



The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis

Clinical Infectious Diseases® 2017;64(1):15–23

Tristan T. Timbrook,[1,4] Jacob B. Morton,[1,4] Kevin W. McConeghy,[2] Aisling R. Caffrey,[1,2,4] Eleftherios Mylonakis,[3] and Kerry L. LaPlante[1,2,4]



Study or Subgroup	mRDT Events	mRDT Total	Conventional Testing Events	Conventional Testing Total	Weight, %	OR (95%CI)
1.1.1 mRDT with ASP						
Bauer et al [17] (2010)	15	82	19	74	5.6	0.65 (.30–1.39)
Bias et al [19] (2015)	3	37	7	55	1.8	0.61 (.15–2.51)
Box et al [20] (2015)	6	64	10	103	3.0	0.96 (.33–2.79)
Forrest et al [24] (2006)	2	119	2	84	0.9	0.70 (.10–5.08)
Forrest et al [23] (2006)	19	72	20	76	6.0	1.00 (.48–2.09)
Forrest et al [25] (2008)	17	95	37	129	7.4	0.54 (.28–1.04)
Heil et al [27] (2012)	5	21	19	61	2.7	0.69 (.22–2.16)
Huang et al [29] (2013)	31	245	52	256	11.8	0.57 (.35–.92)
Lockwood et al [30] (2016)	11	241	14	149	4.9	0.46 (.20–.1.04)
Macvane et al [32] (2015)	5	63	5	50	2.1	0.78 (.21–.2.84)
Macvane et al [33] (2016)	6	23	16	45	2.8	0.64 (.21–.1.95)
Nagel et al [36] (2014)	11	117	19	129	5.3	0.60 (.27–.1.32)
Pardo et al [39] (2016)	5	84	37	252	3.6	0.37 (.14–.97)
Perez et al [15] (2013)	6	107	12	112	3.3	0.50 (.18–1.37)
Revolinksi et al [40] (2015)	8	95	13	133	4.0	0.85 (.34–2.14)
Sango et al [42] (2013)	11	28	7	46	2.8	3.61 (1.19–10.89)
Sothoron et al [43] (2015)	5	67	4	59	1.9	1.11 (.28–4.34)
Suzuki et al [44] (2015)	3	88	19	147	2.3	0.24 (.07– .83)
Walker et al [45] (2016)	8	97	19	98	4.3	0.37 (.16– .90)
Subtotal		**1745**		**2058**	**76.5**	**0.64 (.51– .79)**
Total events	177		331			
Heterogeneity: $\tau^2 = 0.01$ $\chi^2 = 19.00$ ($df = 18$; $P = .39$); $I^2 = 5\%$						
Test for overall effect: $z = 4.14$ ($P < .001$)						
1.1.2 mRDT without ASP						
Beuving et al [18] (2015)	14	114	8	109	4.1	1.77 (.71–4.40)
Felsenstein et al [22] (2016)	5	189	11	194	3.0	0.45 (.15–1.33)
Frye et al [26] (2012)	14	110	17	134	5.7	1.00 (.47–2.14)
Ly et al [31] (2008)	8	101	17	101	4.2	0.43 (.17–1.04)
Maslonka et al [34] (2014)	6	55	10	55	2.9	0.55 (.19–1.64)
Neuberger et al [37] (2008)	1	42	4	42	0.7	0.23 (.02–2.17)
Wang et al [46] (2013)	8	48	8	38	2.9	0.75 (.25–2.23)
Subtotal		**659**		**673**	**23.5**	**0.72 (.46–1.12)**
Total events	56		75			
Heterogeneity: $\tau^2 = 0.08$ $\chi^2 = 7.74$ ($df = 6$; $P = .26$); $I^2 = 23\%$						
Test for overall effect: $z = 1.46$ ($P = .15$)						
Total (95% CI)		**2404**		**2731**	**100.0**	**0.66 (.54– .80)**
Total events	233		406			
Heterogeneity: $\tau^2 = 0.02$ $\chi^2 = 27.22$ ($df = 25$; $P = .34$); $I^2 = 8\%$						
Test for overall effect: $z = 4.27$ ($P < .001$)						
Test for subgoup differences: $\chi^2 = 0.25$ ($df = 1$; $P = .62$); $I^2 = 0\%$						

Meta-analysis of Impact of rapid diagnostic tests

Molecular tests with antibiotic stewardship programs: positive impact

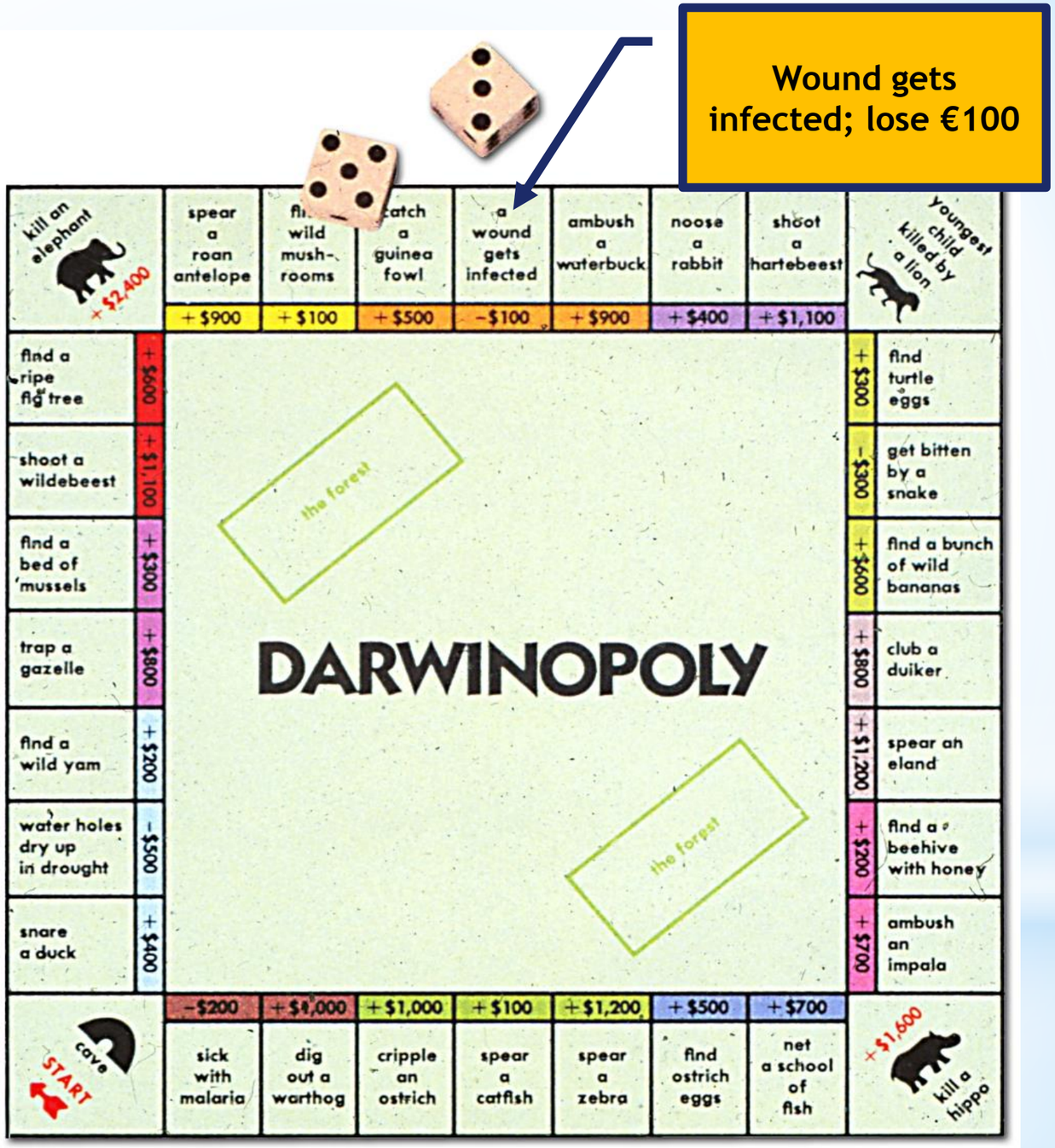
Molecular tests without antibiotic stewardship programs: positive impact

Overall impact is positive

Who is winning the resistance game?

Humans or Bacteria?

Progress is being made (by humans) but bacteria have been on the planet for 1.2 billion years and are very clever at surviving



Summary

* Reservoirs of antimicrobial resistant organisms are increasing
* Carbapenem-resistant organisms continue to emerge and molecular diagnostics can be useful for surveillance
* *C. difficile* guidelines from Europe and the US differ regarding the need for toxin testing if specimens from patients who may be colonized are excluded from testing
* Molecular diagnostics can aid with infection control decisions with tuberculosis particularly for removing patients from respiratory isolation
* Infection control and antimicrobial stewardship go hand in hand

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