The Year in Infection Control

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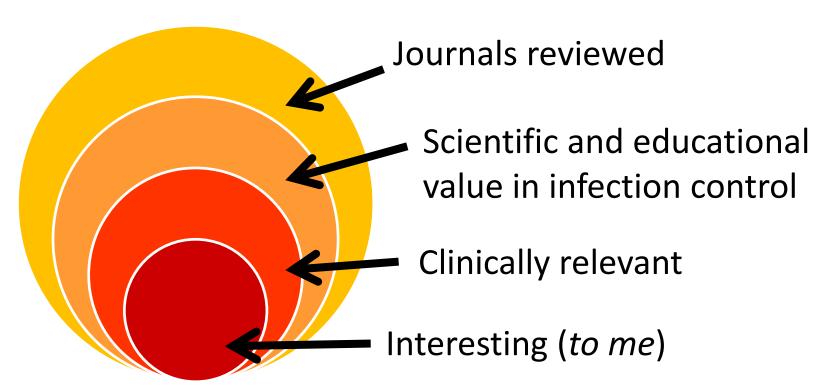


Royal Prince Alfred Hospital Sydney, Australia



1.223 million Pubmed publications last 12 months

Selection process



Topics covered

- Antimicrobial resistance
 Gram-negative >>> Gram-positive
- Infection control practices
 - Environmental cleaning
 - Hand hygiene
 - Contact precautions

ANTIMICROBIAL RESISTANCE

Clinical Review & Education

Table 1. Annual Cases and Deaths for Selected Antimicrobial-Resistant Organisms and *Clostridium difficile* Infection in the United States, 2008-2011^a

JAMA | Special Communication

Antimicrobial Resistance

In the US each year, AMR organisms:

- Cause > 2 million infections
- Associated with 23 000 deaths

In Europe each year, 25 000 deaths

	Cases per Year	Deaths per Year
Streptococcus pneumoniae (resistant to clinically relevant drugs)	1.2 million	7000
Drug-resistant Campylobacter	310 000	28
Clostridium difficile	250 000	14 000
Drug-resistant Neisseria gonorrhoeae	246 000	< 5
Drug-resistant nontyphoidal Salmonella	100 000	38
Methicillin-resistant Staphylococcus aureus	80 461	11 285
Drug-resistant Shigella	27 000	40
Extended spectrum β-lactamase- producing Enterobacteriaceae	26 000	1700
Carbapenem-resistant Enterobacteriaceae	9300	610
Clindamycin-resistant group B Streptococcus	7600	440
Drug-resistant Acinetobacter	7300	500
Multidrug-resistant <i>Pseudomonas</i> aeruginosa (≥3 drug classes)	6700	440

Marston et al. JAMA 2016; 316: 1193-1204

ORIGINAL ARTICLE

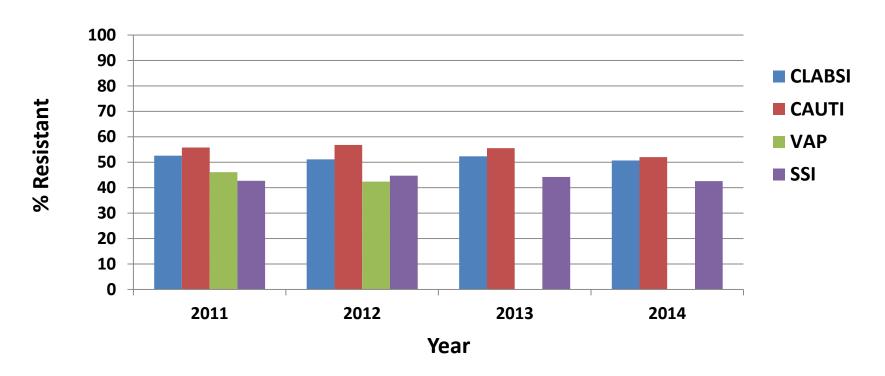
Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011–2014

Lindsey M. Weiner, MPH; Amy K. Webb, MPH, CHES; Brandi Limbago, PhD; Margaret A. Dudeck, MPH, CPH; Jean Patel, PhD; Alexander J. Kallen, MD, MPH; Jonathan R. Edwards, MStat; Dawn M. Sievert, PhD, MS

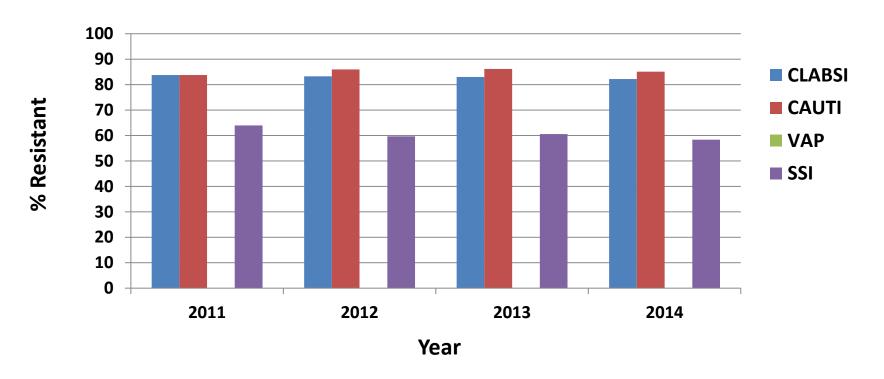
4,515 hospitals reported data

Weiner et al. Infect Control Hosp Epidemiol 2016; 37: 1288-1301

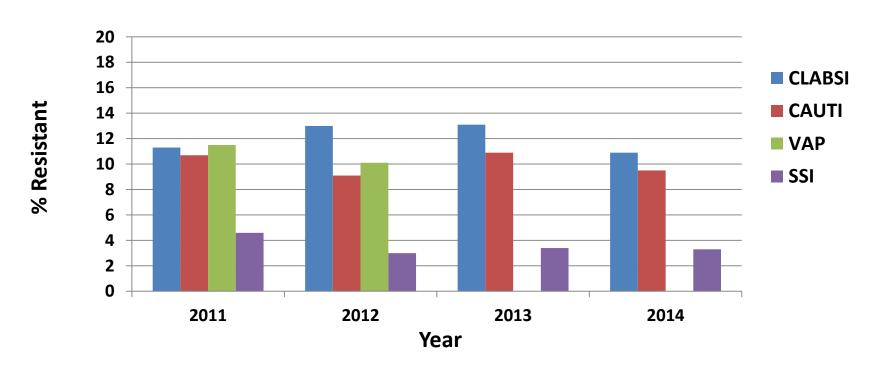
% methicillin-resistant *Staphylococcus aureus* (MRSA)



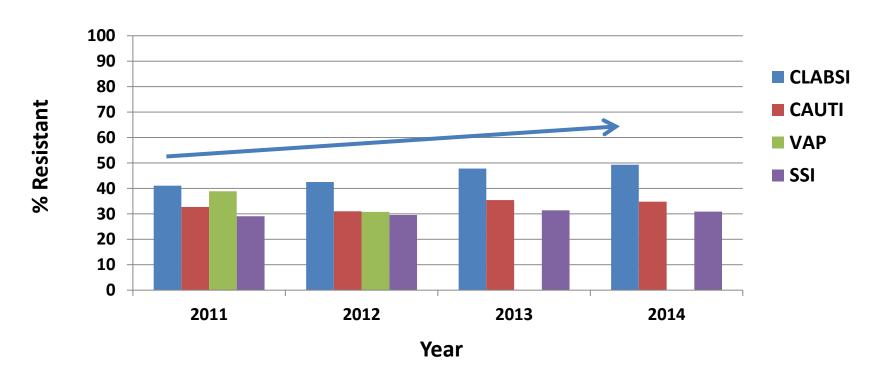
% vancomycin-resistant *Enterococcus faecium* (VRE)



% carbapenem-resistant *Klebsiella* species (CRE)



% fluoroquinolone-resistant *Escherichia coli*



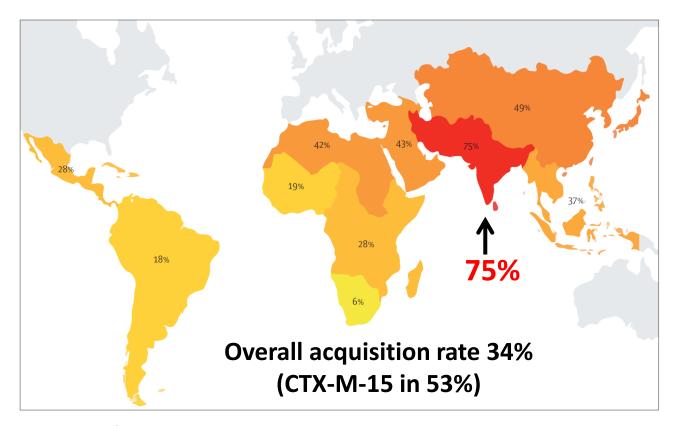
Import and spread of extended-spectrum \(\beta \)-lactamaseproducing Enterobacteriaceae by international travellers (COMBAT study): a prospective, multicentre cohort study

Maris S Arcilla*, Jarne M van Hattem*, Manon R Haverkate, Martin C J Bootsma, Perry J J van Genderen, Abraham Goorhuis, Martin P Grobusch, Astrid M Oude Lashof, Nicky Molhoek, Constance Schultsz, Ellen E Stobberingh, Henri A Verbrugh, Menno D de Jong, Damian C Melles, John Penders

2001 Dutch travellers and 215 household members

- Faecal swabs before and immediately and 1 month after travel
- If any of above ESBL positive, traveller and household members sampled at 3, 6, and 12 months after travel
- Questionnaires at all timepoints for potential risk factors for ESBL acquisition, including:
 - Demographics
 - Illnesses
 - Behaviour before, during and after travel

Percentage of travellers acquiring an ESBL by subregion



Predictors for ESBL acquisition

Risk factor	Adjusted OR (95% CI)	p value
Antibiotic use during travel	2.7 (1.8 – 4.1)	<0.001
(Quinolone use)	6.0 (2.9 – 12.4)	
Diarrhoea during and immediately after travel	2.3 (1.4 – 3.8)	0.001
Pre-existing bowel disease	2.1 (1.1 – 3.9)	0.019
Daily street food	1.8 (1.1 – 3.0)	0.025

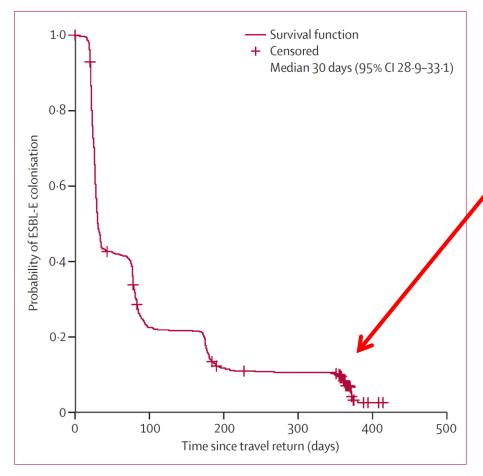


Figure 2: Kaplan-Meier estimate of time to decolonisation of ESBL-E in travellers

11% remained colonised at12 months

Estimated probability of transmitting ESBL to household member was 12% (95% CI 5–18)

Arcilla. Lancet Infect Dis 2017; 17: 78-85

RESEARCH ARTICLE

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Prolonged carriage and potential onward transmission of carbapenemase-producing Enterobacteriaceae in Dutch travelers

Jarne M van Hattem^{‡,1}, Maris S Arcilla^{‡,2}, Martin CJ Bootsma³, Perry J van Genderen⁴, Abraham Goorhuis⁵, Martin P Grobusch⁵, Nicky Molhoek⁶, Astrid ML Oude Lashof⁷, Constance Schultsz¹, Ellen E Stobberingh⁷, Henri A Verbrugh², Menno D de Jong¹, Damian C Melles² & John Penders*,

- Same cohort as previous study
- Acquisition of carbapenemase-producing Enterobacteriaceae (CPE)

van Hattern et al. Future Microbiol 2016; 11: 857-64



Future

MICROBIOLOGY

Traveler	Age	Sex	Countries visited	Duration (days)	Species	ESBL gene(s)	Before travel		1 month after travel	3 months after travel	6 months after travel	12 months after travel
1	64	F	Myanmar	16	Enterobacter cloacae complex	None	_†	IMI-2 ^{†‡}	_†	_†	_†	_+
2a	58	F	Indonesia	22	Escherichia coli	CTX-M-14	_†	OXA- 244 ^{†‡}	OXA- 244 ^{†‡}	OXA-244 ^{†‡}	OXA- 244 ^{§¶}	_§
2b	59	М	Indonesia	22	E. coli	CTX-M-14	_†	_†	_†	OXA-244 ^{†‡}	_§	_§
3	41	M	Turkey, Greece	14	Klebsiella pneumoniae	None	_†	<i>OXA-</i> 48§ [#]	_§	_§	_§	_§
4	37	F	China, Thailand, Vietnam, Japan, Hong Kong and Singapore	22	E. coli	CTX-M-15 and CTX-M-55	_†	<i>NDM</i> -1/2 ^{†‡}	<i>NDM</i> -1/2 ^{†‡}	_†	_+	_†
5	64	F	Myanmar	22	E. coli	CTX-M-15	_†	<i>NDM</i> -7 ^{†‡}	_†	_†	_†	_+

- Acquisition of CPE seen:
 - Outside the Indian subcontinent
 - No healthcare contact during travel

 Consider admission CPE screening not only after recent travel, but even several months after return

Multiple Variants of *Klebsiella pneumoniae* Producing Carbapenemase in One Patient

Michael R. Mulvey, Ph.D.

National Microbiology Laboratory Winnipeg, MB, Canada michael.mulvey@phac-aspc.gc.ca

Louis-Patrick Haraoui, M.D.

McGill University Health Centre Montreal, QC, Canada

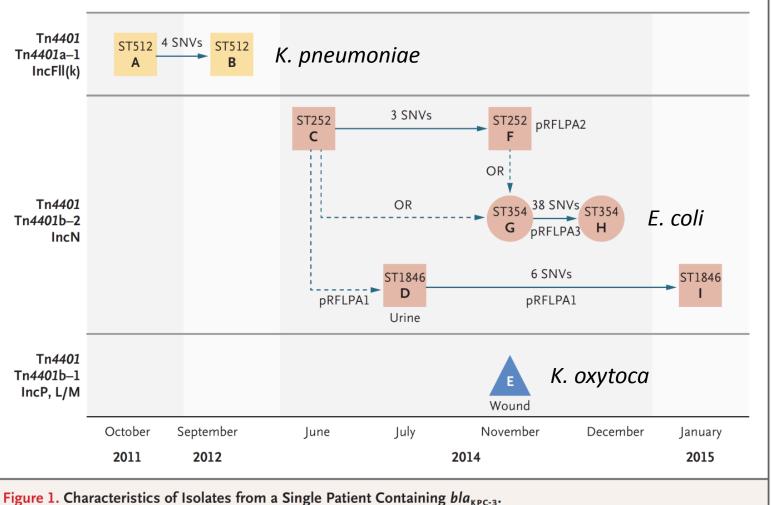
Yves Longtin, M.D.

Jewish General Hospital Montreal, QC, Canada

- 82 yr man
- Admitted to the same hospital 21 times (2011-2015)
- Often grouped with patients colonized with KPC-producing Enterobacteriaceae (KPE)
- Numerous antibiotic courses

Mulvey et al. NEJM 2016; 375: 2408-10

- 14 KPE isolates identified
- 9 available for sequencing:
 - 7 rectal swabs
 - 1 urine
 - 1 wound swab
- 3 species (*K. pneumoniae, K. oxytoca, and E. coli*) identified, including:
 - 3 different K. pneumoniae sequence types
 - 3 different incompatibility (Inc) group plasmids carrying Tn4401



- Multiple isolates may have arisen from:
 - Spread of resistance element within the host and/or
 - Exposure to other KPE-colonized patients
- Limitations of outbreak investigations with traditional epidemiologic and molecular tools
- Genome sequencing necessary

Prevalence, risk factors, outcomes, and molecular epidemiology of *mcr*-1-positive Enterobacteriaceae in patients and healthy adults from China: an epidemiological and clinical study

Yang Wang*, Guo-Bao Tian*, Rong Zhang*, Yingbo Shen*, Jonathan M Tyrrell, Xi Huang, Hongwei Zhou, Lei Lei, Hong-Yu Li, Yohei Doi, Ying Fang, Hongwei Ren, Lan-Lan Zhong, Zhangqi Shen, Kun-Jiao Zeng, Shaolin Wang, Jian-Hua Liu, Congming Wu, Timothy R Walsh, Jianzhong Shen

- Until recently, colistin resistance reported to be mediated by chromosomal mutations and possibly imposed a fitness cost
- mcr-1 gene confers transferable colistin resistance

- 2 hospitals in Zhejiang and Guangdong
- mcr-1 in up to 1% of infecting isolates (2007 to 2015)
- Risk factors for infection:
 - Male sex (p=0.011)
 - Immunosuppression (p=0.011)
 - Antibiotic use
 - Carbapenems (p=0.002)
 - Fluoroquinolones (p=0.017)

- Colonisation rates:
 - Healthy volunteers 0.7%
 - Inpatients 3%
- Risk factor for colonisation Antibiotic use
- mcr-1 transferred between bacteria at high frequencies (10–1 to 10–3)
- Colistin not yet used in humans in China
- In 2017, colistin will be formally banned from animal feeds

Prevalence of mcr-1 in Escherichia coli and Klebsiella pneumoniae recovered from bloodstream infections in China: a multicentre longitudinal study

Jingjing Quan*, Xi Li*, Yan Chen*, Yan Jiang, Zhihui Zhou, Huichuan Zhang, Lu Sun, Zhi Ruan, Ye Feng, Murat Akova, Yunsong Yu

- E. coli and K. pneumoniae bloodstream infections
- 28 hospitals in China

- Proportion *mcr-1*-positive (2066 isolates):
 - E. coli 20 of 1495 (1%)
 - K. pneumoniae 1 of 571 (<1%)</p>
- All mcr-1-positive resistant to colistin except for 1 E. coli isolate
- Clonally diverse sporadic

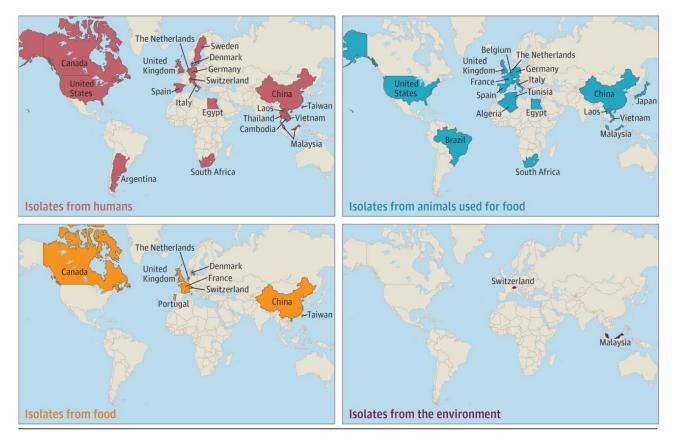
- Resistance to other antibiotics
 - 100% tigecycline sensitive
 - 20 (95%) carbapenem and piperacillin-tazobactam sensitive
 - 1 mcr-1-positive E. coli isolate also produced NDM-5
- No prior history of colistin use
- Zero 30 day mortality

Investigation of First Identified *mcr-1* Gene in an Isolate from a U.S. Patient — Pennsylvania, 2016

Kelly E. Kline, MPH^{1,2}; Jordan Shover¹; Alexander J. Kallen, MD³; David R. Lonsway, MMSc³; Sharon Watkins, PhD¹; Jeffrey R. Miller, MD^{1,4}

- May 2016, mcr-1-positive E. coli first isolated from patient in US
- Woman with UTI
- ESBL with reduced colistin susceptibility
- Repeated admissions 2016
- 100 community and hospital contacts screens negative

Recovery of *mcr-1* Enterobacteriaceae June 2016



RAPID COMMUNICATIONS

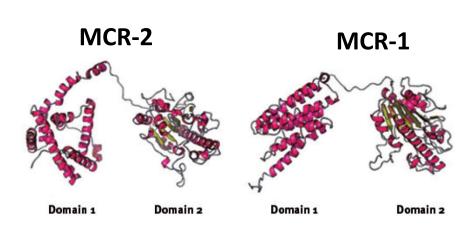
Identification of a novel plasmid-mediated colistin-resistance gene, *mcr-2*, in *Escherichia coli*, Belgium, June 2016

BB Xavier 123, C Lammens 123, R Ruhal 123, S Kumar-Singh 134, P Butaye 567, H Goossens 123, S Malhotra-Kumar 123

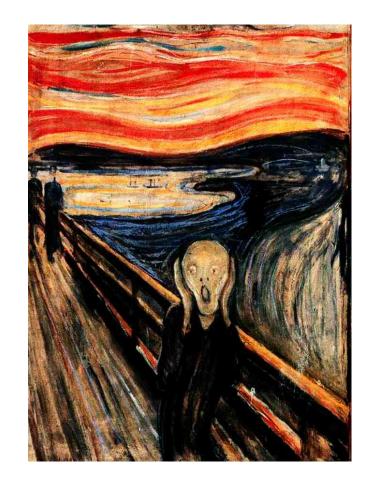
- 1. Laboratory of Medical Microbiology, Wilrijk, Belgium
- 2. Vaccine & Infectious Disease Institute, Wilrijk, Belgium
- 3. University of Antwerp, Wilrijk, Belgium
- 4. Molecular Pathology group, Cell Biology and Histology, Wilrijk, Belgium
- 5. Ghent University, Faculty of Veterinary Medicine, Ghent, Belgium
- 6. CODA-CERVA, Brussels, Belgium
- 7. Ross University School of Veterinary Medicine, Basseterre, Saint Kitts and Nevis

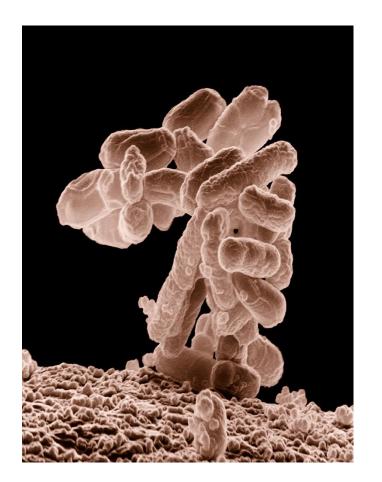
Correspondence: Surbhi Malhotra-Kumar (surbhi.malhotra@uantwerpen.be)

- Porcine and bovine colistin-resistant *E. coli* 2011-2012
- *mcr-1* in 12% (n = 13) of *E. coli*
- Novel plasmid-mediated colistin resistance gene mcr-2
 - 77% nucleotide identity to mcr-1
- ? Originated from Moraxella catarrhalis



Xavier et al. Euro Surveill 2016; 21 (27): pii = 30280



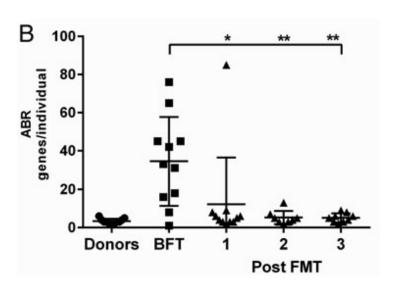


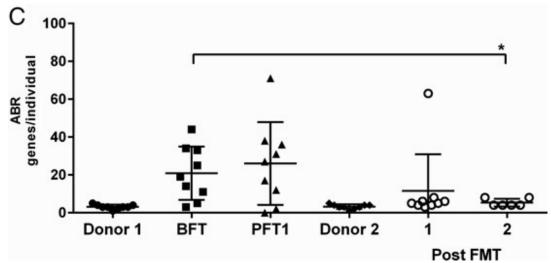
Fecal Microbial Transplants Reduce Antibiotic-resistant Genes in Patients With Recurrent *Clostridium difficile* Infection

Braden Millan,^{1,a} Heekuk Park,^{1,a} Naomi Hotte,¹ Olivier Mathieu,² Pierre Burguiere,² Thomas A. Tompkins,² Dina Kao,^{1,b} and Karen L. Madsen^{1,b}

¹Department of Medicine, University of Alberta, Edmonton, and ²Lallemand Health Solutions, Montreal, Quebec, Canada

- Gut microbiota enormous reservoir of antibiotic resistance (ABR) genes
- Aim:
 - To analyze the gut resistome in patients with recurrent *C. difficile* infection (RCDI) undergoing FMT (n = 20)
 - To examine how FMT influences the ABR profile of the recipients





Millan et al. Clin Infect Dis 2016; 62: 1479-86

- Following successful FMT, the resistome of recipient became more similar to the resistome of donor
- Maintained up to a year after FMT
- Limitations
 - No control group
 - Clinical outcomes MRO infection and transmission

UN commits to tackling antimicrobial resistance

The UN held a meeting on antimicrobial resistance on Sept 21, 2016, in New York. This meeting is only the fourth time that a health-care topic has been addressed by the UN. Ammara Mushtaq reports.

"...antimicrobial resistance is an existing reality everywhere... [and] ...is a multidimensional issue..."



UN Secretary-General Ban Ki-Moon

Mushtaq. Lancet Infect Dis 2016; 16: 1229-1230

INFECTION CONTROL PRACTICES

Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and *Clostridium difficile* (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study

Deverick J Anderson, Luke F Chen, David J Weber, Rebekah W Moehring, Sarah S Lewis, Patricia F Triplett, Michael Blocker, Paul Becherer, J Conrad Schwab, Lauren P Knelson, Yuliya Lokhnygina, William A Rutala, Hajime Kanamori, Maria F Gergen, Daniel J Sexton; for the CDC Prevention Epicenters Program

Anderson et al. Lancet 2017; 389: 805-14

Aim: To determined the effect of three enhanced strategies for terminal room disinfection on acquisition and infection due to:

- MRSA
- VRE
- C. difficile
- Multidrug-resistant Acinetobacter

- Pragmatic, cluster-randomised, crossover trial
- 9 US hospitals
- Rooms terminally disinfected with:
 - Reference (quaternary ammonium)
 - UV (quaternary ammonium and UV-C)
 - Bleach
 - Bleach and UV-C
- Bleach for all *C. difficile* rooms

- Every strategy used at each hospital
- 4 consecutive 7-month periods
- Randomly assigned sequence of strategies
- Primary outcomes
 - Incidence of infection or colonisation with all target organisms among exposed patients
 - Incidence of *C. difficile* infection among exposed patients

Intention-to-treat analysis

	Reference	UV	Bleach	Bleach + UV
Total no.	4916	5178	5438	5863
RR (95% CI)				
All target organisms	Reference	0·70 (0·50 to 0·98)	0·85 (0·69 to 1·04)	0·91 (0·76 to 1·09)
C. difficile	-	-	Reference	1·0 (0·57 to 1·75)
MRSA	Reference	0·78 (0·58 to 1·05)	1·00 0·82 to 1·21)	0·97 (0·78 to 1·22)
VRE	Reference	0·41 (0·15 to 1·13)	0·43 (0·19 to 1·00)	0·36 (0·18 to 0·70)

Anderson et al. Lancet 2017; 389: 805-14

- Enhanced terminal cleaning resulted in 10–30% reduction in acquisition of a multidrug-resistant organism or *C. difficile*
- Largest risk reduction with UV-C device added to the standard disinfectant strategy
 - Incident cases from 2.3% to 1.6%
- C. difficile infection not reduced after adding UV to bleach (unlike previous studies)

Enhanced performance feedback and patient participation to improve hand hygiene compliance of health-care workers in the setting of established multimodal promotion: a single-centre, cluster randomised controlled trial

Andrew James Stewardson*, Hugo Sax*, Angèle Gayet-Ageron, Sylvie Touveneau, Yves Longtin, Walter Zingg, Didier Pittet

- 15-month baseline period
- 67 wards randomised (1:1:1) to 1 of 3 groups:
 - Control (22)
 - Enhanced performance feedback (24)
 - Enhanced performance feedback plus patient participation (21)
- Primary outcome hand hygiene compliance

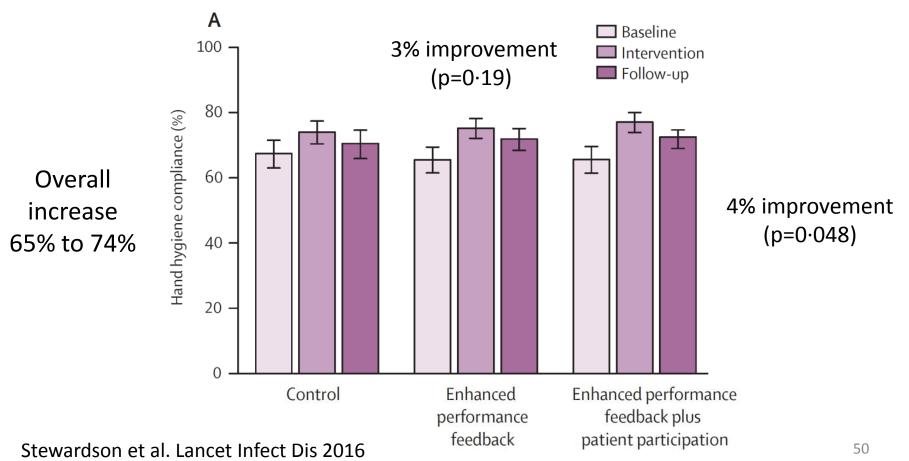
Enhanced performance feedback

- Immediate, individualised feedback
 - Verbal
 - Where feasible, individualised card
- Intermittent, aggregated feedback
 - Reports and posters
 - 3 monthly
- Ward-level benchmarking and goal setting (80%)

Patient participation

- Patient welcome pack
 - Brochure
 - Individual bottle of alcohol-based handrub
- Patient education about hand hygiene
- Invited to ask health-care workers to perform hand hygiene
- Posters and healthcare worker badges

Figure 2: Overall hand hygiene compliance (A)



 No clinically significant effect for either intervention (a-priori threshold of 15% not reached)

- Possible explanations:
 - Direct observation
 - Cross-contamination
 - Did patients really participate?
 No episodes of patients reminding health-care workers to perform hand hygiene observed

CONTROVERSIES!

Do we need contact precautions ??

- Contact precautions aim to reduce transmission of MROs by direct or indirect contact
- Common practice
- Increasingly controversial:
 - Costs
 - Concerns regarding patient safety
 - Disputable benefits regarding transmission
- Evaluation of effectiveness and cost-benefit ratio

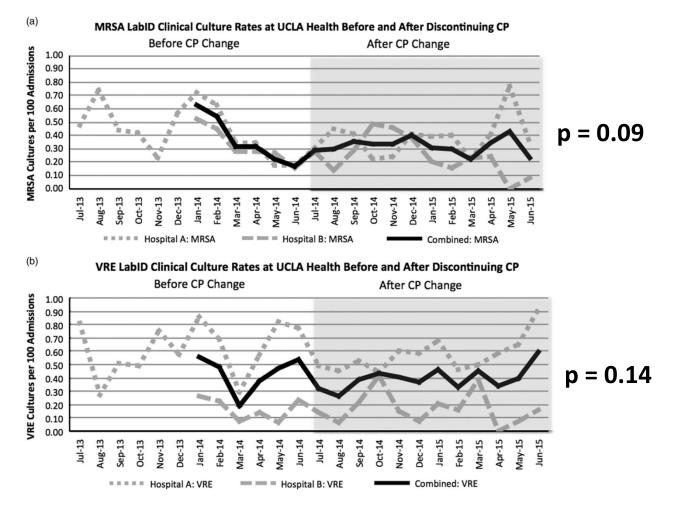
Elimination of Routine Contact Precautions for Endemic Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant *Enterococcus*: A Retrospective Quasi-Experimental Study

Elise M. Martin, MD;¹ Dana Russell, MPH;² Zachary Rubin, MD;¹ Romney Humphries, PhD;³ Tristan R. Grogan, MS;⁴ David Elashoff, PhD;⁴ Daniel Z. Uslan, MD, FIDSA, FSHEA¹

Aim: To evaluate the impact of discontinuation of contact precautions (CP) for MRSA and VRE and expansion of chlorhexidine gluconate (CHG) use on the health system

- Retrospective, non-randomized, observational, quasi-experimental study
- Two California hospitals
- All beds at hospital A and majority at hospital B are single-occupant, private rooms

- July 2014 Routine CP for endemic MRSA and VRE discontinued
- May 2014 Daily 2% CHG bathing in all units
- Outcome Hospital-wide laboratory-identified clinical culture rates 1 year before and after



- Before change, CP for MRSA or VRE in:
 - 29% intensive care unit
 - 19% medicine/surgery beds
- When combining isolation, gown and CHG costs, \$643,776 saving in 1 year
- Estimated nursing time 45,277 hours/year (estimated cost, \$4.6 million)

Caveats:

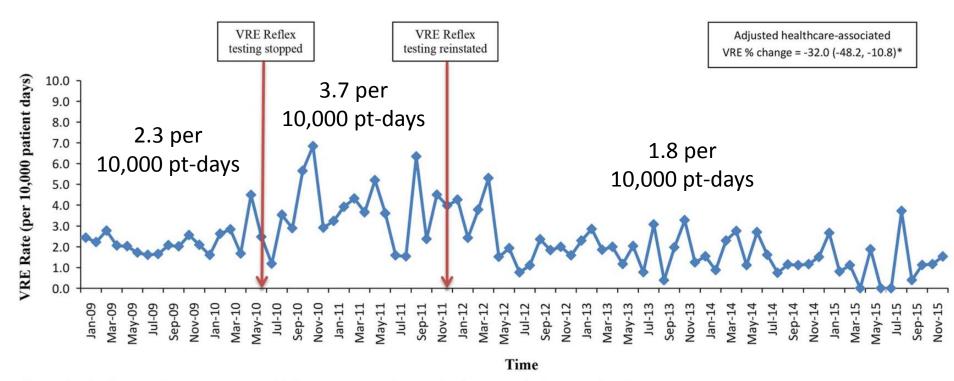
- Near-universal CHG bathing
- HH compliance rates high
 (>90% Hosp A and 64-74% Hosp B)
- Single-occupant patient rooms
- Short follow up
- Reproducible in hospitals with higher rates?

Reinstatement of Reflex Testing of Stool Samples for Vancomycin-Resistant Enterococci (VRE) Resulted in Decreased Incidence of Hospital-Associated VRE

- 1,250-bed academic tertiary care hospital in Saint Louis,
 Missouri
- VRE rate between January 2009 and December 2015

- Reflex screening of stool for C. difficile testing
 - Jan 2009 to July 2010 Yes
 - July 2010 Ceased
 - Jan 2012 to Dec 2015 Yes

Outcome - positive VRE urine or blood culture



*Rate adjusting for overall temporal trend and VRE prevalence on admission by Autoregressive integrated moving average.

FIGURE 1. Monthly incidence of healthcare-associated vancomycin resistant enterococci (VRE) infections, January 2009 - December 2015

Prospective Validation of Cessation of Contact Precautions for Extended-Spectrum β-Lactamase-Producing *Escherichia coli*¹

Sarah Tschudin-Sutter, Reno Frei, Friedbert Schwahn, Milanka Tomic, Martin Conzelmann, Anne Stranden, Andreas F. Widmer

Basel, Switzerland

Aim: To determine nosocomial transmission of ESBL–*E. coli* after discontining contact precautions

- Hospitals (acute and geriatrics) ceased contact precautions for ESBL-E. coli patients - 2012
- Patient inclusion in study to December 2013
- Screened hospital patients who shared rooms with ESBL-E. coli patients

- 231 contact patients exposed to 211 index patients
- ESBL-*E. coli* from 24 contact patients and strain identity for 11 (PFGE) – overall transmission rate of 4.8% (11/231)

Table. Characteristics and exposures for hospitalized contact patients with and without transmission of ESBL-producing *Escherichia*

coli from index patients, Basel, Switzerland*

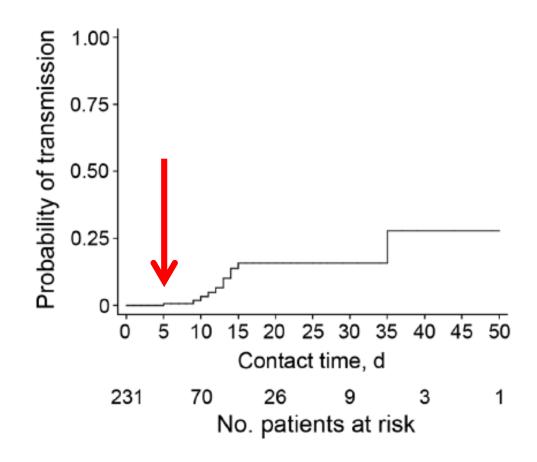
	Contact patients with transmission of	Contact patients without transmission	
Patient characteristics and exposures	ESBL-producing E. coli, n = 11†	of ESBL-producing E. coli, n = 220†	p value
Contact patient characteristics			
Age, y, median (IQR)	81 (77–82)	75 (64–82)	0.153
Charlson Comorbidity Index, median (IQR)	2 (1–4)	2 (1–3)	0.399
Contact time, d, median (IQR)	13 (10–15)	8 (5–12)	0.006
Intensive care unit stay	0	54 (24.8)	0.122
Received any antimicrobial drug	4 (36.4)	93 (42.3)	0.765
Received systemic antimicrobial drugs with activity against ESRL <i>E. coli</i>	1 (9.1)	19 (8.6)	1.000

Contact time, d, median (IQR) 0.006

Tschudin-Sutter et al. Emerg Infect Dis 2016; 22: 1094-97

Exposure > 5 days associated with increased odds for transmission

OR 10.2, 95% CI 1.3–80.9 p = 0.03



NOTE:

- High adherence to standard precautions hand hygiene compliance > 90%
- Infrastructure
 - Acute hospital 9% in rooms with 4 beds and remaining in rooms with 1–2 beds
 - Geriatric hospital 48% in rooms with 4 beds and remaining in rooms with 1–2 beds
- Lower ESBL rates than other settings

Summary – Antibiotic resistance

- Community reservoirs
 - Understanding the epidemiology
- Transmission dynamics complex
 - WGS
- Untreatable Gram-negatives
- Novel approaches
 - Microbiome
- Global action

Summary – Infection control practices

Horizontal approaches – get the basics right!

- Environmental cleaning
 - Good quality evidence emerging
- Hand hygiene
 - Ongoing challenges to improve compliance

Vertical approaches

- Contact precautions
 - Controversy for endemic MROs
 - Watch this space...

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QUESTIONS??

