

European approaches to MDR-GNR prevention and control

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THE END OF
ANTIBIOTICS IS NIGH

What's the problem?



“CRE are nightmare bacteria.”

Dr Tom Frieden, CDC Director



“If we don't take action, then we may all be back in an almost 19th Century environment where infections kill us as a result of routine operations.”

Dame Sally Davies, Chief Medical Officer



“If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine where treatable infections and injuries will kill once again.”

David Cameron, Prime Minister, UK



“The rise of antibiotic-resistant bacteria, however, represents a serious threat to public health and the economy.”

Barack Obama, President USA

CRE in the UK and US



PHE Gateway number: 2013-499
To: Chief Executive Officer
CC: Director of Nursing
Medical Director

27 February 2014

Dear Chief Executive Officer,

Re: Addressing the infection risk of other carbapenem-resistant organisms

We are taking the unusual step of writing to address the risk posed to trusts and Enterobacteriaceae and other carbapenem-resistant organisms represent one of the most currently feared, and the failure to control them has substantial human health and financial implications. Management of these infections is extremely difficult to treat as they are resistant to most antibiotics. Management of these infections is also significantly more costly for the health service.

In order to minimise the wide spread of these infections, it is important that you be grateful if you could ensure, as a national 'Acute trust toolkit for carbapenemase-producing Enterobacteriaceae'.

Additionally, to ensure that trusts are fully aware of the risk, next week NHS England will be publishing 'Addressing rising trends and outbreaks of carbapenemase-producing Enterobacteriaceae' and information that will support trusts in the 'Key Information' appendix. These infections are already causing significant numbers of infections, outbreaks and antimicrobial resistance. The National Resistance and Healthcare Association (NRAHA) has been working since 2000 and confirming up to 25 positive samples on a voluntary basis. PHE will continue to work with trusts available to professional colleagues and national efforts to address the public health risk.

The 'Acute trust toolkit for the early detection of carbapenemase-producing Enterobacteriaceae' is available at: http://www.hpa.org.uk/web/HPAwebHPAwebStandard/HPAweb_C/1317140378529



Acute trust management of carbapenemase-producing Enterobacteriaceae



Patient Safety Alert

Alert reference number: NHSPSA/Re/2014/004
Alert stage: Two - Resources

Enterobacteriaceae are a large family of bacteria that usually live harmlessly in the gut of all humans and animals, but, in the wrong place, can cause serious infections. Worldwide, a small but increasing number of strains of enterobacteriaceae have become resistant to carbapenem antibiotics, which have been defined by WHO as critically important antibiotics. Carbapenemases are enzymes made by some strains of these bacteria, which allow them to destroy carbapenem antibiotics and cause resistance. Increasing trends in sporadic infections, clusters and outbreaks of carbapenemase-producing Enterobacteriaceae (CPE) have been observed in a number of NHS trusts in England. There is a high risk of this problem becoming more widespread unless early and decisive action is taken by trusts. These bacteria represent a significant challenge in terms of prevention, treatment and control. Inadequate measures to prevent and control transmission can have serious consequences for both patients, who may require more complex treatment to manage their infection, and hospitals in terms of ward closures and protracted patient stays. As a result of the escalating problem, Public Health England (PHE) is providing national support for ongoing efforts to control and reverse rising trends with the aim of minimising morbidity and preventing further outbreaks. Because the PHE resources are now available NHS England has been able to proceed to issuing a Stage 2 alert without a previous Stage 1 alert.

PHE have recently published a toolkit for acute trusts to assist them with the early detection, management and control of carbapenemase-producing Enterobacteriaceae. A key aspect of the control measures is to take special precautions for patients recently treated in countries known to have high levels of CPE or in UK hospitals with recent clusters or outbreaks of CPE. This alert is to bring this significant infection prevention and control challenge to the attention of the NHS and to signpost the toolkit developed to support the NHS in both controlling existing transmission problems and preventing further spread.

The toolkit along with 'UK Standards for Microbiology Investigations: Laboratory Detection and Reporting of Bacteria with Carbapenem-Hydrolyzing β -lactamases (Carbapenemases)' can be found at: www.hpa.org.uk/web/HPAwebHPAwebStandard/HPAweb_C/1317140378529

BSAC, antibiotic susceptibility testing guidance is available at: www.bsac.org.uk/wp-content/uploads/2012/08/AST-testing-and-reporting-guidance-v1-Final.pdf

Implementation advice on the toolkit can be obtained from local PHE Centres: www.gov.uk/government/publications/phe-centre-addresses-and-phone-numbers/phe-local-and-regional-contact-details

Patient Safety | Domain 5
www.england.nhs.uk/patientsafety

Contact us: patientsafety.enquiries@nhs.net
Visit our website: www.england.nhs.uk/patientsafety
Report incidents: www.england.nhs.uk/reportingincidents



Stage Two: Resources
Addressing rising trends and outbreaks in carbapenemase-producing Enterobacteriaceae
6th March 2014

Actions

Who: Chief Executives of NHS trusts and foundation trusts providing acute care and independent hospitals.

When: To commence immediately and completed by 30 June 2014

1. Bring this alert to the notice of the Director for Infection Prevention and Control (DIPIC) and infection control staff to instigate the development of the board level CPE management plan.
2. In discussion with relevant clinical experts establish if there are / have been cases of CPE in the organisation and consider if immediate action is required locally to reduce the risk of such an incident / outbreak occurring.
3. In the light of the local situation the Infection Prevention and Control Committee to plan for local adoption and dissemination of the Acute Trust CPE toolkit to influence clinical practice. This will include advising front line staff of the issue and the Trust's plans for addressing CPE.

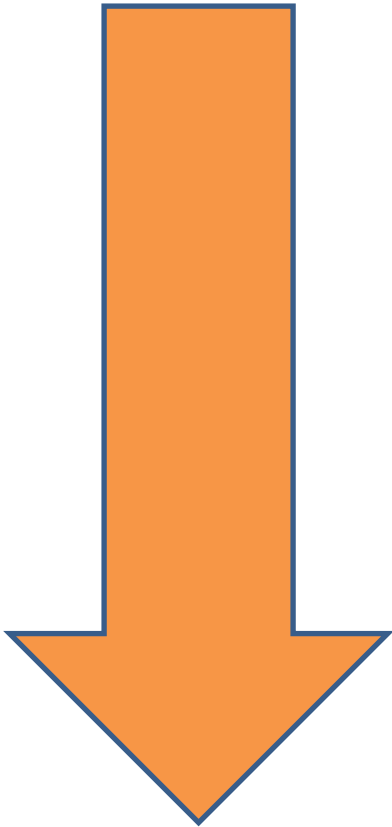
Note: This alert is being sent to GPs for information

Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

2012 CRE Toolkit

National Center for Enteric and Zoonotic Infections Diseases
Division of Healthcare Quality Promotion

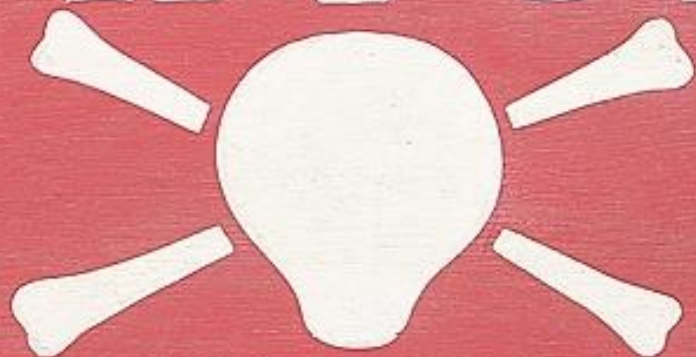
Universal or targeted approach?



Evidence-free zone

Guidelines \neq Policy

DANGER



MINES

Acronym minefield

CPE

MDR-GNR

CPC

ESBL

MDR-GNB

CRO

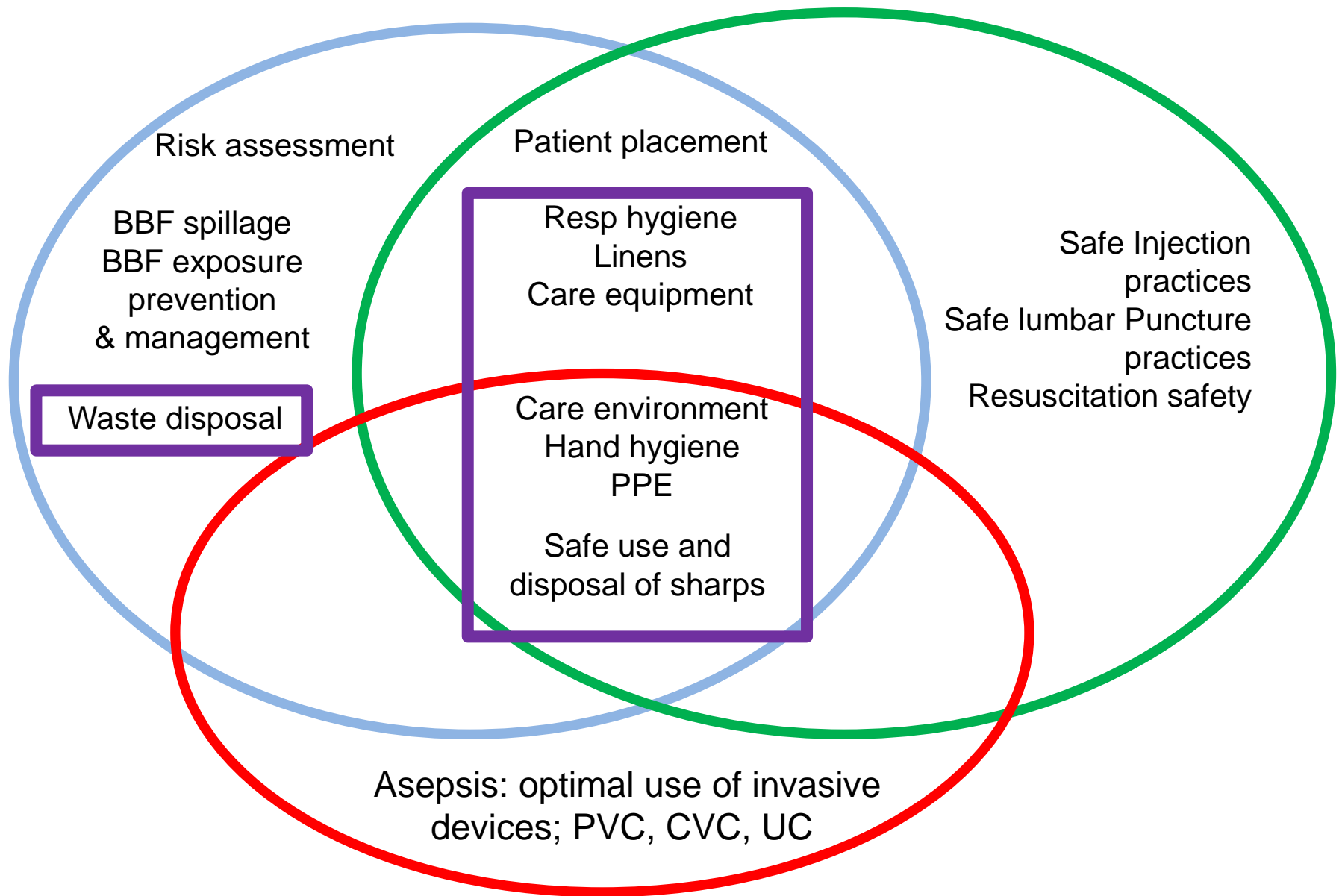
CPE

CRE

CRC

KPC

CRAB

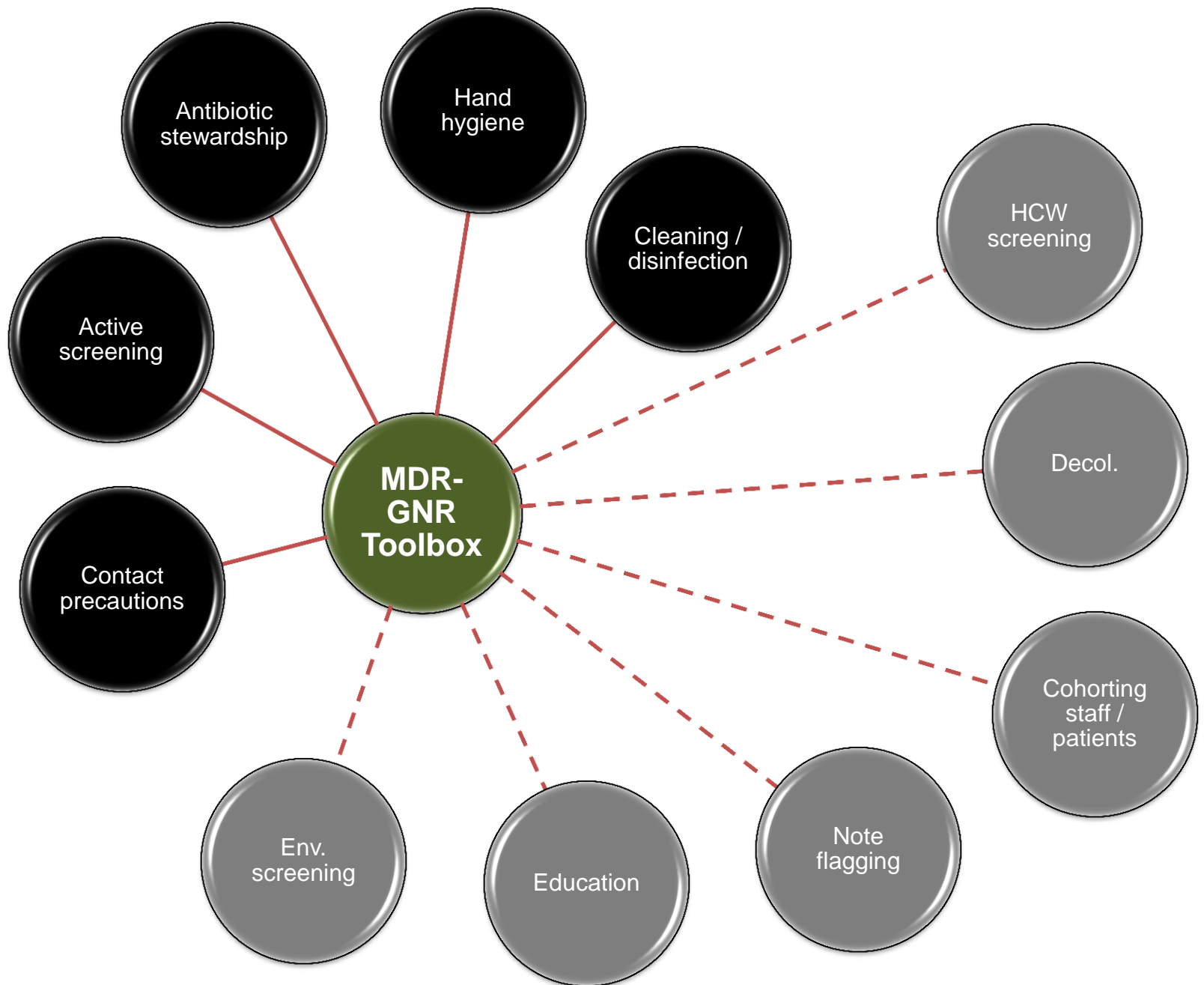


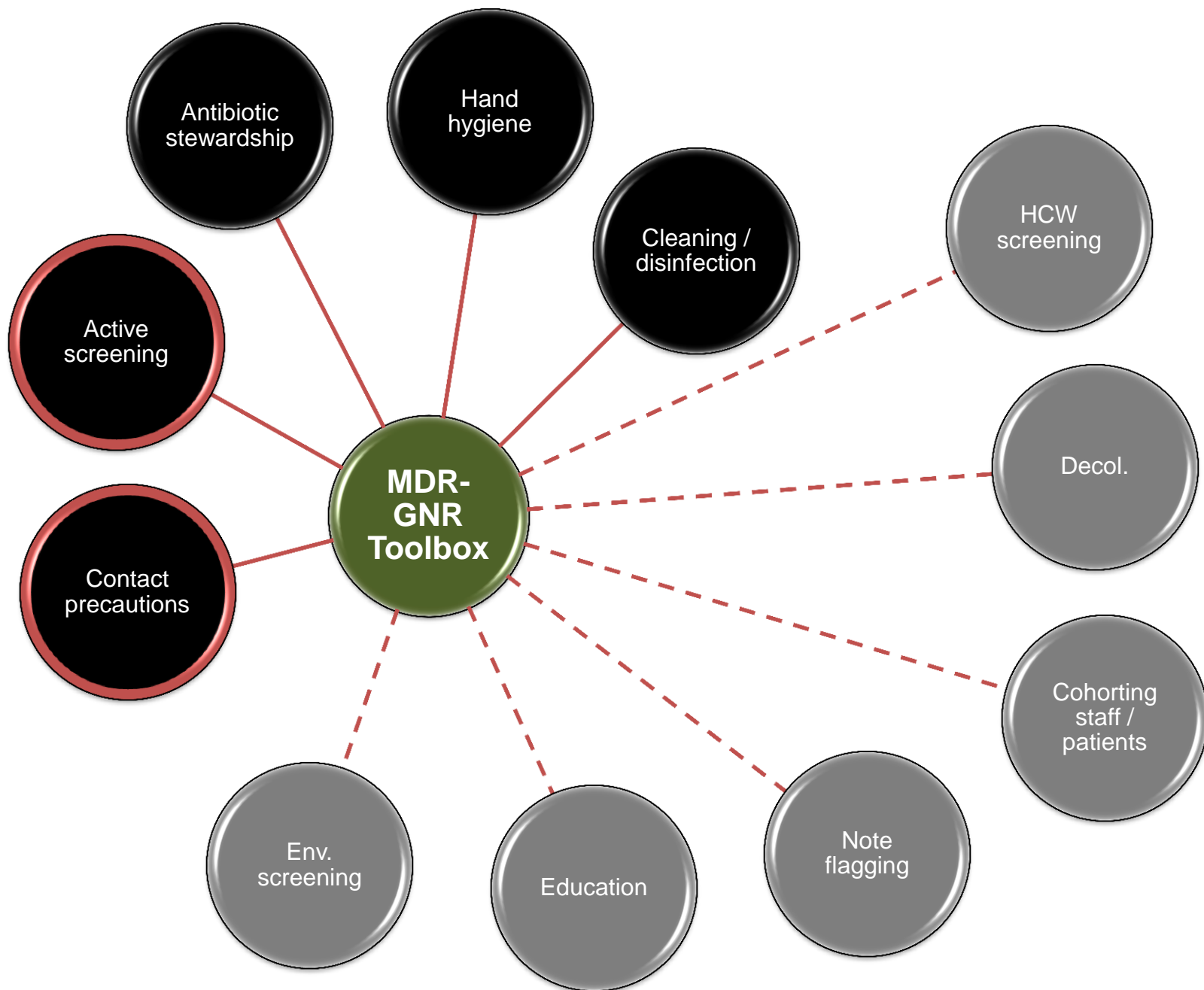
Health Protection Scotland: <http://www.documents.hps.scot.nhs.uk/hai/infection-control/ic-manual/ipcm-p-v2-3.pdf>

Centres for Disease Control: <http://www.cdc.gov/HAI/settings/outpatient/outpatient-care-gl-standard-precautions.html>

UK Epic3: <http://www.sciencedirect.com/science/article/pii/S0195670113600122>

WHO: www.who.int/csr/resources/publications/EPR_AM2_E7.pdf





Who do I screen?

[UK PHE CPE Toolkit](#) screening triggers:

- a) an inpatient in a hospital abroad, or
- b) an inpatient in a UK hospital which has problems with spread of CPE (if known), or
- c) a 'previously' positive case.

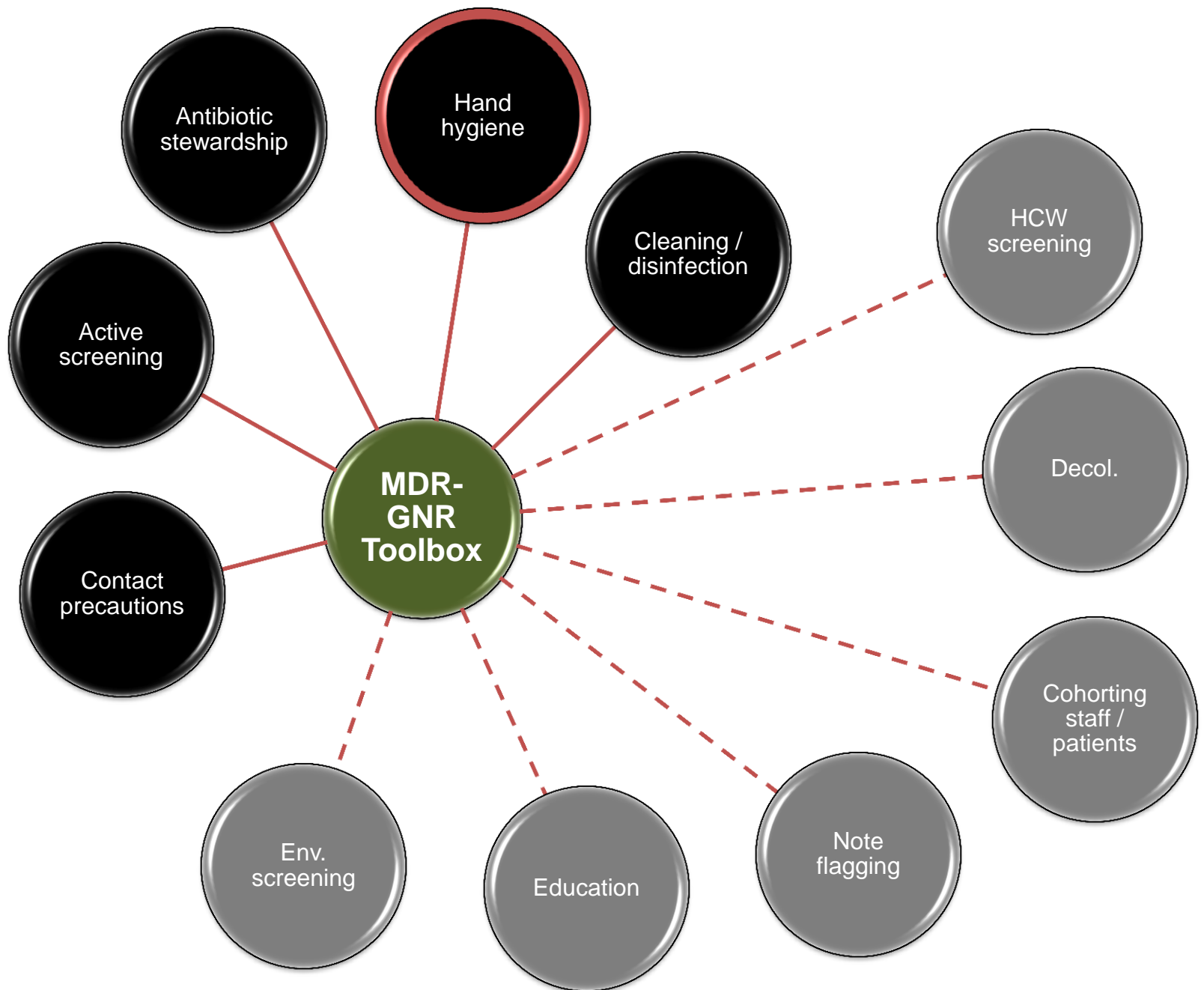
Also consider screening admissions to high-risk units such as ICU, and patients who live overseas.

How do I screen?

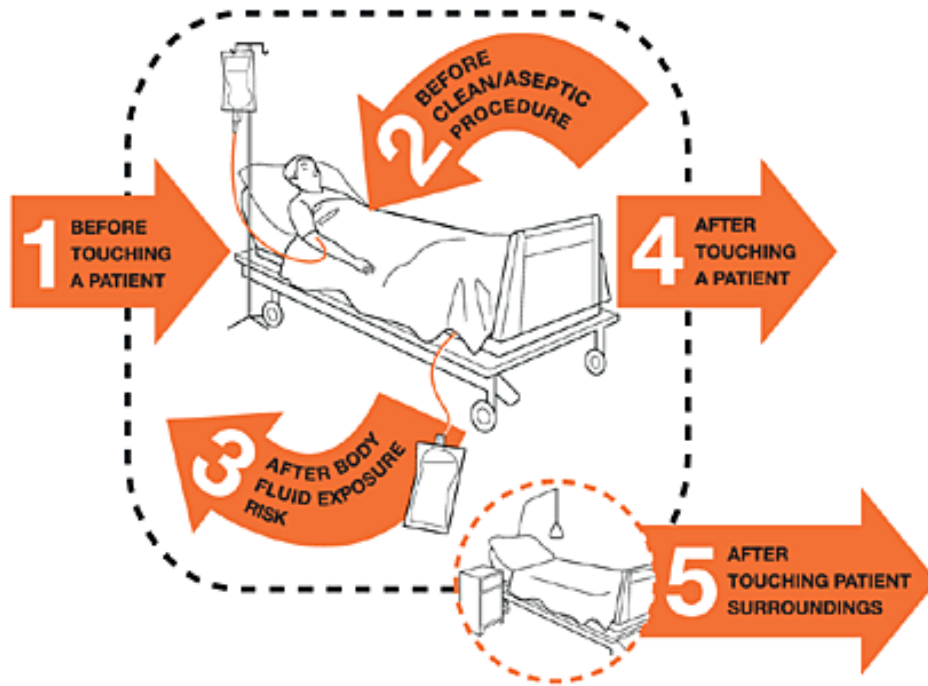
- Rectal swab is the best sample
 - Insert no more than 2cm into rectum
 - Twist gently and withdraw
 - Ideally want to see faeces on swab.
- Patient and staff education as to why this is needed in order to overcome taboos
- Alternate specimen is stool sample, but have to wait for the patient to 'go'

Does screening and isolation work?

	All MDROs	MRSA	VRE	ESBLs
Baseline trend	–	↑	–	–
Hygiene intervention step-change	–	–	–	–
Hygiene intervention trend change	↓	↓	–	–
Screening step-change	–	–	–	–
Screening trend change	–	↑	–	–
Rapid vs. conventional step-change	↑	–	–	↑
Rapid vs. conventional trend-change	–	–	–	–

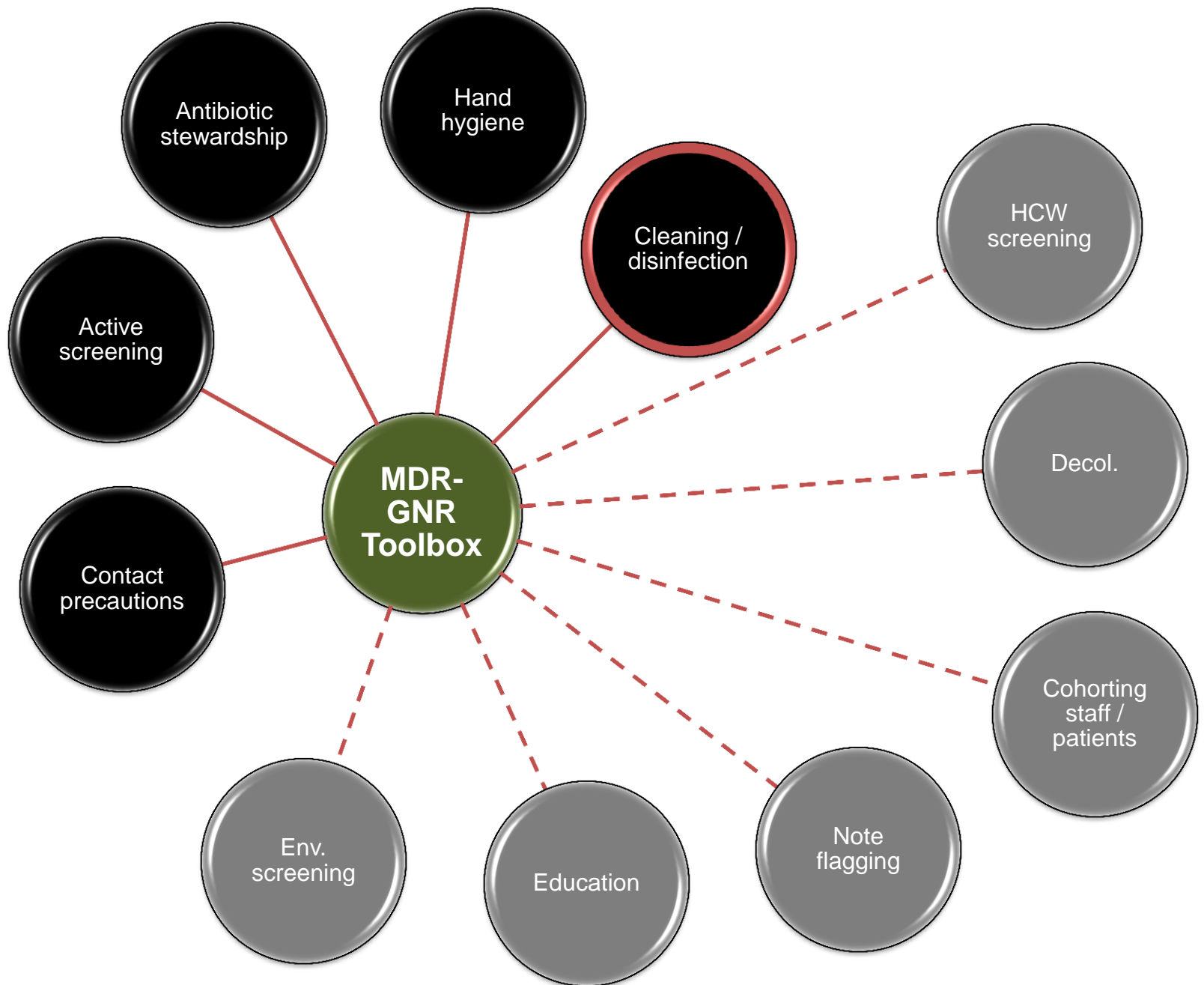


Hand hygiene

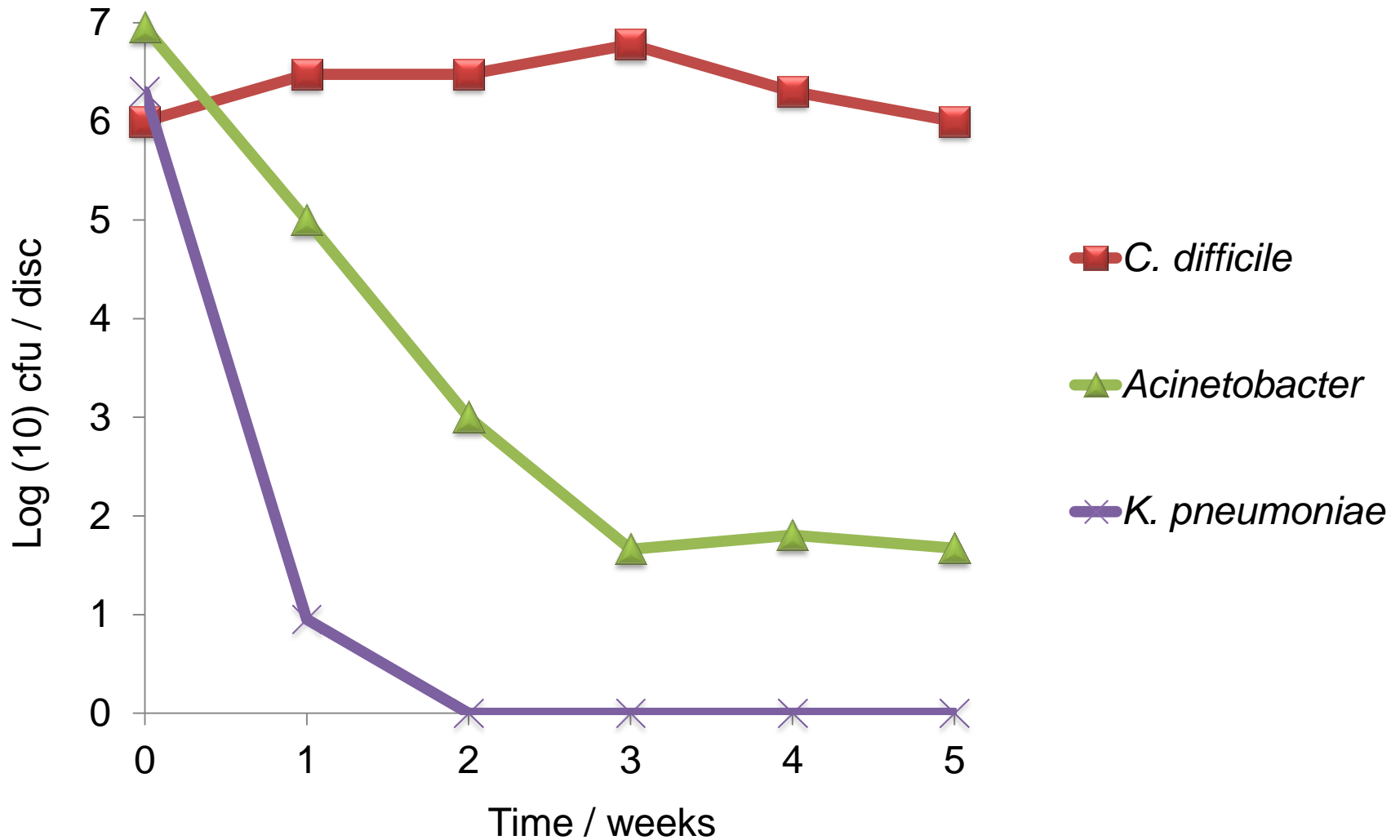


40%

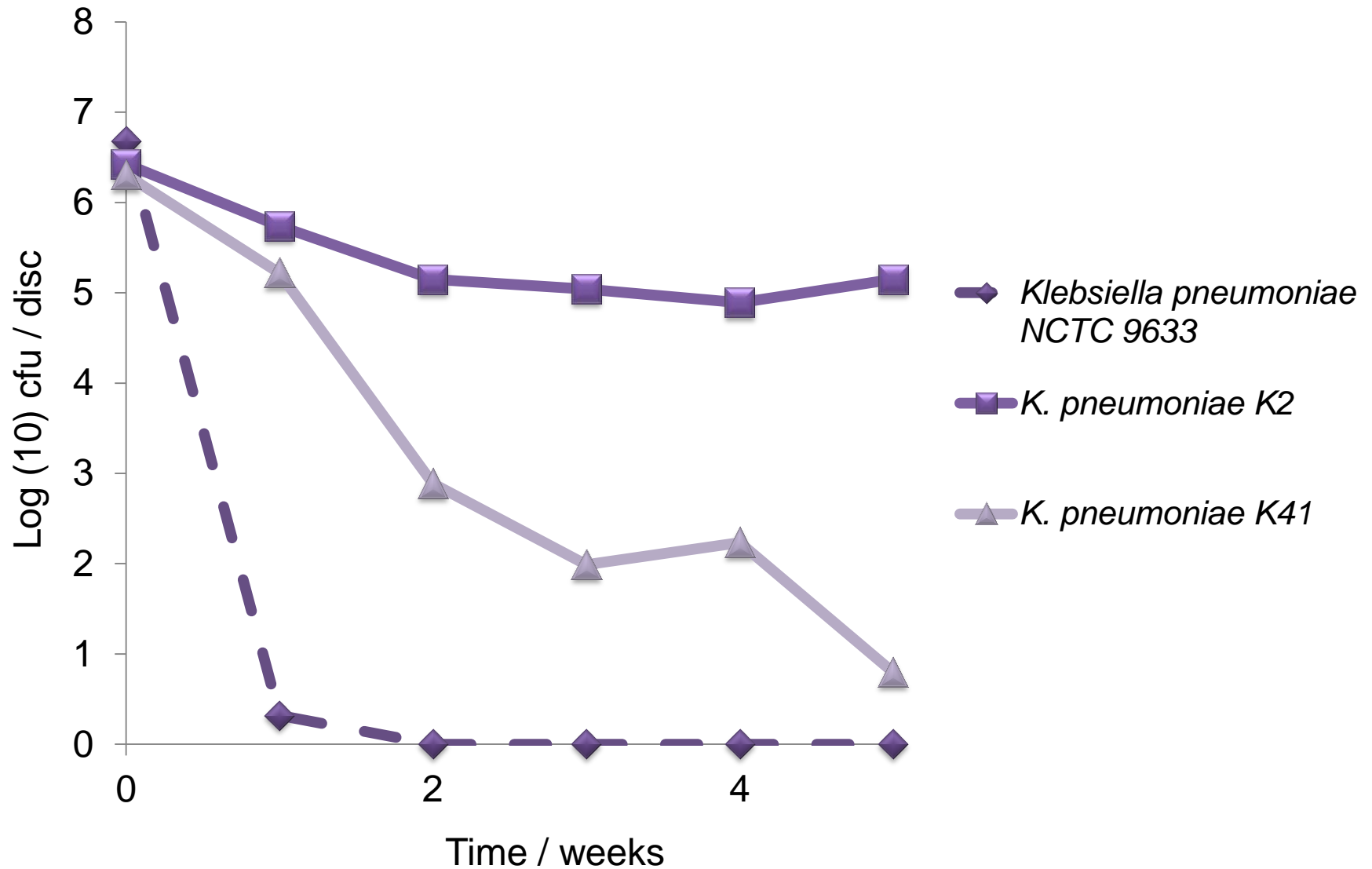
Median hand hygiene compliance
from 95 studies.



Surface survival

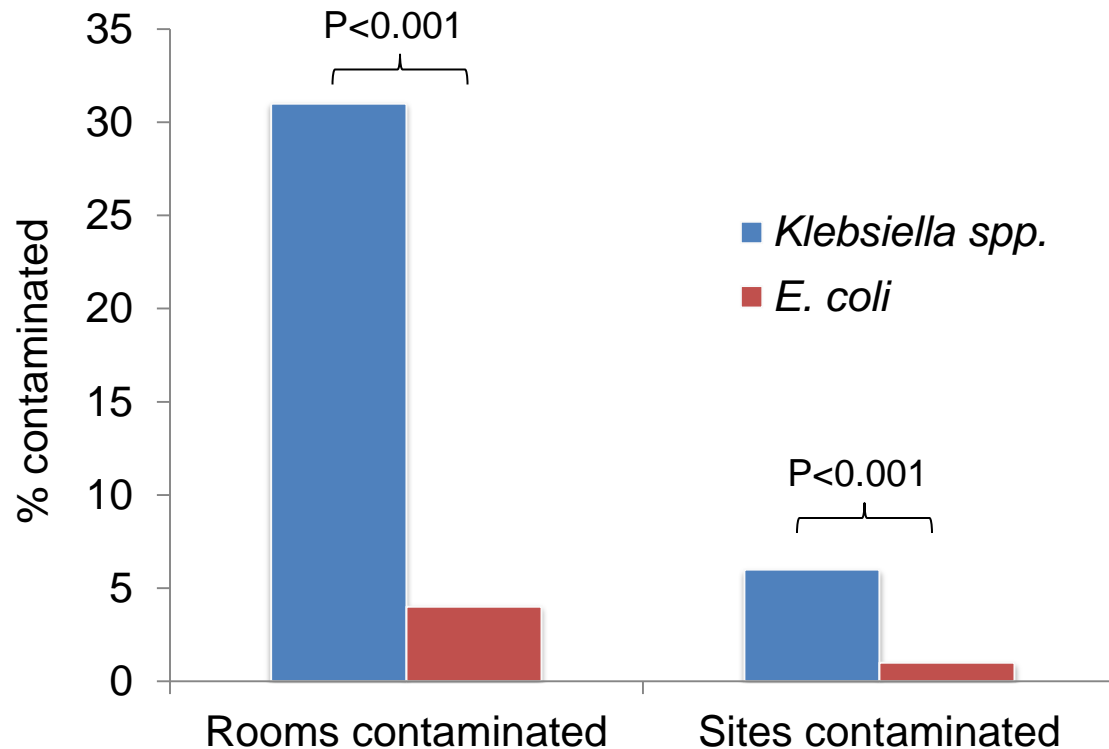


Surface survival – strain variation



K. pneumoniae vs. *E. coli*

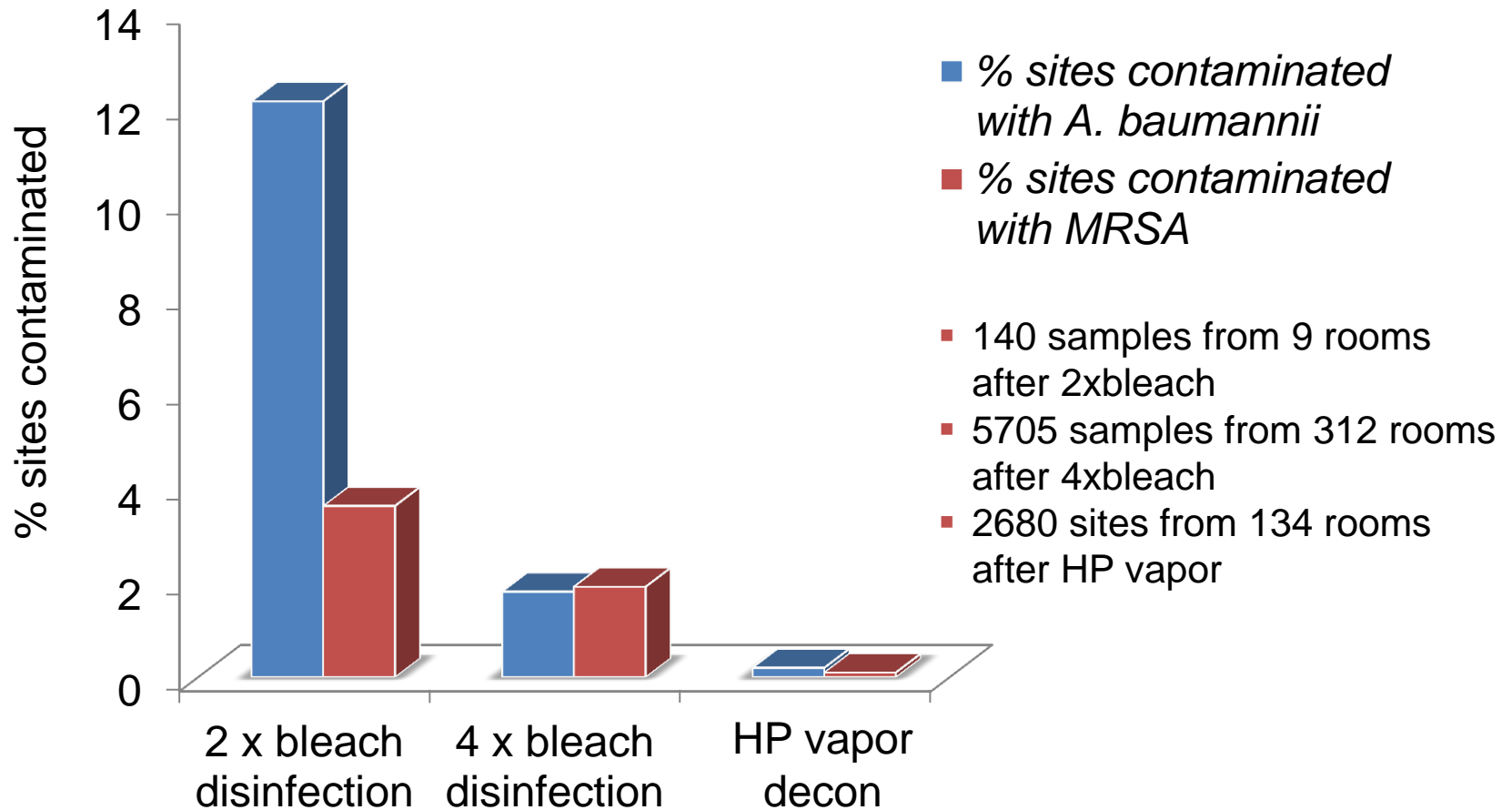
- *K. pneumoniae* seems to be more environmental than *E. coli*.^{1,2}
- Surface contamination on five standardized sites surrounding patients with ESBL-producing *Klebsiella* spp. (n=48) or ESBL-producing *E. coli* (n=46).¹



Risk factors for ESBL-E contamination = ESBL-KP, urinary catheter; carbapenem therapy was protective.³

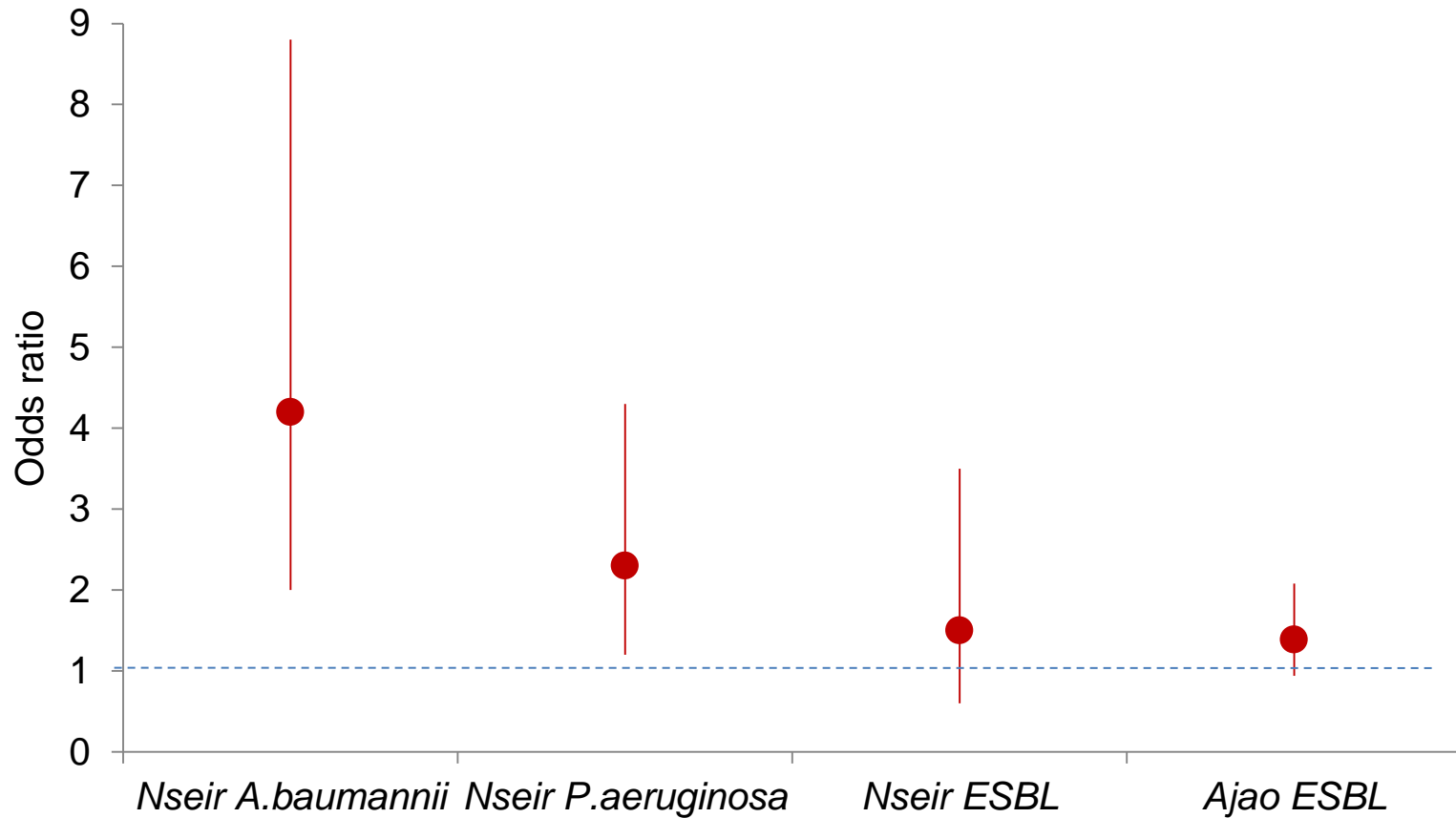
1. Guet-Revillet *et al.* *Am J Infect Control* 2012;40:845-848.
2. Gbaguidi-Haore. *Am J Infect Cont* 2013;41:664-665.
3. Freeman *et al.* *Antimicrob Resist Infect Control* 2014;**3**:5.

Persistent contamination



26.6% of rooms remained contaminated with either MRSA or *A. baumannii* following 4 rounds of bleach disinfection

Enterobacteriaceae “less environmental”



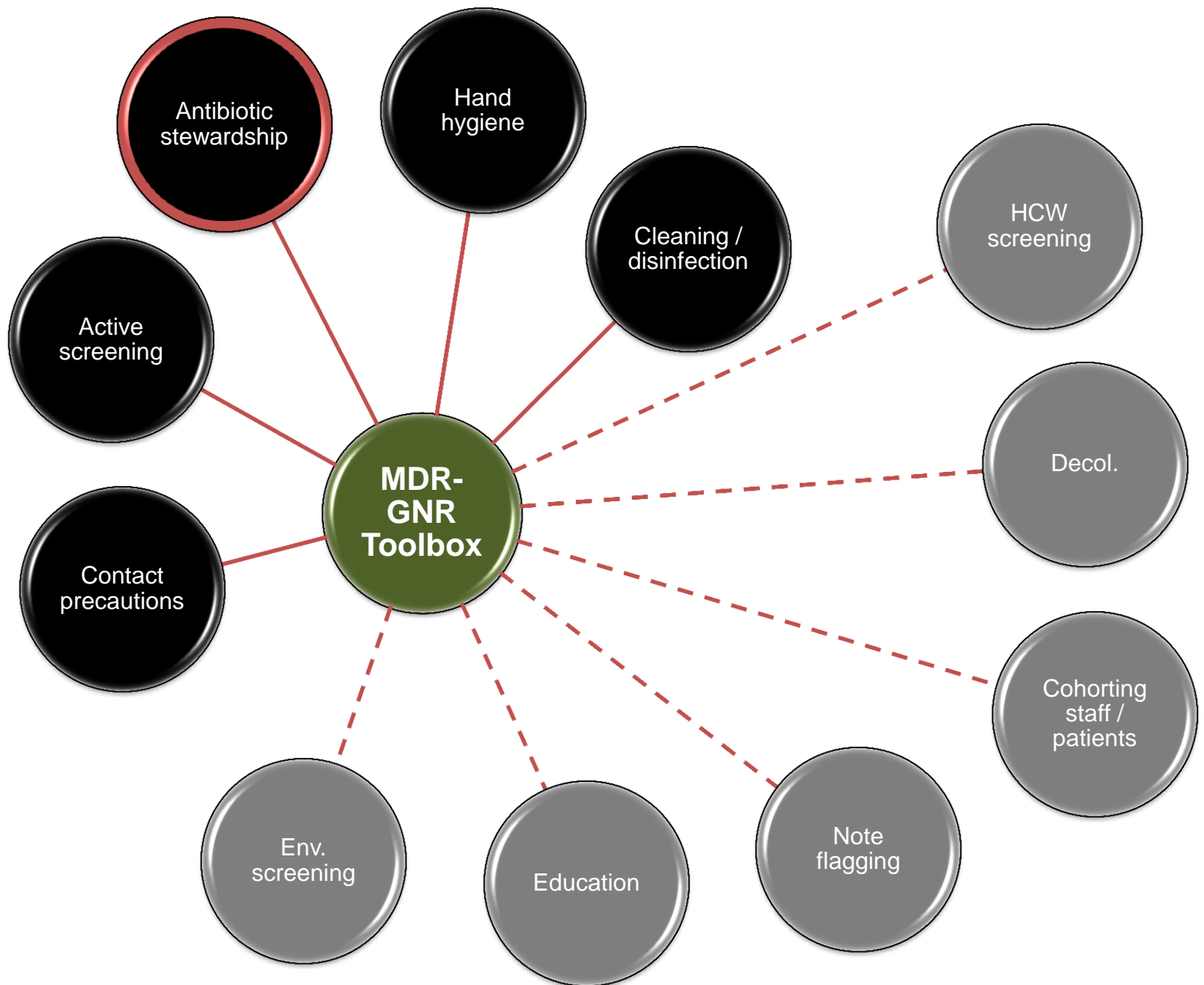
Nseir *et al. Clin Microbiol Infect* 2011;17:1201-1208.

Ajao *et al. Infect Control Hosp Epidemiol* 2013;34:453-458.

MDR-GNR cleaning & disinfection checklist

- Clean / declutter
- Monitor cleaning process (e.g. fluorescent markers)
- Enhanced daily disinfection using bleach
- All equipment disinfected before leaving room
- Terminal disinfection using bleach or, ideally, H₂O₂ vapor¹⁻³

1. Gopinath *et al.* *Infect Control Hosp Epidemiol* 2013;34:99-100.
2. Snitkin *et al.* *Sci Transl Med* 2012;4:148ra116.
3. Verma *et al.* *J Infect Prevent* 2013;7:S37.

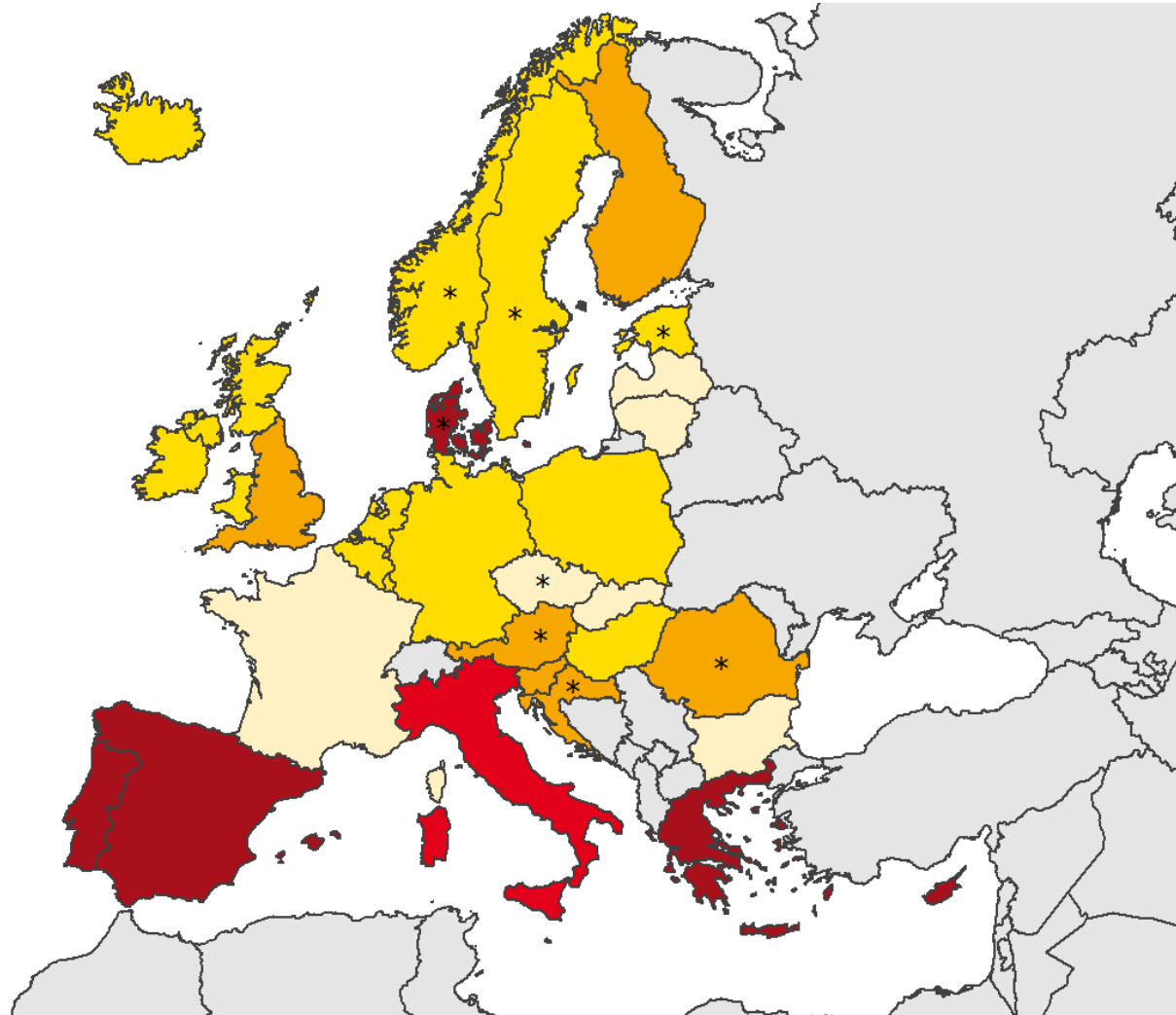
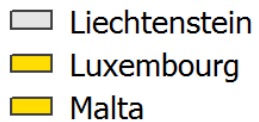


Carbapenem use, Europe

Carbapenem use
(% of patients)

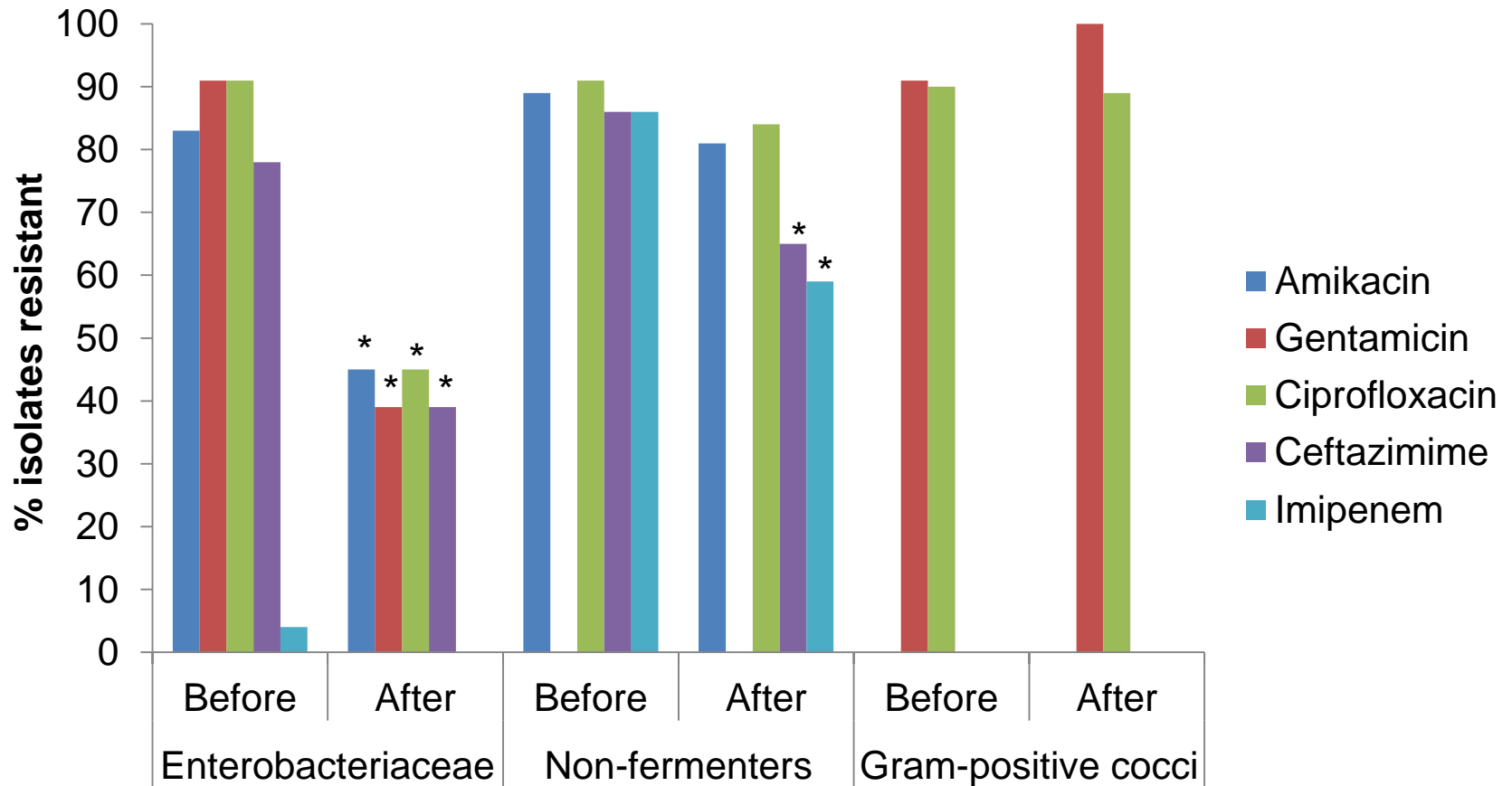


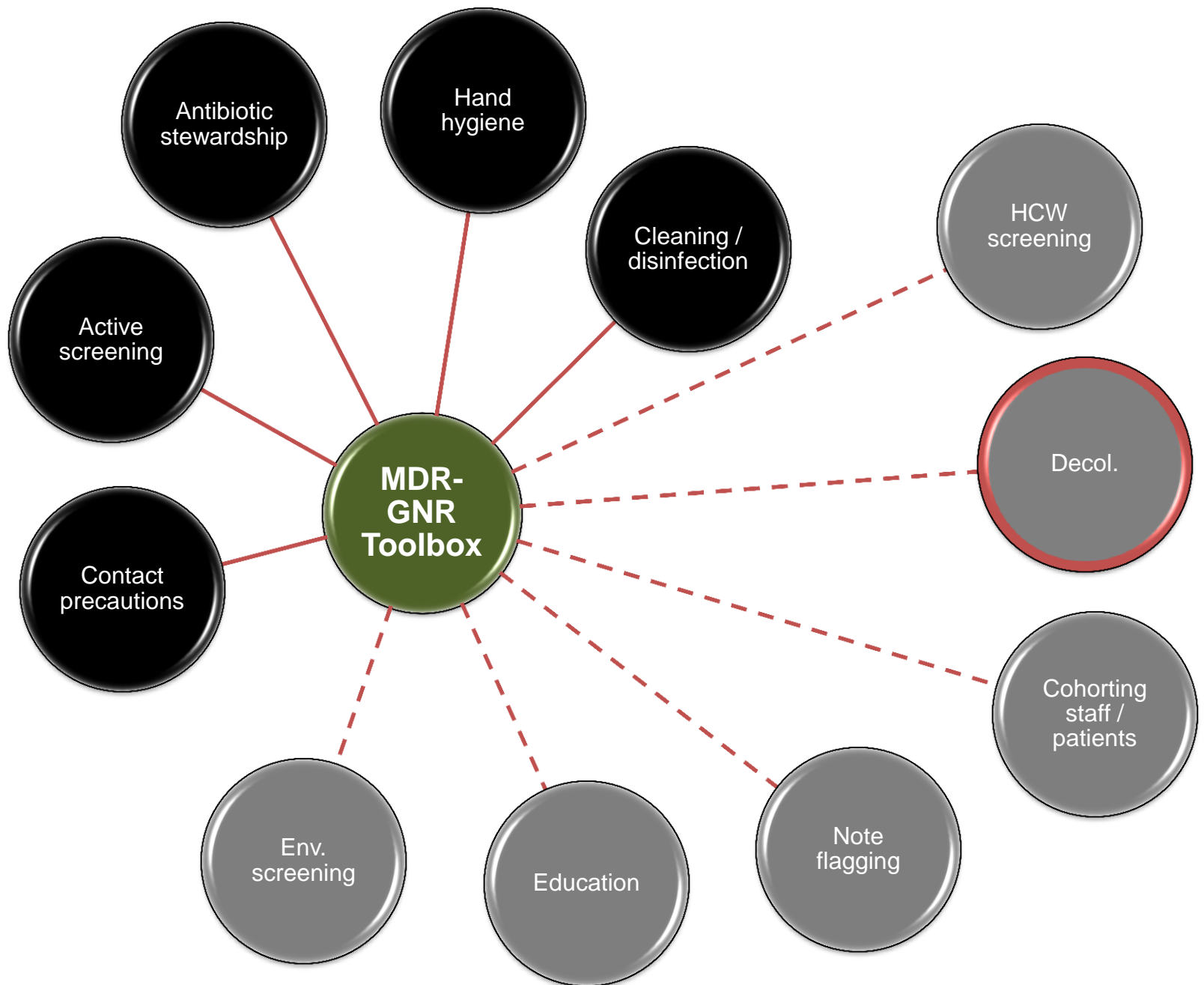
Non-visible countries



Antimicrobial stewardship – impact

Evaluating impact of 6 month antimicrobial stewardship intervention on an ICU by comparing bacterial resistance for matched 6 month periods either side of intervention.





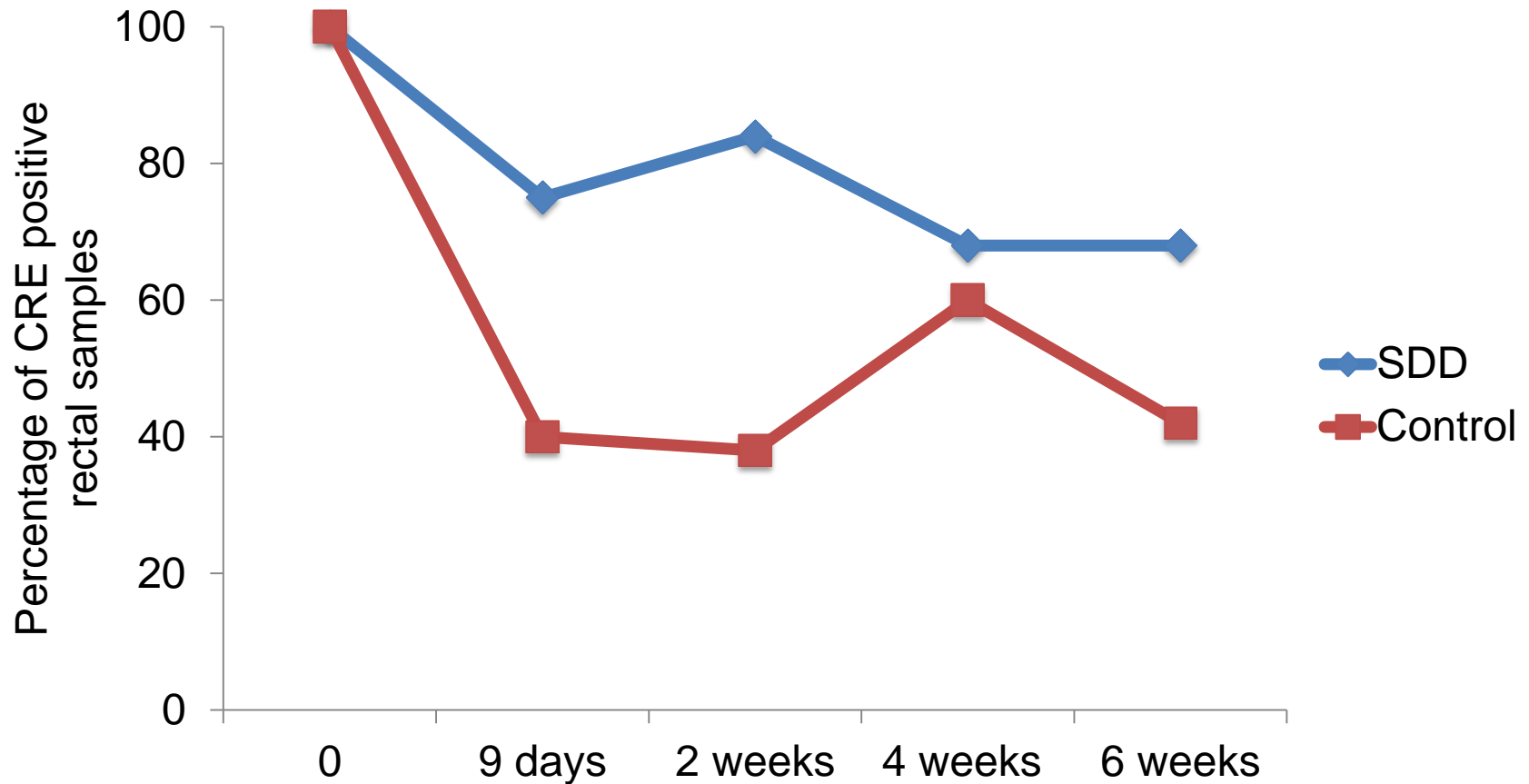
Deisolation?

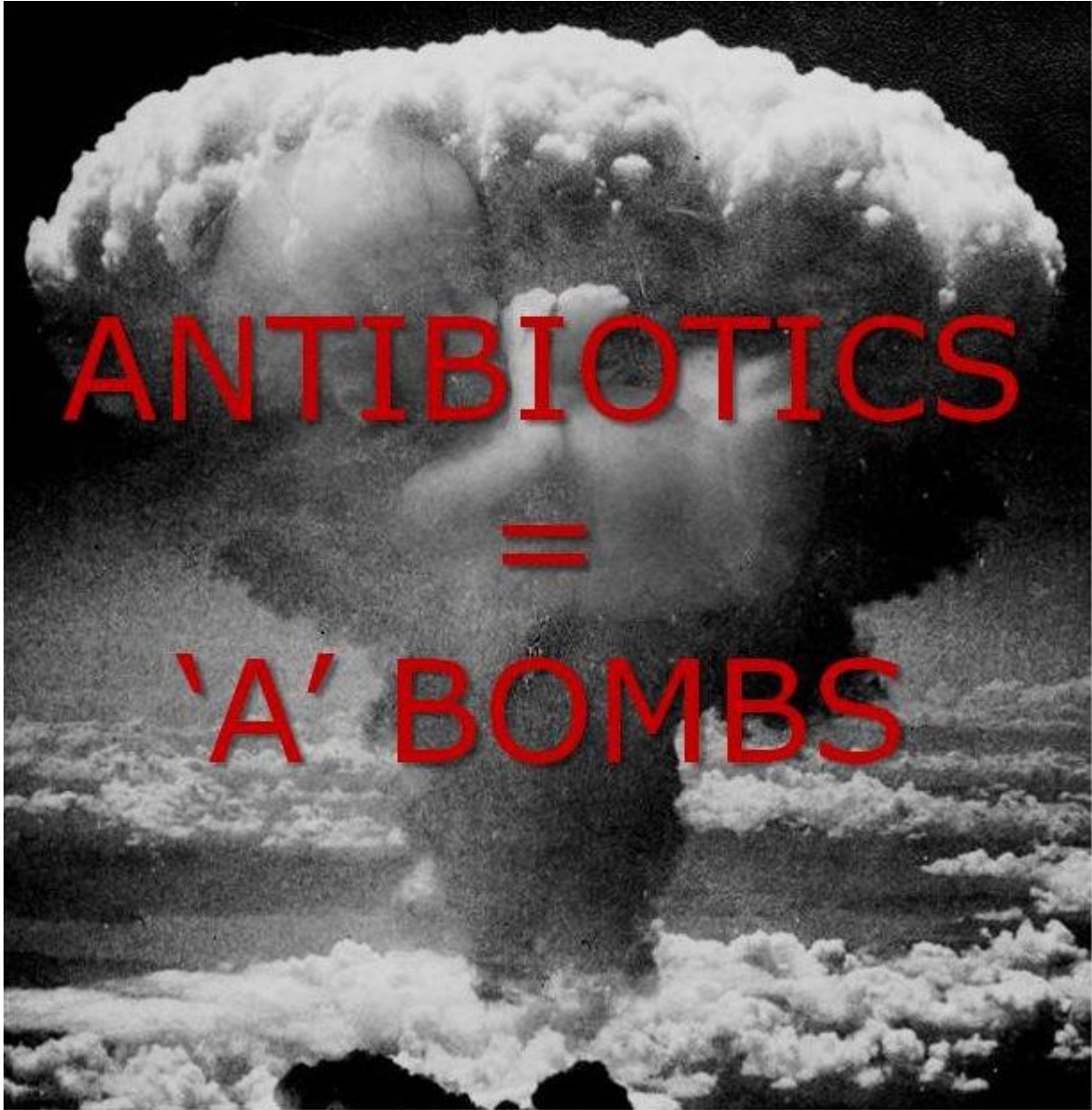
Author	Year	Setting	N pts	Organism	Duration of colonization
Bird ¹	1998	Elderly care facilities, Scotland	38	ESBL <i>K. pneumoniae</i>	Mean 160 days (range 7-548)
Pacio ²	2003	Long term care facility, USA	8	Resistant Gram-negative rods	Median 77 days (range 47-189)
Zahar ³	2010	Paediatric hospital, France	62	ESBL Enterobacteriaceae	Median 132 days (range 65-228)
O'Fallon ⁴	2009	Long term care facility, USA	33	Resistant Gram-negative rods	Median 144 days (range 41–349)
Zimmerman ⁵	2013	Patients discharged from hospital, Israel	97	CRE	Mean 387 days

1. Bird *et al. J Hosp Infect* 1998;40:243-247.
2. Pacio *et al. Infect Control Hosp Epidemiol* 2003;24:246-250.
3. Zahar *et al. J Hosp Infect* 2010;75:76-78.
4. O'Fallon *et al. Clin Infect Dis* 2009;48:1375-1381.
5. Zimmerman *et al. Am J Infect Control* 2013;41:190-194.

'Selective' digestive decontamination

20 CRE colonized patients in each arm given gentamicin + polymyxin (SDD arm) or placebo (Control arm)





ANTIBIOTICS

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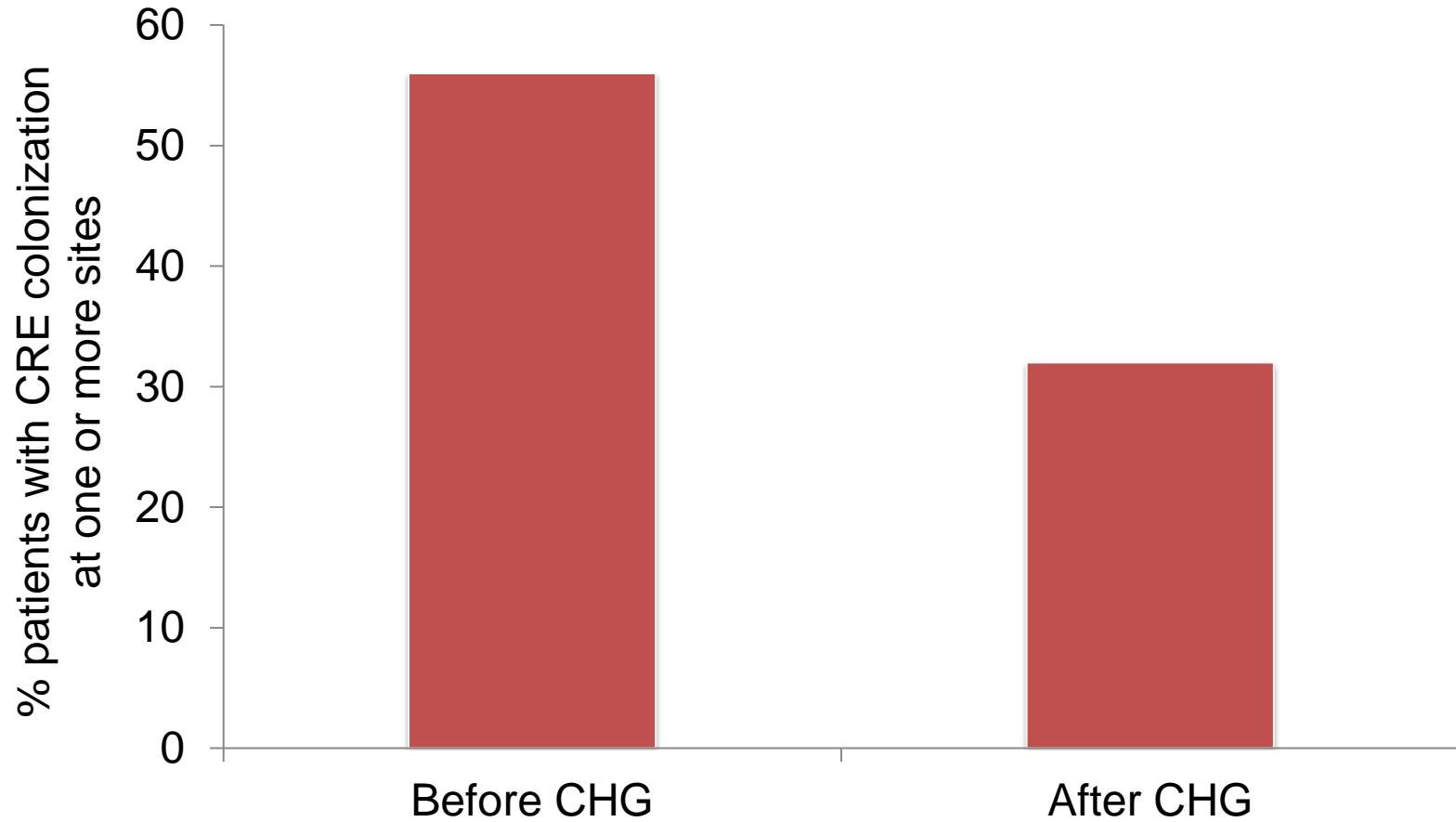
'A' BOMBS

Decolonisation using faecal microbiota transplantation (FMT)

- 82 year old colonised with CRE.
- Carriage was delaying her admission to a nursing home.
- Single dose of FMT decolonised her at 7 and 14 days.

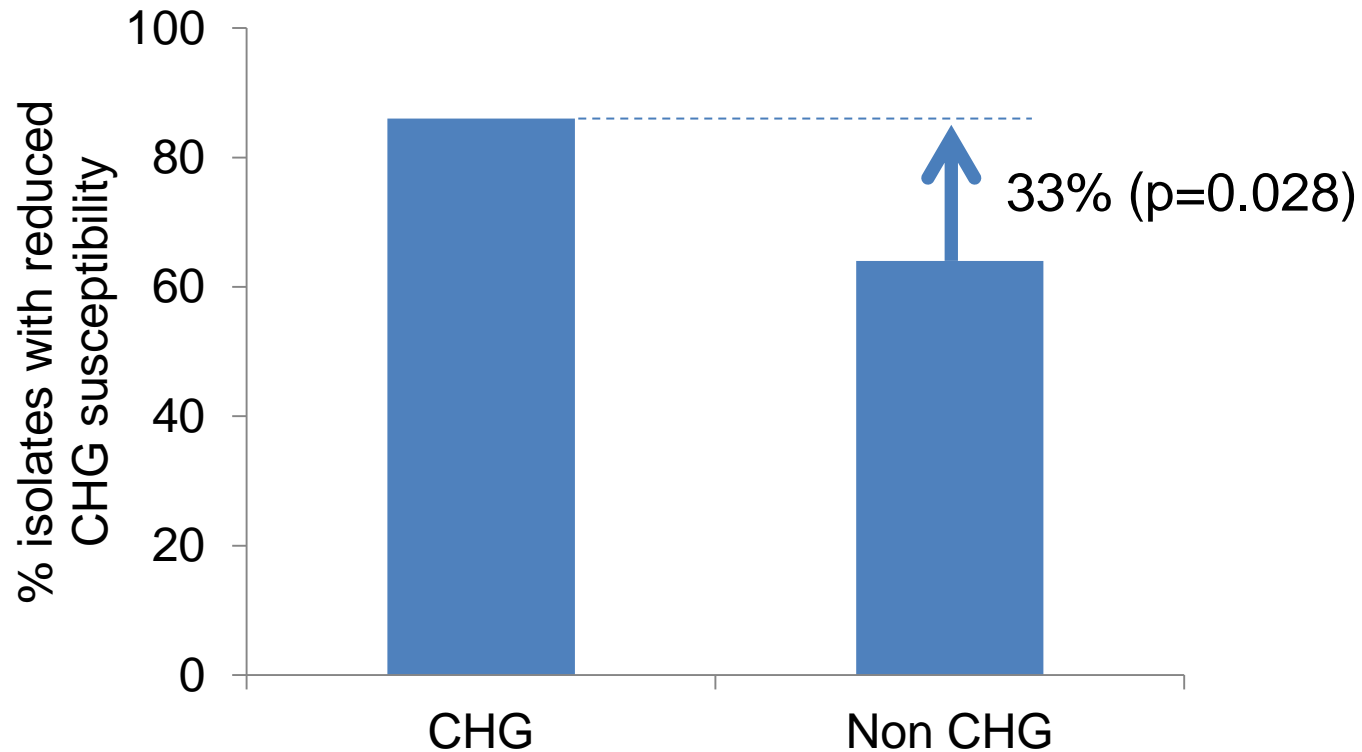
Chlorhexidine – efficacy

Impact of chlorhexidine gluconate (CHG) daily bathing on skin colonization with KPC-producing *K. pneumoniae* in 64 long-term acute care patients.

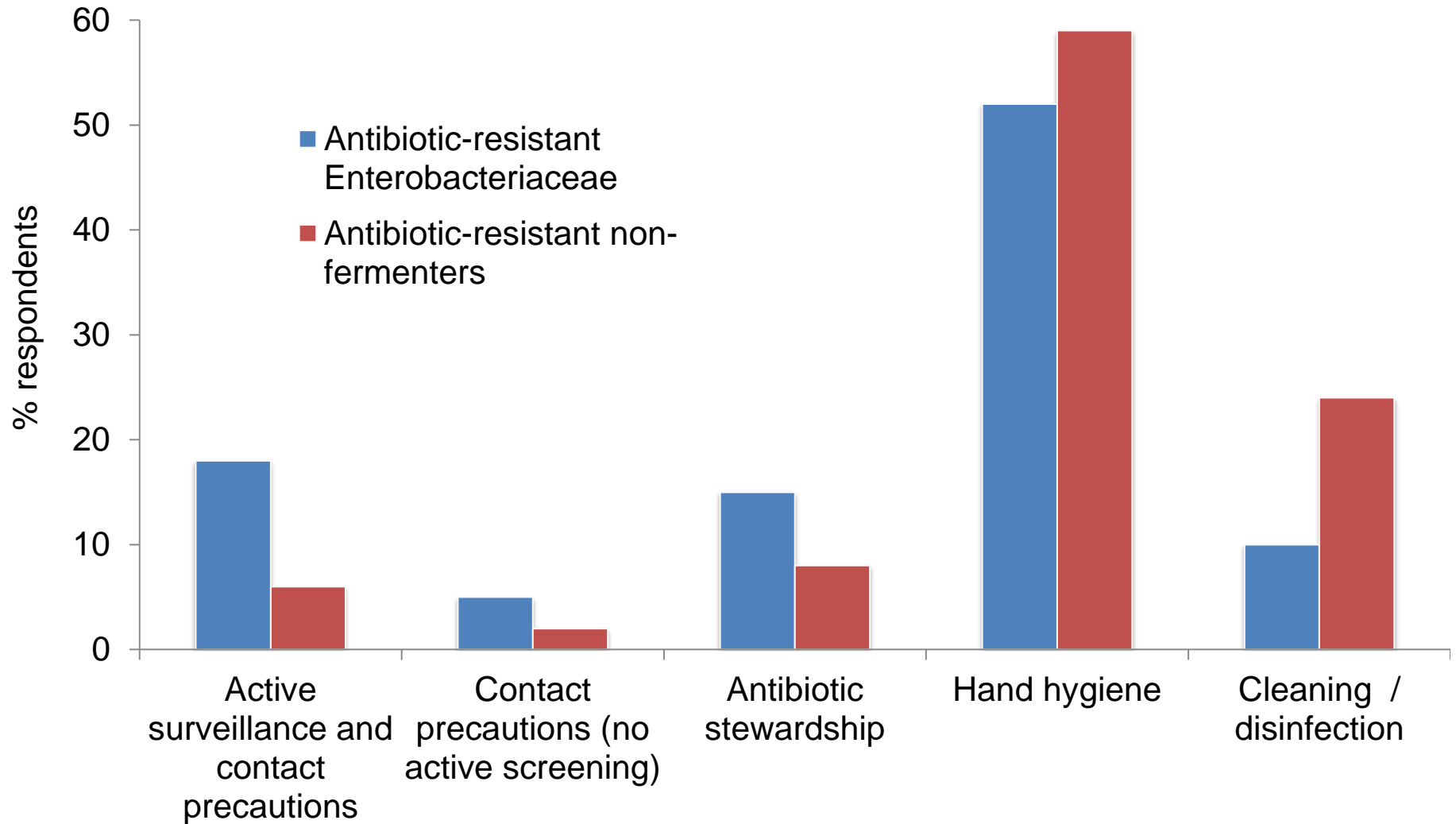


Chlorhexidine – reduced susceptibility

Proportion of BSI isolates with reduced susceptibility to chlorhexidine on units using chlorhexidine gluconate (CHG) daily bathing (n=28) or not (n=94).



Which do you consider to be the most important measure to prevent transmission?



[Data from around 150 webinar participants, mainly in the US, 2014.](#)



Type	n studies	Failure rate	Odds ratio
Bundled intervention	75	28%	1.9
Single intervention	11	45%	

What works? NIH



Hand
hygiene

Active
surveillance

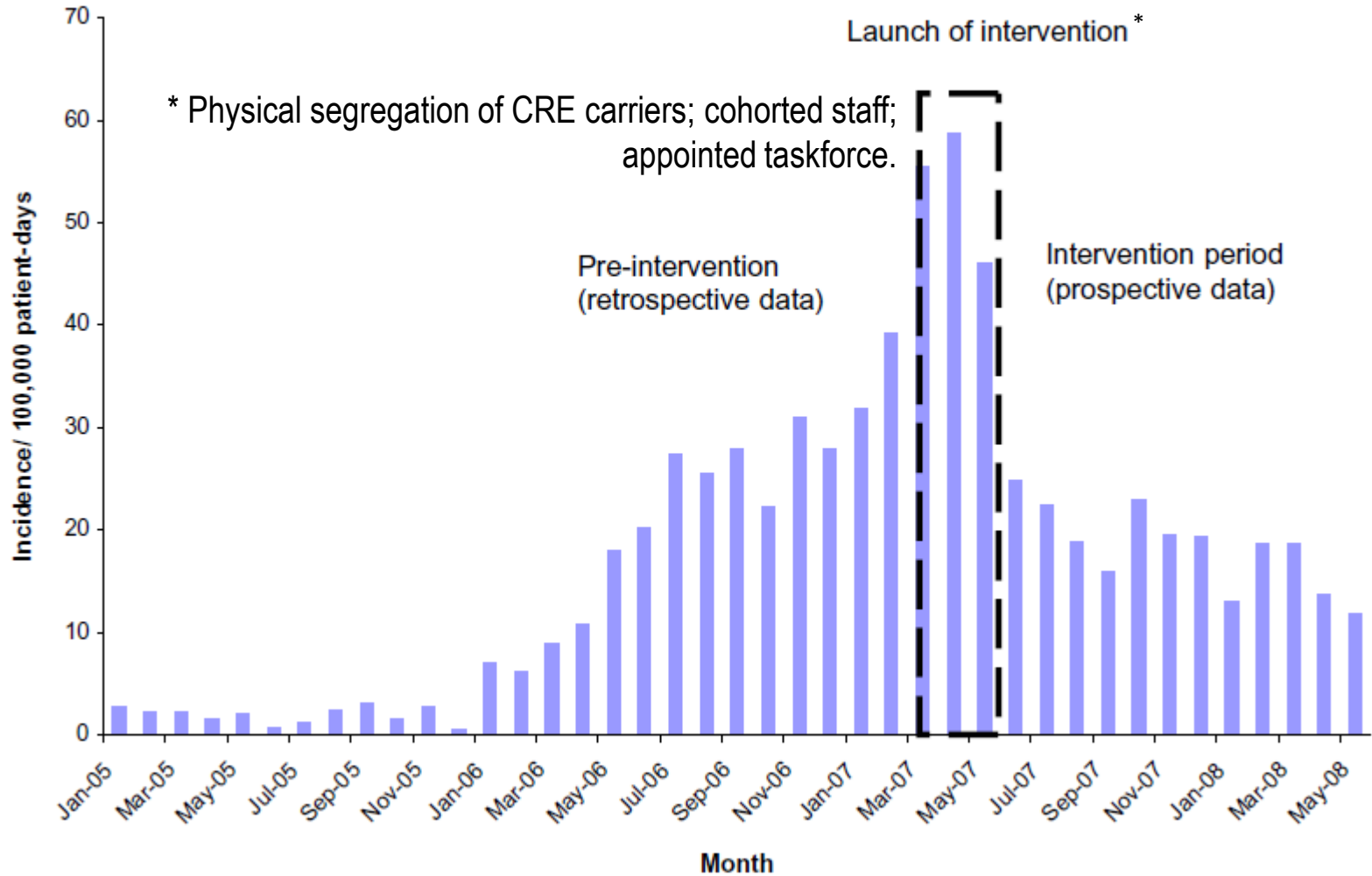
Isolation &
cohorting

Cleaning &
disinfection

Also:

- Daily chlorhexidine baths
- 'Enforcers' for hand hygiene compliance
- Communication with all staff
- Hydrogen peroxide vapor
- Characterisation of outbreak strains (WGS)

What works? Israel



Summary

1. Enterobacteriaceae (mainly *K. pneumoniae*) and non-fermenters (mainly *A. baumannii*) have fundamental differences in their epidemiology – and require a different approach to control.
2. We still don't really know what works to control MDR-GNR.
3. A “kitchen sink” approach (aka bundle) should be deployed!
4. Effective strategies should include:
 - Hand hygiene
 - Screening & contact precautions
 - Antimicrobial stewardship
 - Cleaning & disinfection

European approaches to MDR-GNR prevention and control

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