3M Infection Prevention Solutions

# Filling the gaps in the guidelines to control resistant Gram-negative bacteria

3M Learning Connection

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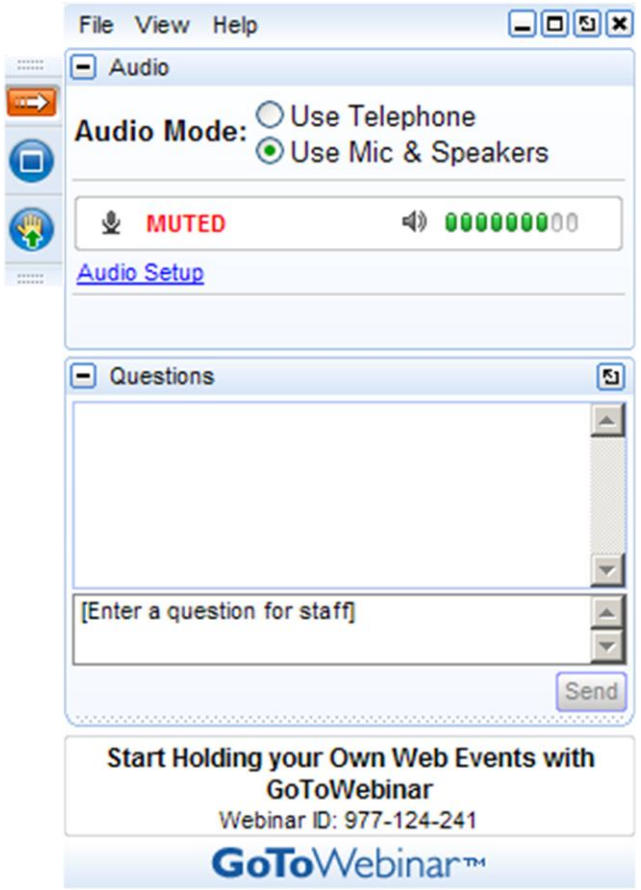
3M

# House Keeping

## Questions

From the GoToWebinar page:

- Click on the orange box with a white arrow to expand your control panel (upper right-hand corner of your screen).
- Type a question in the question box and click send.



# House Keeping

**Continuing Education**

Each 1 hour web meeting qualifies for 1 contact hour for nursing. 3M Health Care Provider is approved by the California Board of Registered Nurses CEP 5770.

**Post webinar eMail**

- Link to Course Evaluation
- CE Certificate Included
- Forward eMail to Others in Attendance

# Disclosure

I am employed part-time by Bioquell and received payment from 3M for this webinar.

1. Aug 19: CRE and friends: what's the problem and how to detect them?

2. Sept 16: Not all resistant Gram-negative bacteria are created equal: Enterobacteriaceae vs. non-fermenters

3. Oct 7: Filling the gaps in the guidelines to control resistant Gram-negative bacteria

# Learner objectives

1. Provide an overview of the available guidelines to control CRE and other resistant Gram-negative bacteria.

2. Identify gaps in the guidelines, in terms of definitions of standard precautions, outbreak epidemiology and who should be on the guidelines writing dream team.

3. Discuss controversial areas in terms of effective interventions: patient isolation, staff cohorting and selective digestive decontamination.

# Rising threat from MDR-GNB

% of all HAI caused by GNBs.

% of ICU HAI caused by GNBs.

| **Non-fermenters** | ***Acinetobacter baumannii***<br>***Pseudomonas aeruginosa***<br>***Stenotrophomonas maltophilia*** |
|---|---|
| Enterobacteriaceae | *Klebsiella pneumoniae*<br>*Escherichia coli*<br>*Enterobacter cloacae* |

Hidron et al. *Infect Control Hosp Epidemiol* 2008;29:966-1011.
Peleg & Hooper. *N Engl J Med* 2010;362:1804-1813.

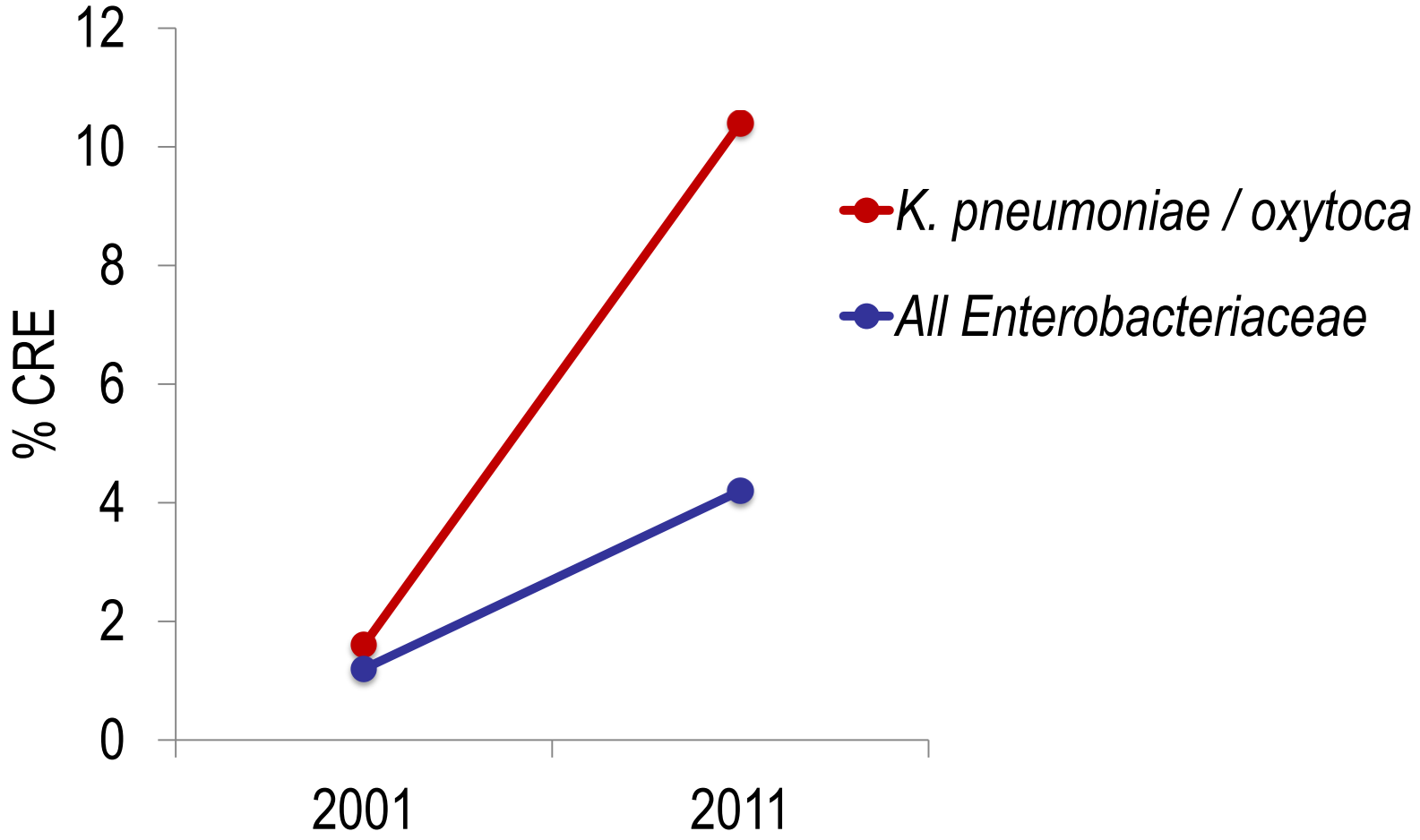
| Enterobacteriaceae (e.g. *Klebsiella pneumoniae*) vs. non-fermenters (e.g. *Acinetobacter baumannii*). | |
|---|---|
| **Share** | **Differ** |
| Gram stain reaction | Risk factors & at-risk population |
| Concerning AMR | Potential for epidemic spread |
| | Infection profile & mortality |
| | Prevalence |
| | Colonisation site & duration |
| | Transmission routes |
| | Resistance profile & mechanisms |

# Infection prevention and control challenges

| Pathogen | CRE[1] | CRAB[2] | MRSA | VRE | *C. difficile* |
|---|---|---|---|---|---|
| Resistance | +++ | +++ | + | + | +/- |
| Resistance genes | Multiple | Multiple | Single | Single | n/a |
| Species | Multiple | Single | Single | Single | Single |
| HA vs CA | HA & CA | HA (ICU) | HA | HA | HA |
| At-risk pts | All | ICU | Unwell | Unwell | Old |
| Virulence | +++ | +/- | ++ | +/- | + |
| Environment | +/- | +++ | + | ++ | +++ |

1. Carbapenem-resistant Enterobacteriaceae.
2. Carbapenem-resistant *Acinetobacter baumannii*.

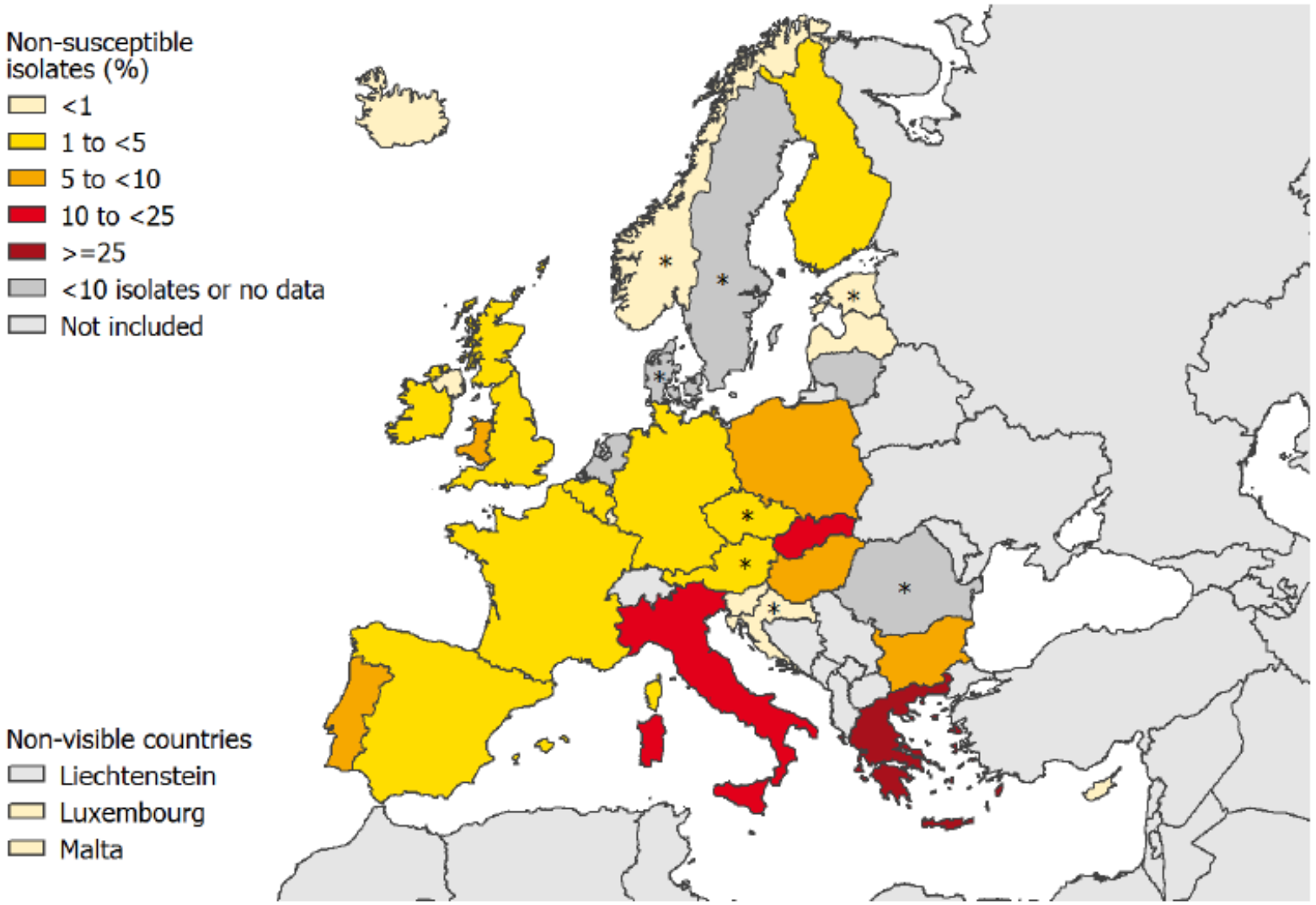
# CRE in the USA




NHSN / NNIS data; *MMWR* 2013;62:165-170.

# CRE in Europe

## Enterobacteriaceae non-susceptible to carbapenems (n=2,787)

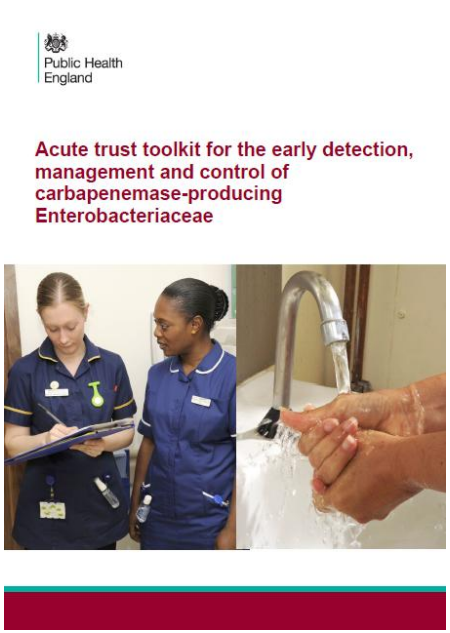



ECDC point prevalence survey 2013.

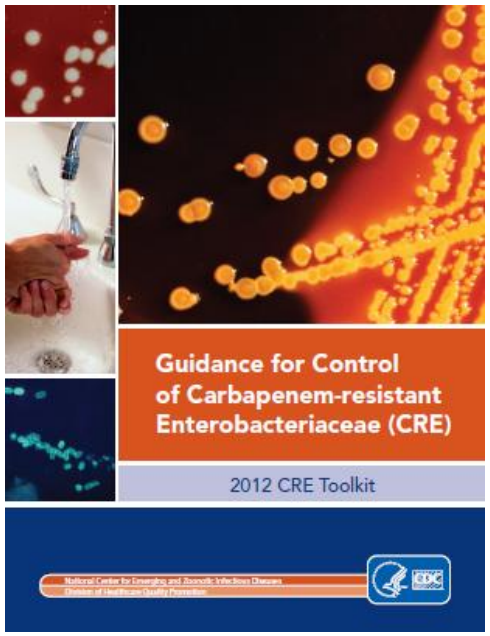
Poll: Do you know where to get guidelines for controlling multidrug-resistant Gram-negative bacteria?

A) Yes
B) No

# Available guidelines (not exhaustive list!)



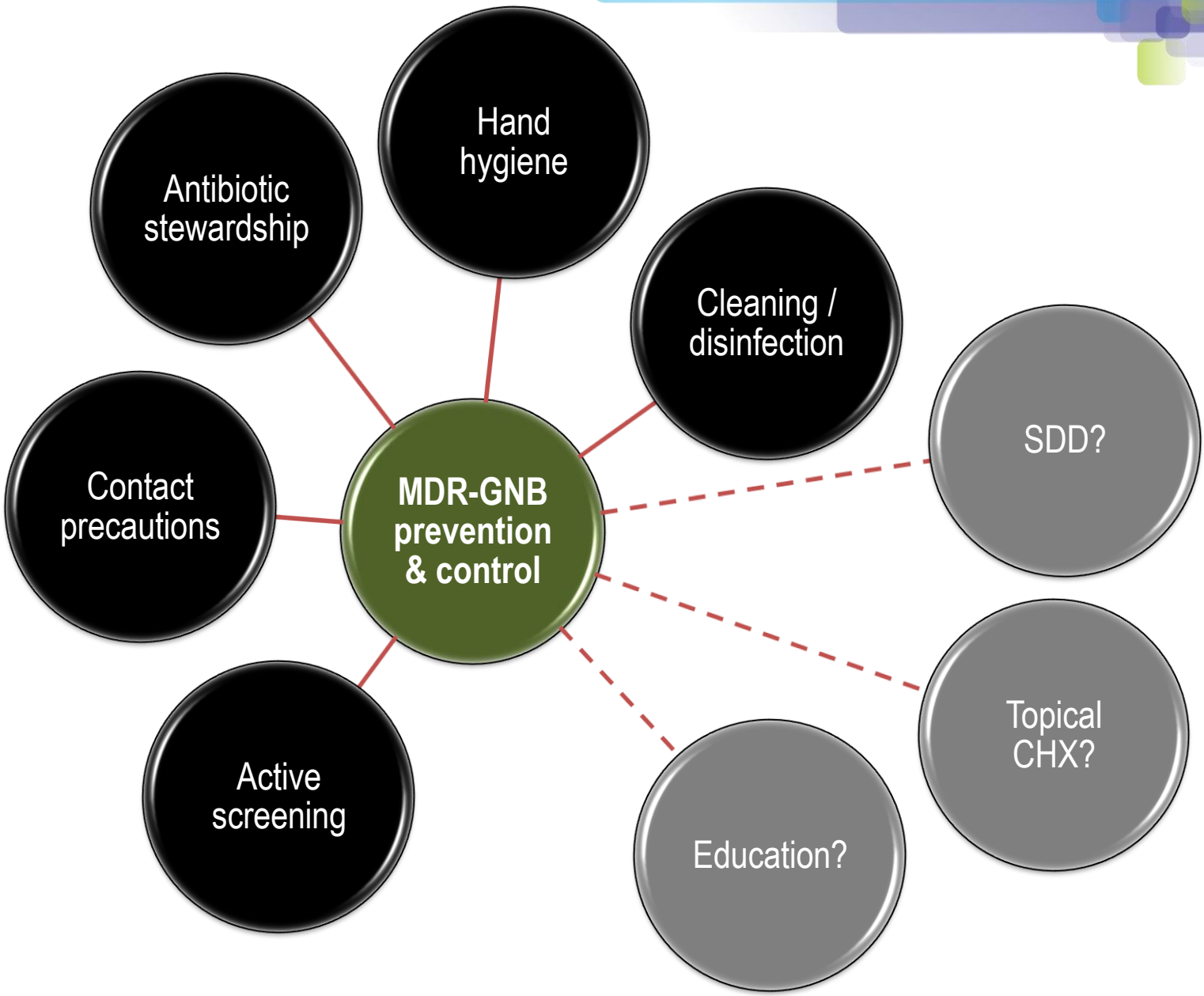

UK CRE Toolkit




US CRE Toolkit


ESCMID Guidelines

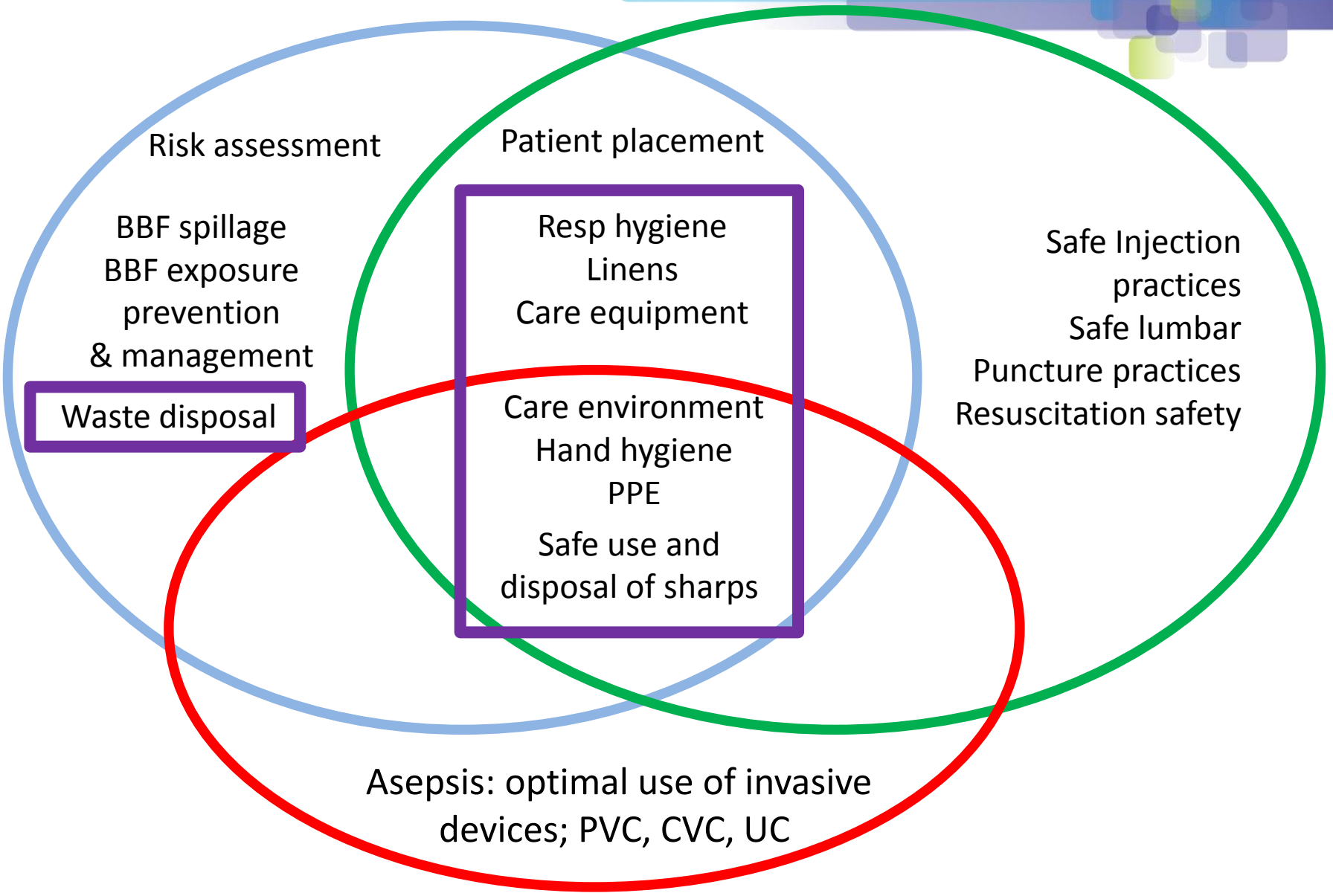
# Guidelines ≠ Policy




Tacconelli *et al. Clin Microbiol Infect* 2014;20 Suppl 1:1-55

# CRE toolkits in the US and UK compared

| | | US Toolkit | UK Tookit |
|---|---|---|---|
| Isolation | Contact precautions, confirmed cases | Recommended | Recommended |
| | Preemptive contact precautions | Suggested | Recommended |
| | Contact precautions for duration of stay | No recommendation | Recommended |
| Screening | Screen 'high risk' patients on admission | Suggested | Recommended |
| | Point prevalence on high risk units | Recommended | Suggested |
| | Contact screening | Recommended | Recommended |
| | Screen staff / household contacts | No recommendation | Not recommended |
| Other | 'Enhanced' infection control measures | Recommended | Recommended |
| | Enhanced disinfection | No recommendation | Recommended |
| | Cohort patients and staff | Suggested | Recommended |
| | Flag patient record & inform receiving facilities | Recommended | Recommended |
| | Tiered local approach | Recommended | Recommended |
| | Develop action plan, education of all staff | Recommended | Recommended |
| | Implement antimicrobial stewardship | Recommended | Recommended |
| | Topical decolonisation during outbreaks | Suggested | Suggested |




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-standared-precautions.html
UK Epic3: http://www.sciencedirect.com/science/article/pii/S0195670113600122
WHO: www.who.int/csr/resources/publications/EPR_AM2_E7.pdf

JIP

# Outbreak Column 15: Carbapenemase-producing Enterobacteriaceae

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Outbreak Column 15 covers the often confusing 'carbapenemase producing Enterobacteriaceae' (CPE), the epidemic curve which has yet to reach base camp. Although there is no doubt that this family of organisms presents a formidable public health challenge, there is some debate about what needs to be done to prevent and control outbreaks. Although the challenge from CPE has only been recognised since the mid-1990s (Queenan and Bush, 2007), the task for the Outbreak Column appears equally as daunting as that presented by *Staphylococcus aureus* – which has been a nosocomial challenge for considerably longer (Curran, 2014a). The high-reliability characteristic '*deference to expertise*' (Weick et al, 1999), is being demonstrated in this column in that it has been co-authored by Dr Jon Otter, whose personal expertise has enabled the topic to be tackled from a more learned perspective.

In this review, we provide:

- A synopsis of the CPE challenge
- An assessment of the strengths and weaknesses of the available guidance and toolkits
- Guidance on developing a strategy to prevent CPE outbreaks

To supplement this column an online appendix is available to the readers. This is a narrative review that drew from the following three sources of information: The online appendix is available at http://jip.sagepub.com/supplemental.

- Reviews of CPE epidemiology
- National and international guidelines to control the organisms
- Outbreak reports

## The challenge from antibiotic resistant Enterobacteriaceae

Gram-negative bacteria of the Enterobacteriaceae family, more commonly *Klebsiella pneumoniae* and *Escherichia coli*, were found to be the most frequent organisms detected in relation to healthcare associated infections in recent national prevalence surveys (Health Protection Agency, 2012; Health Protection Scotland, 2012; Zarb et al, 2012). The Enterobacteriaceae are also a substantial cause of infections in community settings (Farrell et al, 2003). These organisms have become sequentially resistant to several classes of antibiotics: first beta-lactams, then extended spectrum beta-lactams (ESBLs) and most recently the carbapenems (Carmeli et al, 2010; Ho et al, 2010; Peleg and Hooper, 2010). Of note it was only resistance to the third generation carbapenems that posed a therapeutic challenge, as these antibiotics are first-line treatments. Although non-Enterobacteriaceae Gram-negative bacteria that are resistant to carbapenems, such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, represent both a therapeutic challenge and an infection control problem at times, they are largely restricted to intensive care units and other high risk settings (Dijkshoorn et al, 2007; Loveday et al, 2014a; Paterson, 2006). CPE present the most serious threat to a broader group of patients, with the additional capacity for spread outside of hospitals. Effective therapy for CPE is more difficult and can be limited to older, less effective and less well-tolerated agents such as colistin (Carmeli et al, 2010).

## Resistance mechanisms

Enterobacteriaceae may be resistant to carbapenems either through the production of an acquired carbapenemase, or the production of an extended-spectrum beta-lactamase (ESBL)/AmpC combined with porin loss (Nordmann and Poirel, 2013).

Key differentiation:

- Carbapenem-resistant Enterobacteriaceae (CRE) are resistant to carbapenems by any mechanism, including the production of an acquired carbapenemase, or the production of an ESBL/AmpC combined with porin loss
- Carbapenemase-producing Enterobacteriaceae (CPE) are resistant to carbapenems by means of an acquired carbapenemase.

The key issues with CPE arise because higher levels of resistance are produced by acquired carbapenemases (typically KPC, VIM, IMP, NDM and OXA-48 types); the organisms themselves are, like all Gram negatives, easily transmissible, plus they have the potential for horizontal gene transfer between related bacteria (Ho et al, 2010; Gupta et al, 2011; Canton et al, 2012; Nordmann and Poirel, 2013). Horizontal gene transfer between bacteria means cross-infection and

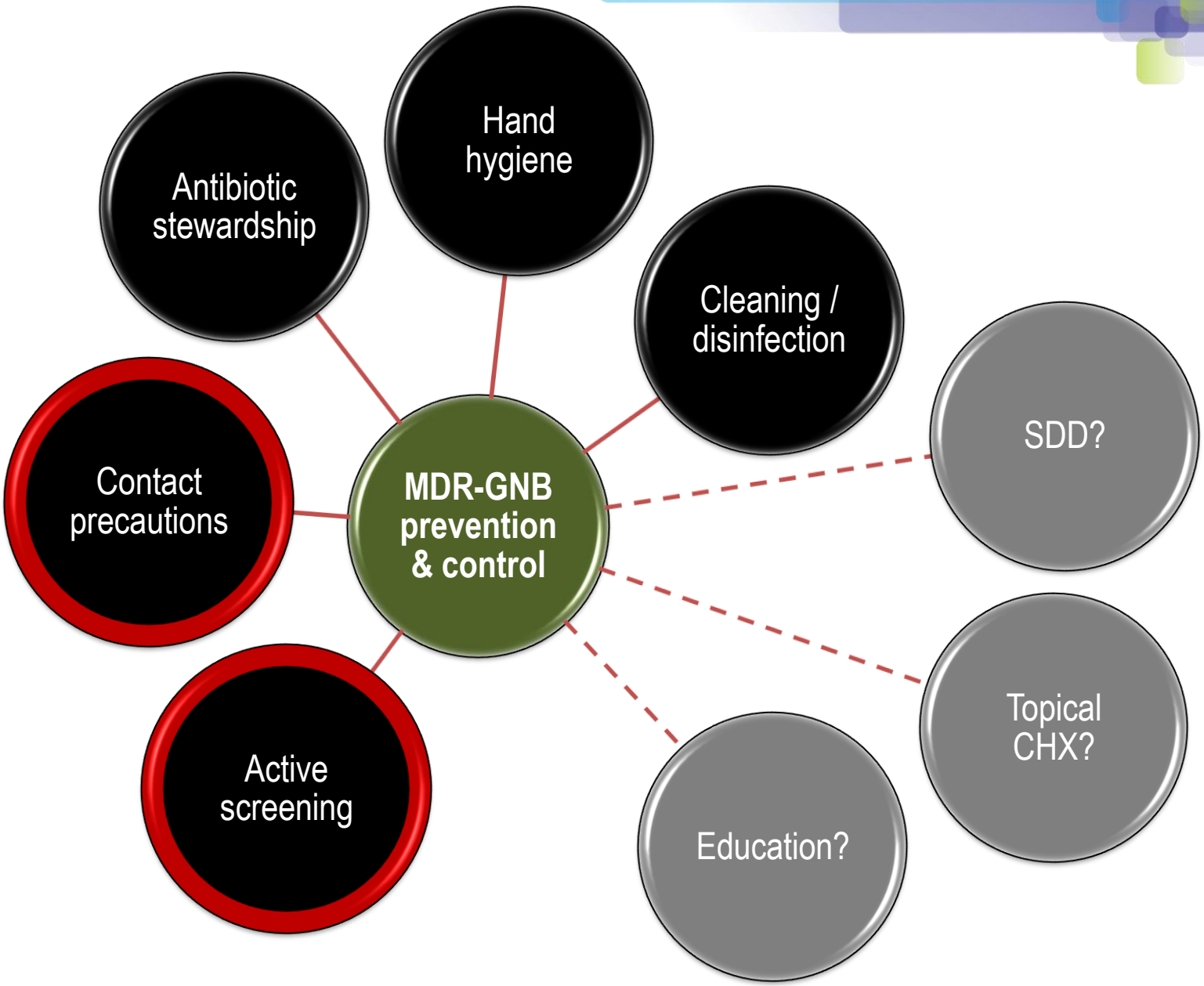
Peer reviewed opinion/comment

- Standardise standard precautions.
- Avoid an 'acronym minefield'.
- Simple outbreak epidemiology.
- Guideline writing dream team.
- "Road-test" guidelines.

Curran & Otter. *J Infect Prevent* 2014;15:193-198.

# Poll: How do you detect outbreaks of Gram-negative bacteria?

A. Passive surveillance only (clinical cultures)
B. Periodic review of clinical cultures
C. Active surveillance

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Poll: Who should be screened on admission for carriage of CRE?

A. Nobody
B. Admissions to high-risk units (e.g. ICU)
C. Admissions that meet screening triggers (e.g. returning overseas travellers)
D. Everybody

# Who do I screen?

UK PHE CPE Toolkit screening triggers:

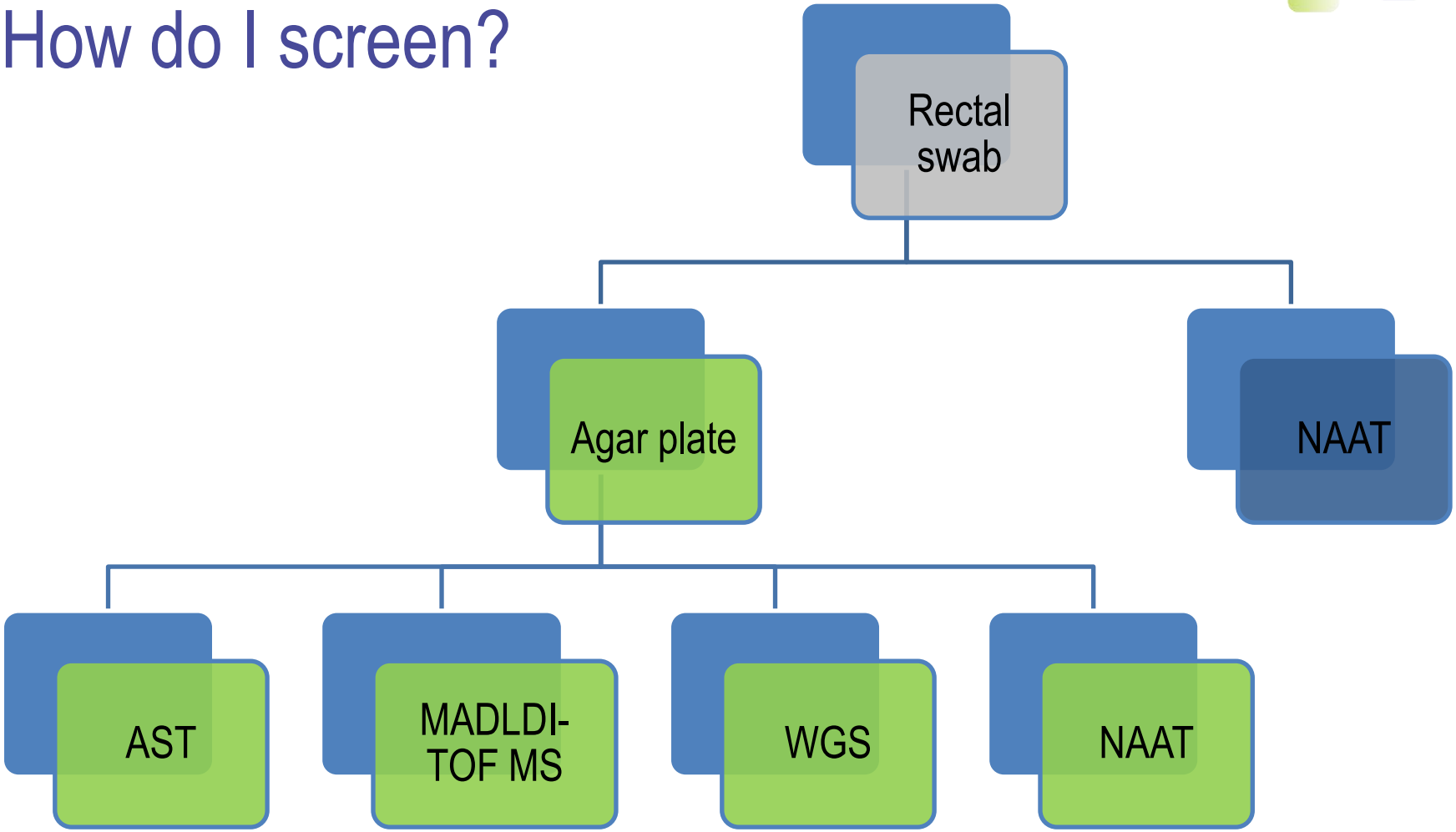
a) an inpatient in a hospital abroad, or

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?




NAAT = nucleic acid amplification techniques
AST = antimicrobial susceptibility testing
MALDI-TOF = Matrix-assisted laser desorption /ionization – time of flight mass spectrometry
WGS = whole genome sequencing

# You have positive case: now what?

**‘Contact precautions’**

Single room+glove/gown
Consider staff cohort

**Contact tracing**

Trigger for screening contacts or whole unit?

**Flagging**

Patient notes flagged
Receiving unit informed

**Education**

Staff
Patient / visitor

# Does screening and isolation work?

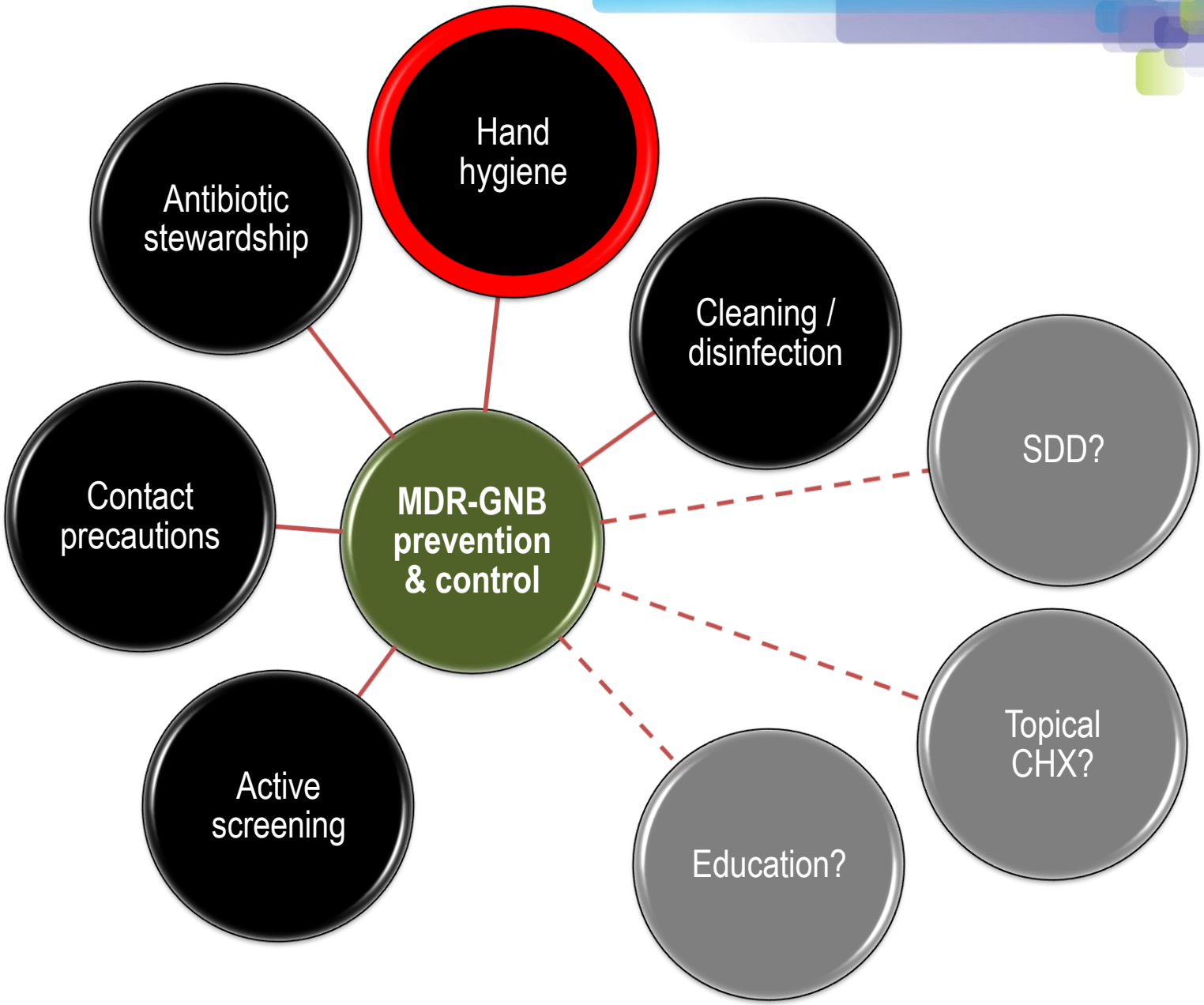
| | All MDROs | MRSA | VRE | ESBLs |
|---|---|---|---|---|
| Baseline trend | – | ↑ | – | – |
| Hygiene intervention step-change | – | – | – | – |
| Hygiene intervention trend change | ↓ | ↓ | – | – |
| Screening step-change | – | – | – | – |
| Screening trend change | – | ↑ | – | – |
| Rapid vs. conventional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

Derde *et al. Lancet Infect Dis* 2014;14:31-39.

# Deisolation?

| Author | Year | Setting | N pts | Organism | Duration of colonization |
|---|---|---|---|---|---|
| Bird[1] | 1998 | Elderly care facilities, Scotland | 38 | ESBL *K. pneumoniae* | 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.

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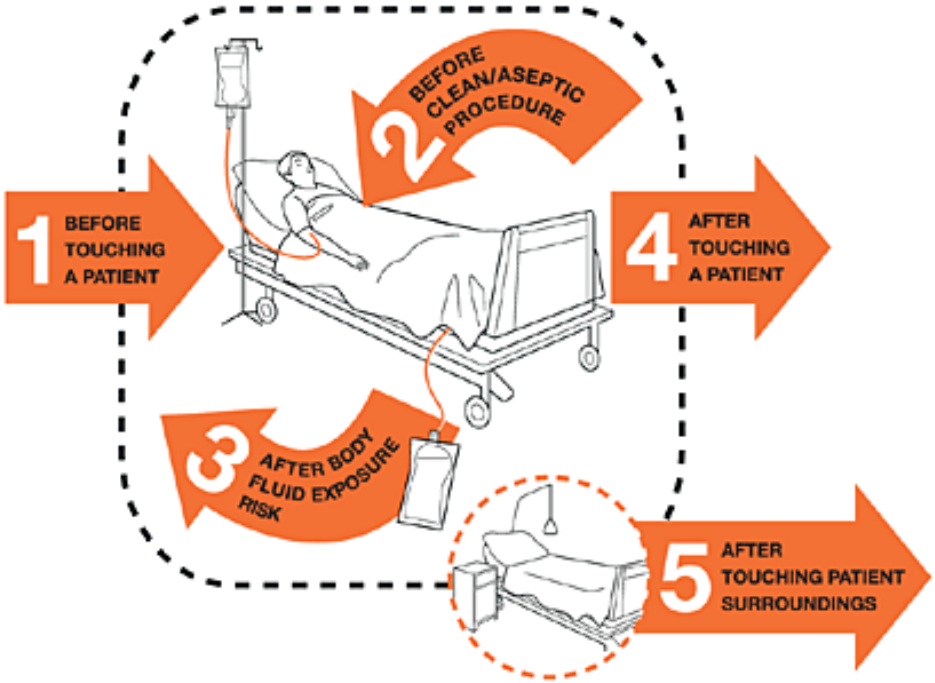
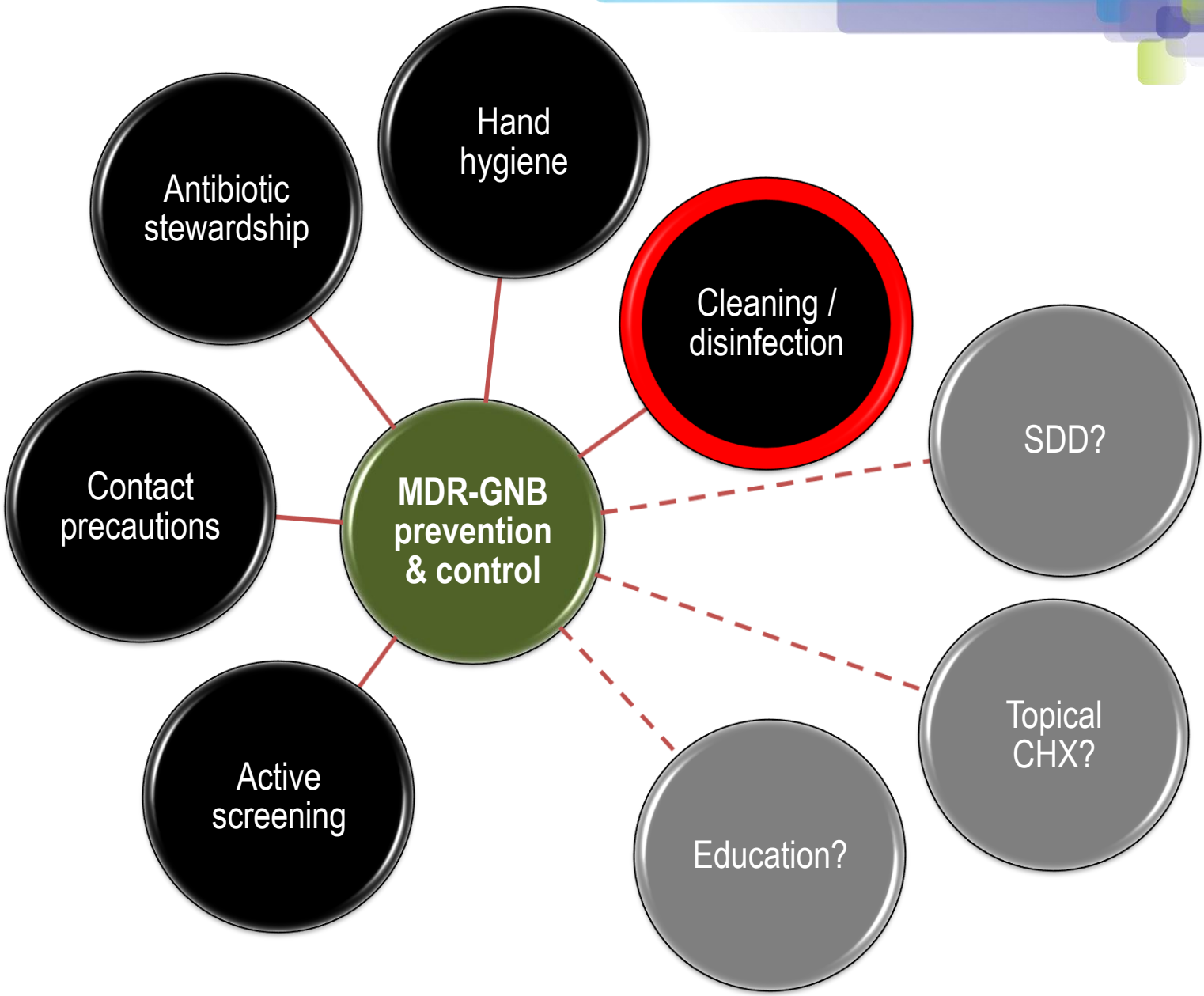
# Hand hygiene




# 40%

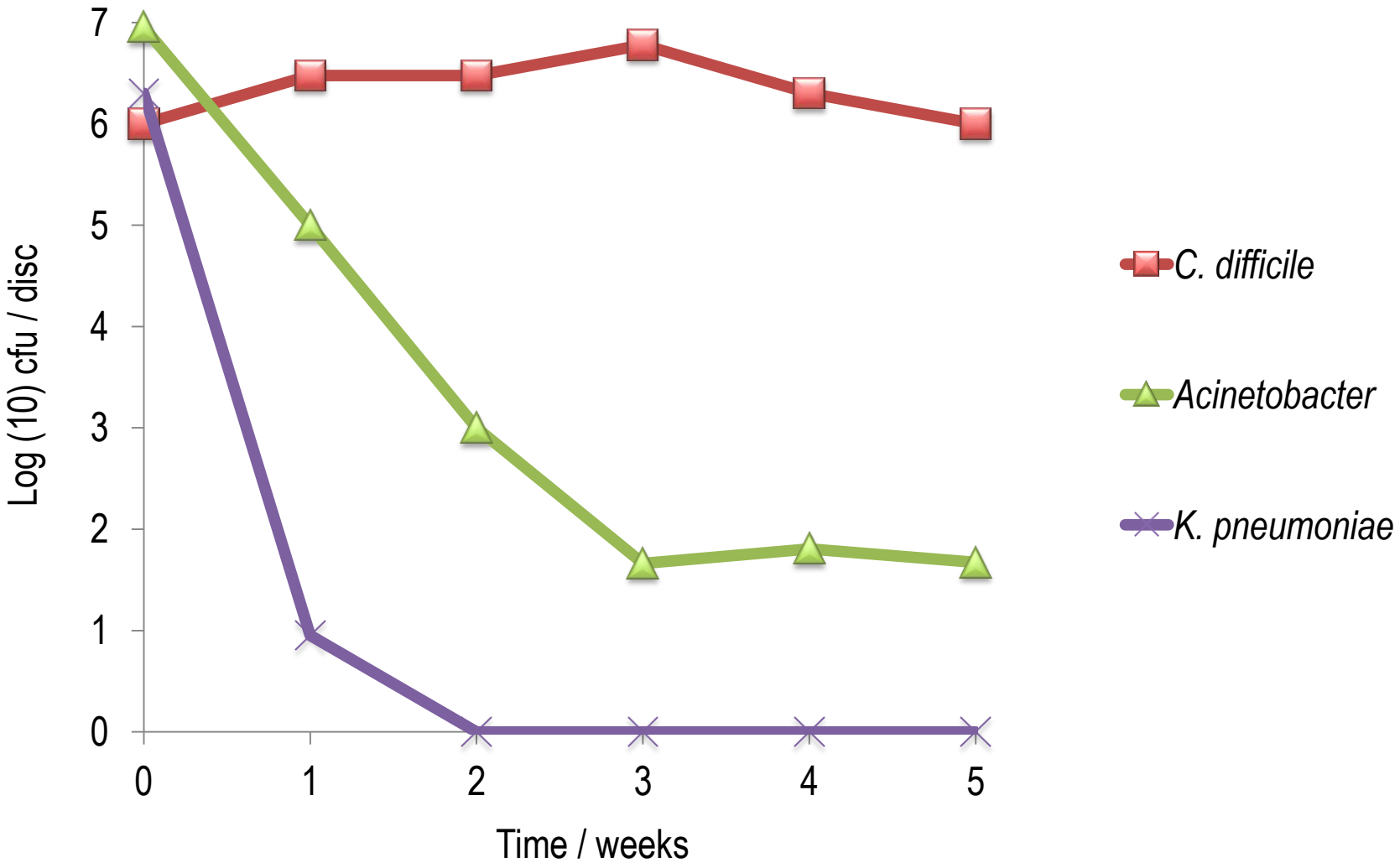
Median hand hygiene compliance from 95 studies.

Erasmus *et al. Infect Control Hosp Epidemiol* 2010;31:283-294.



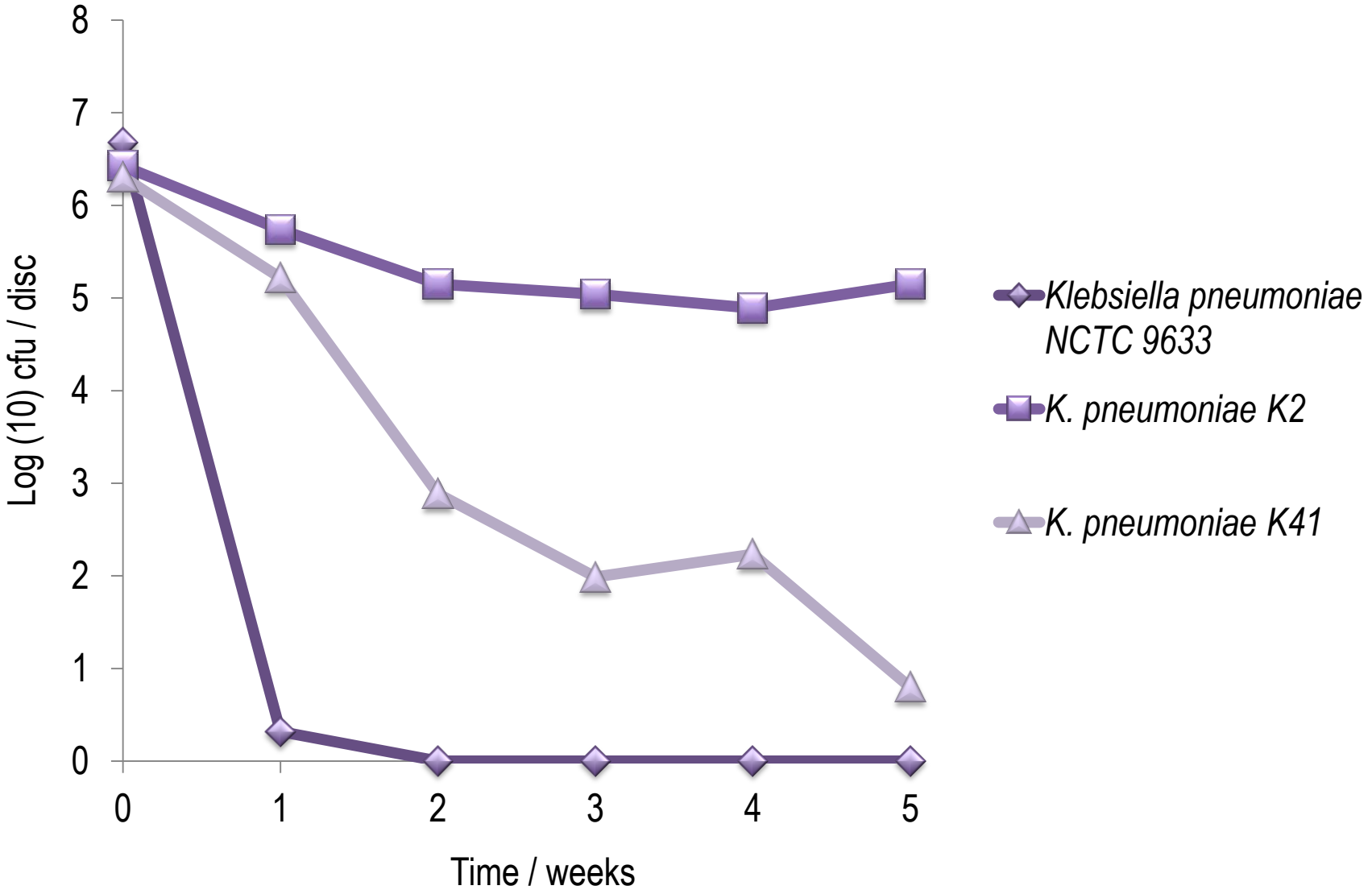

Tacconelli *et al. Clin Microbiol Infect* 2014;20 Suppl 1:1-55

# Surface survival




Otter & French. *J Clin Microbiol* 2009;47:205-207.

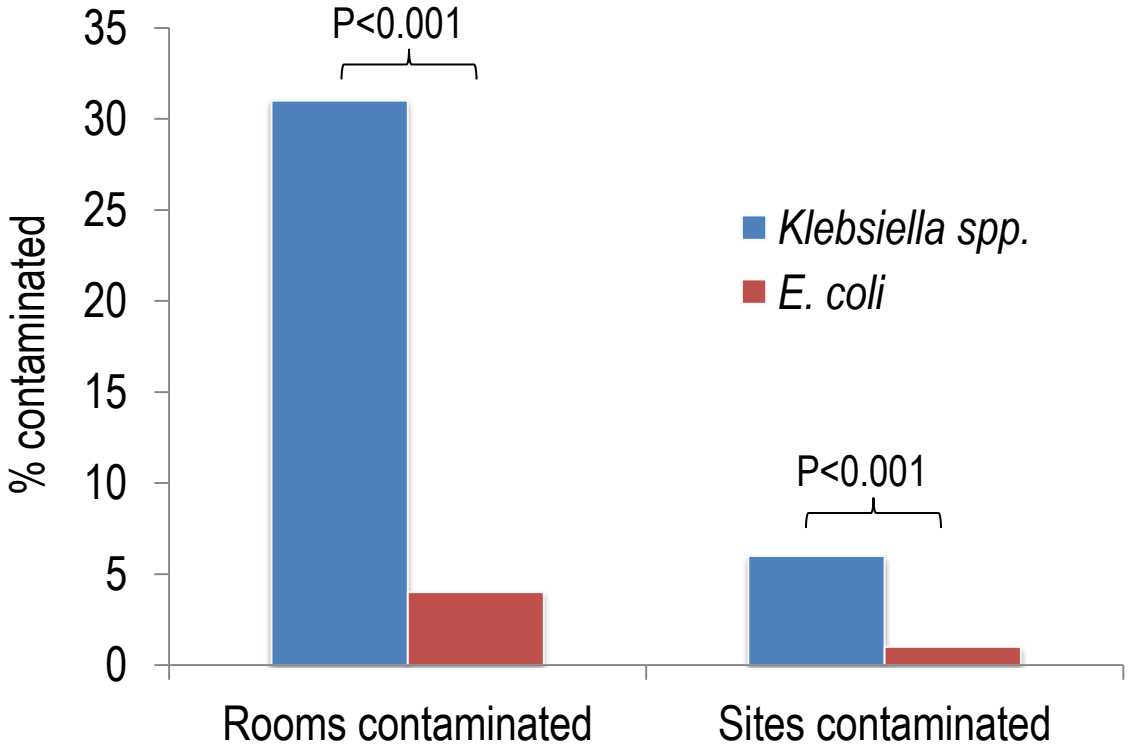
# Surface survival – strain variation




Otter & French. *J Clin Microbiol* 2009;47:205-207.

# *K. pneumoniae* vs. *E. coli*

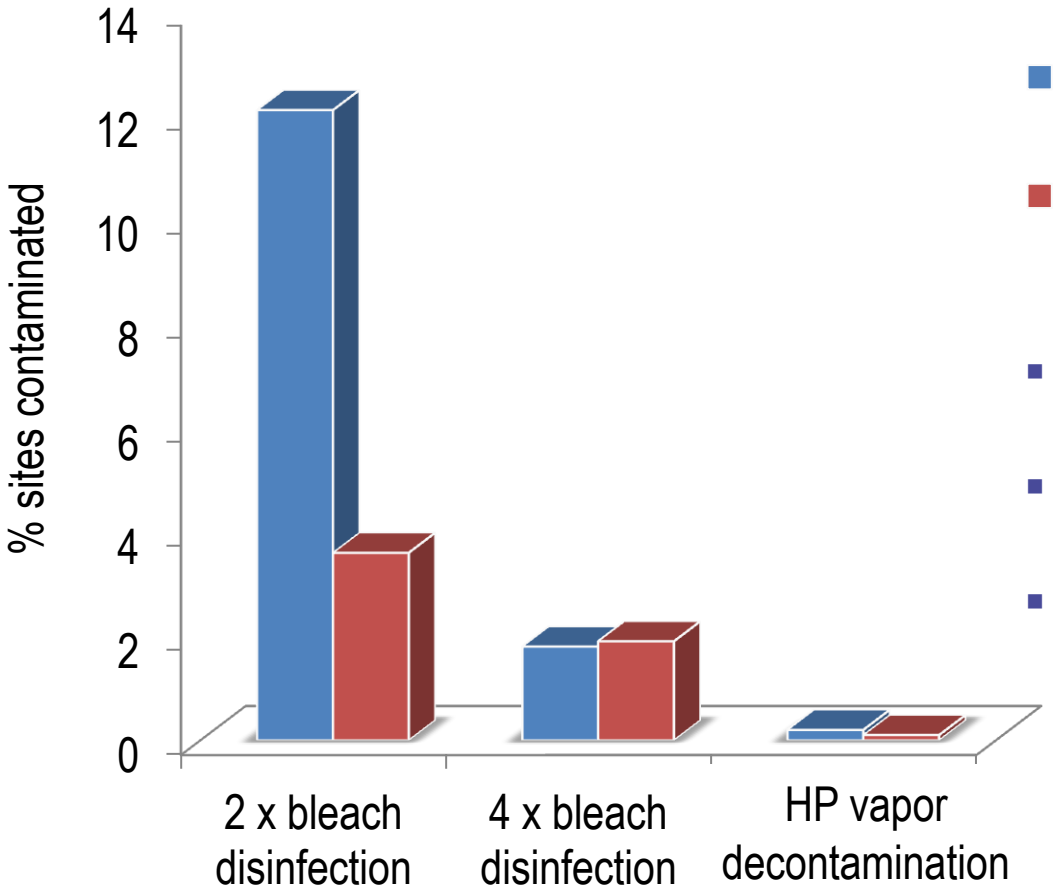
- *K. pneumoniae* seems to be more environmental than *E. coli.*[1,2]
- Surface contamination on five standardized sites surrounding patients with ESBL-producing *Klebsiella* spp. (n=48) or ESBL-producing *E. coli* (n=46).[1]




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



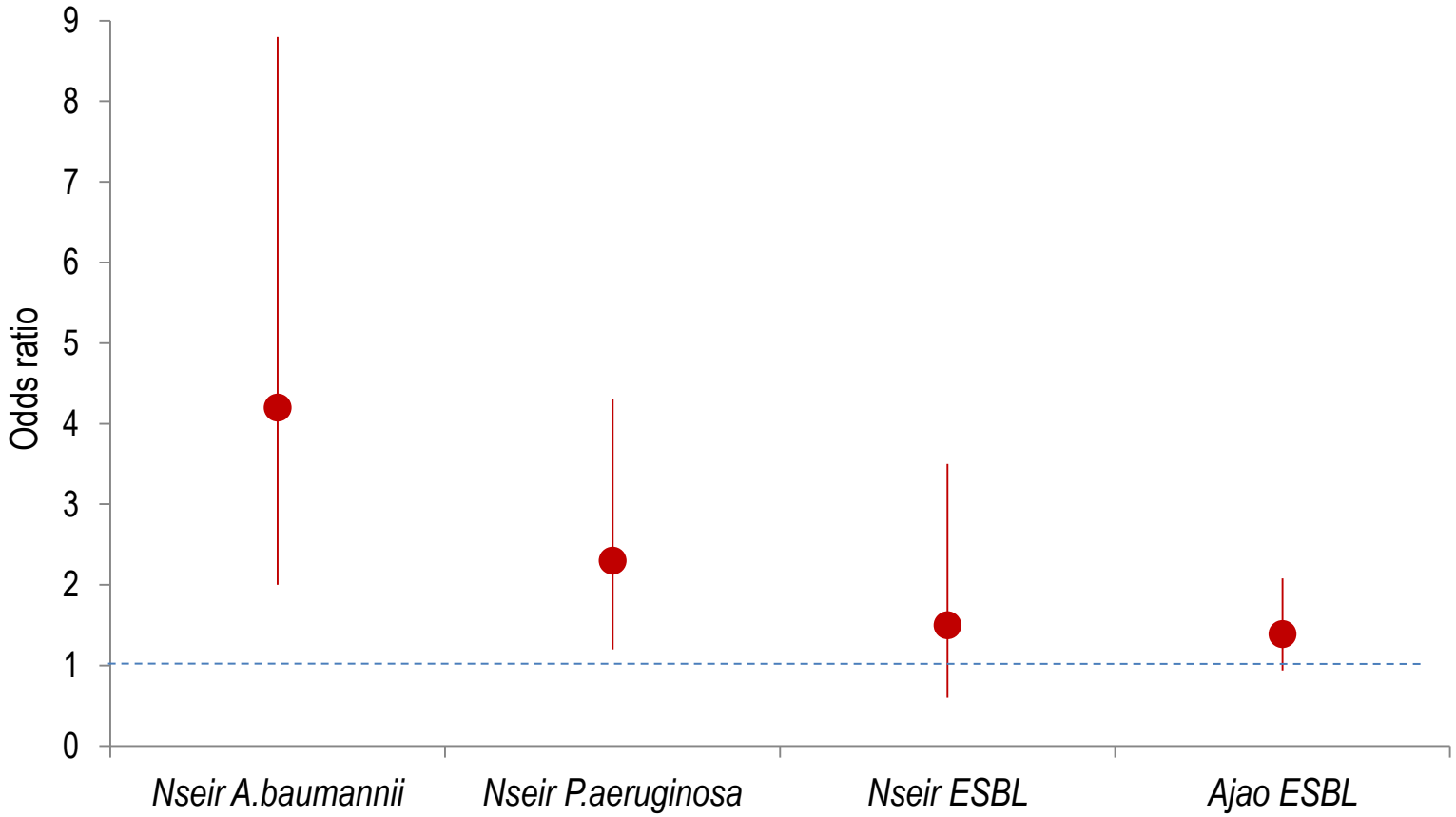

- *% sites contaminated with A. baumannii*
- *% sites contaminated with MRSA*

- 140 samples from 9 rooms after 2xbleach
- 5705 samples from 312 rooms after 4xbleach
- 2680 sites from 134 rooms after HP vapor

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

Manian *et al. Infect Control Hosp Epidemiol* 2011;32:667-672.

# Enterobacteriaceae are “less environmental”

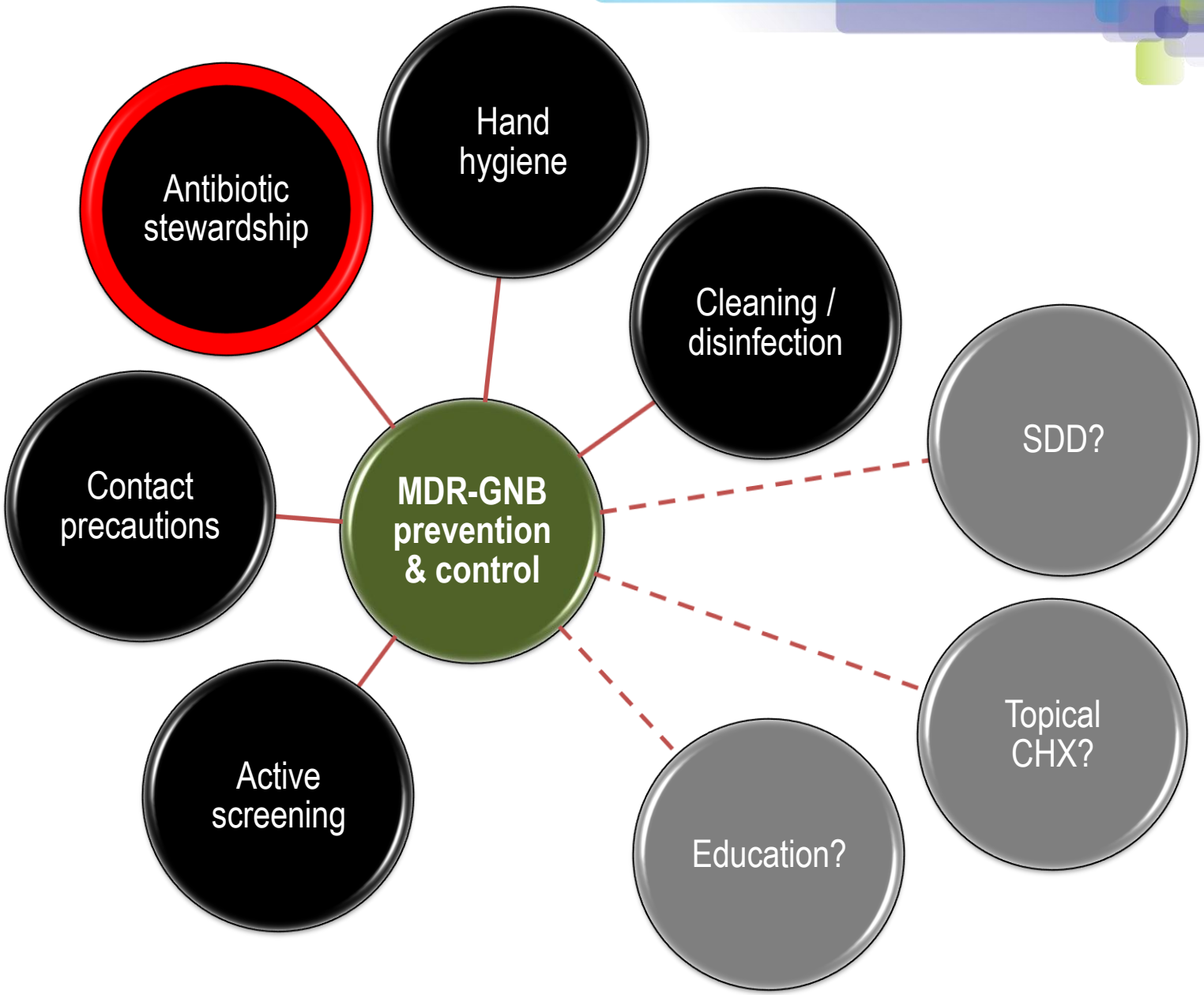



Nseir *et al. Clin Microbiol Infect* 2011;17:1201-1208.
Ajao *et al. Infect Control Hosp Epidemiol* 2013;34:453-458.

# MDR-GNB cleaning & disinfection checklist

- ❑ Clean / declutter
- ❑ Monitor cleaning process (e.g. ATP bioluminescence)
- ❑ Enhanced daily disinfection using bleach
- ❑ All equipment disinfected before leaving room
- ❑ Terminal disinfection using bleach or, ideally, $H_2O_2$ vapor[1-3]

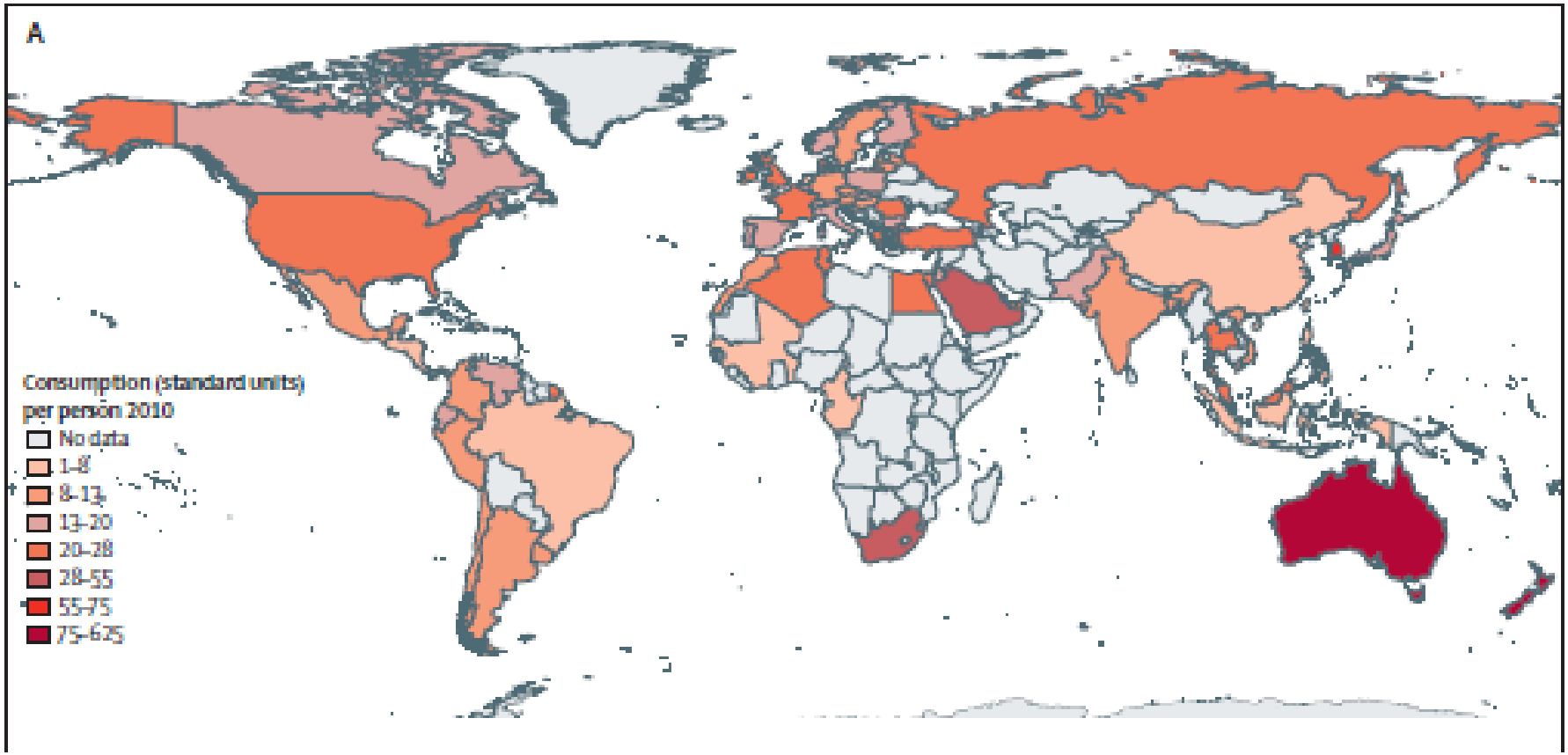

1. Gopinath *et al. Infect Control Hosp Epidemiol* 2013;34:99-100.
2. Snitkin *et al. Sci Transl Med* 2012;4:148ra116.
3. Verma *et al. J Infect Prevent* 2013;7:S37.




Tacconelli *et al. Clin Microbiol Infect* 2014;20 Suppl 1:1-55

# Antibiotic consumption

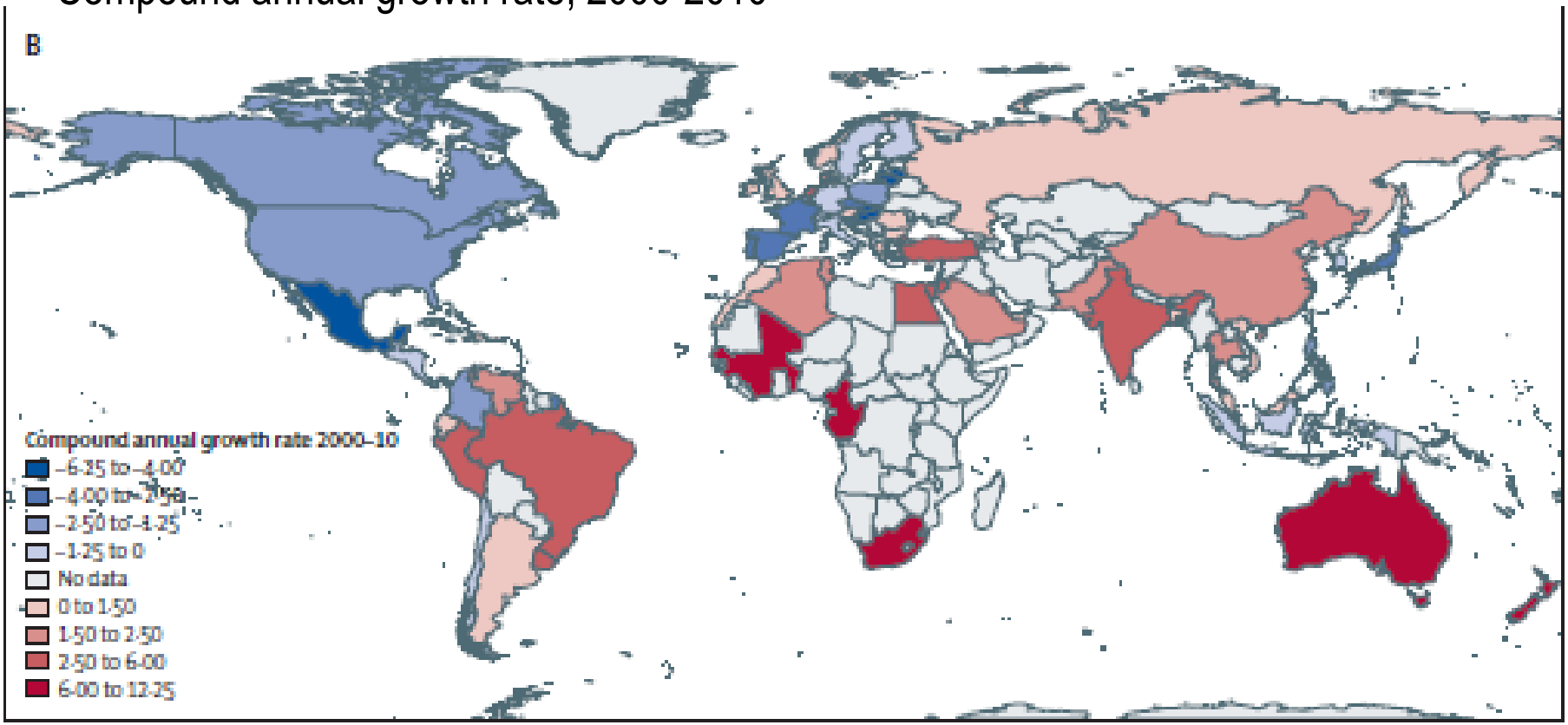
Consumption (standard units) per person, 2010




Van Boeckel *et al. Lancet Infect Dis* 2014;14:742-750

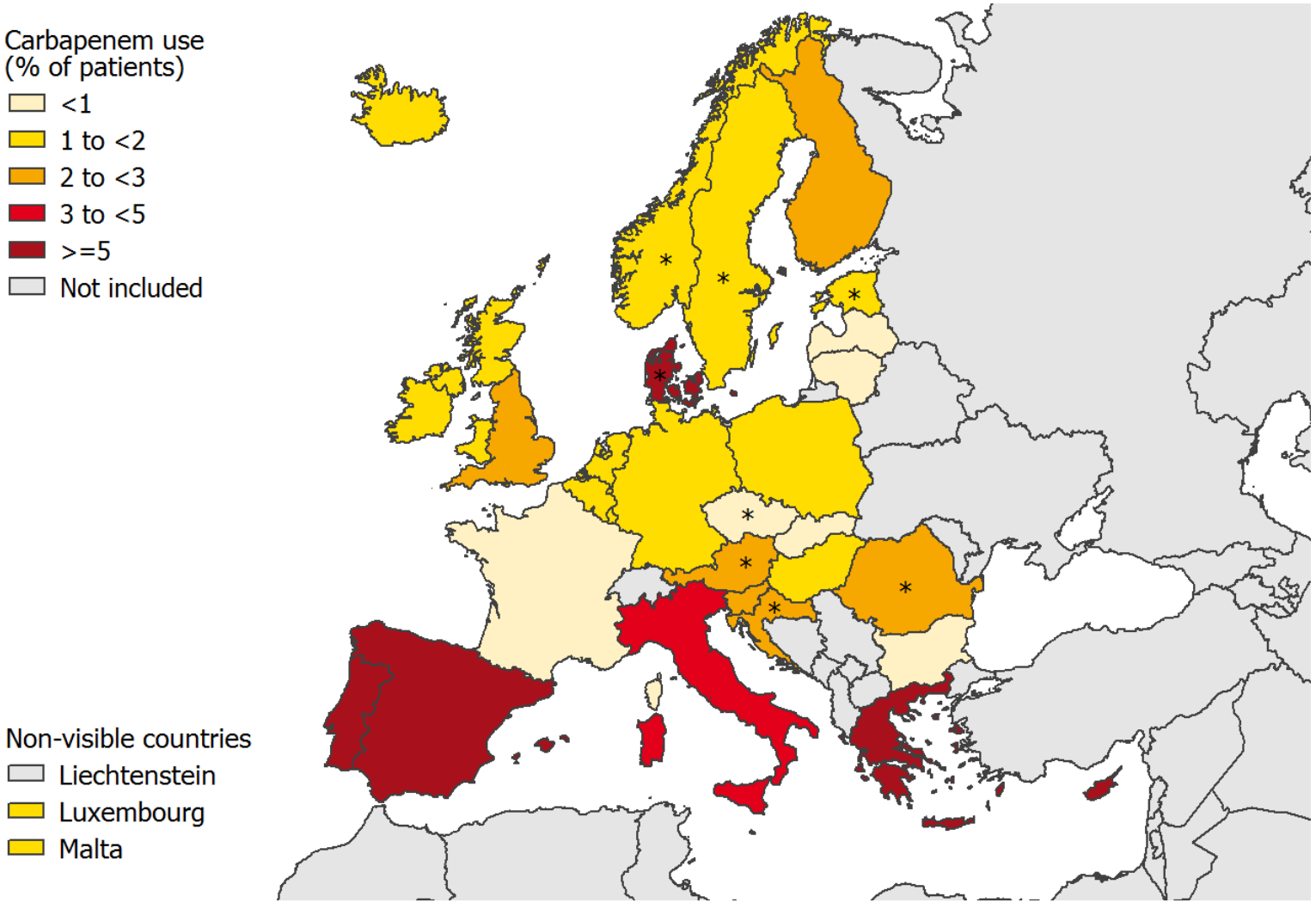
# Antibiotic consumption

Compound annual growth rate, 2000-2010




Van Boeckel *et al. Lancet Infect Dis* 2014;14:742-750

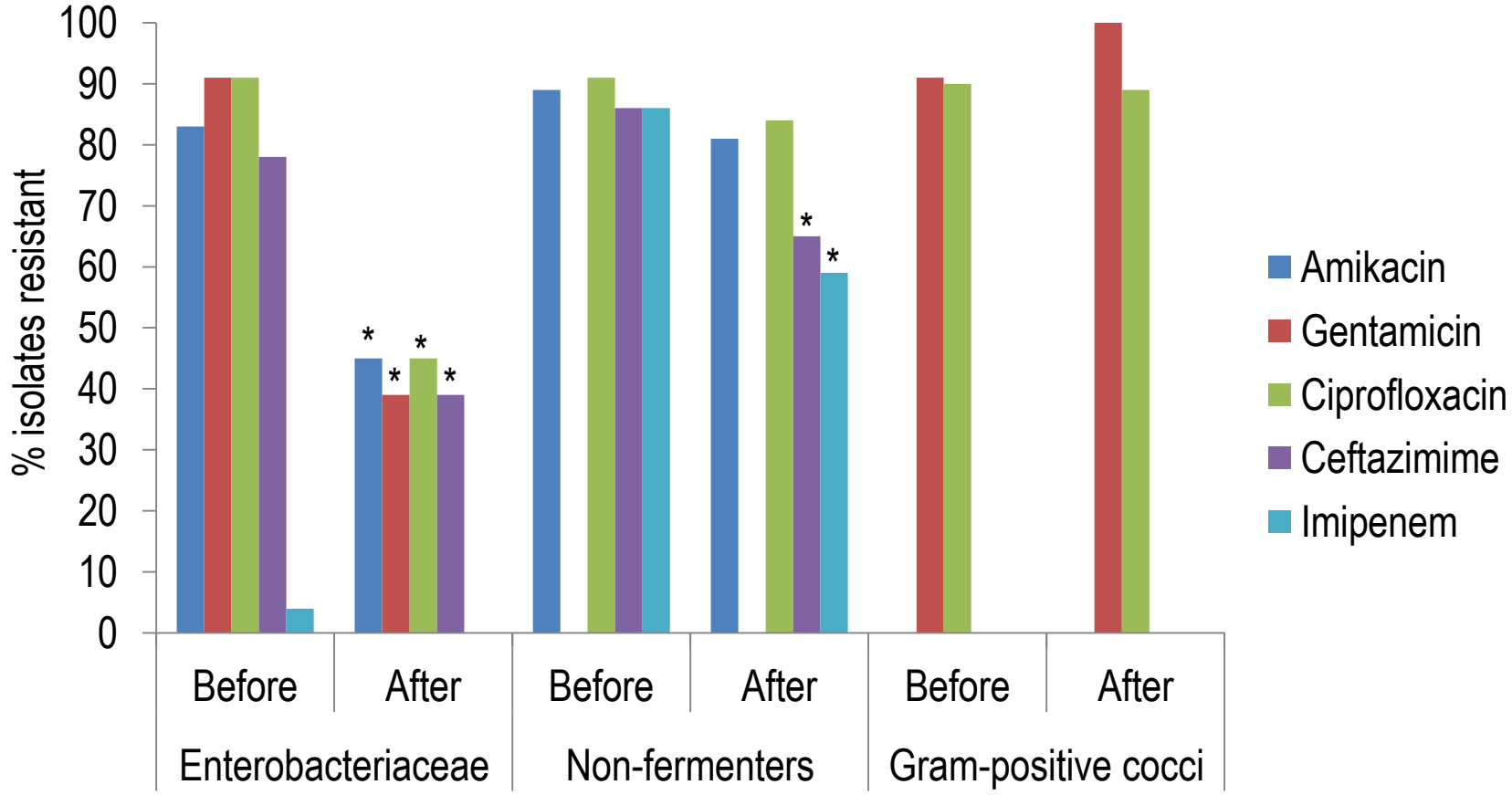
# Carbapenem use, Europe



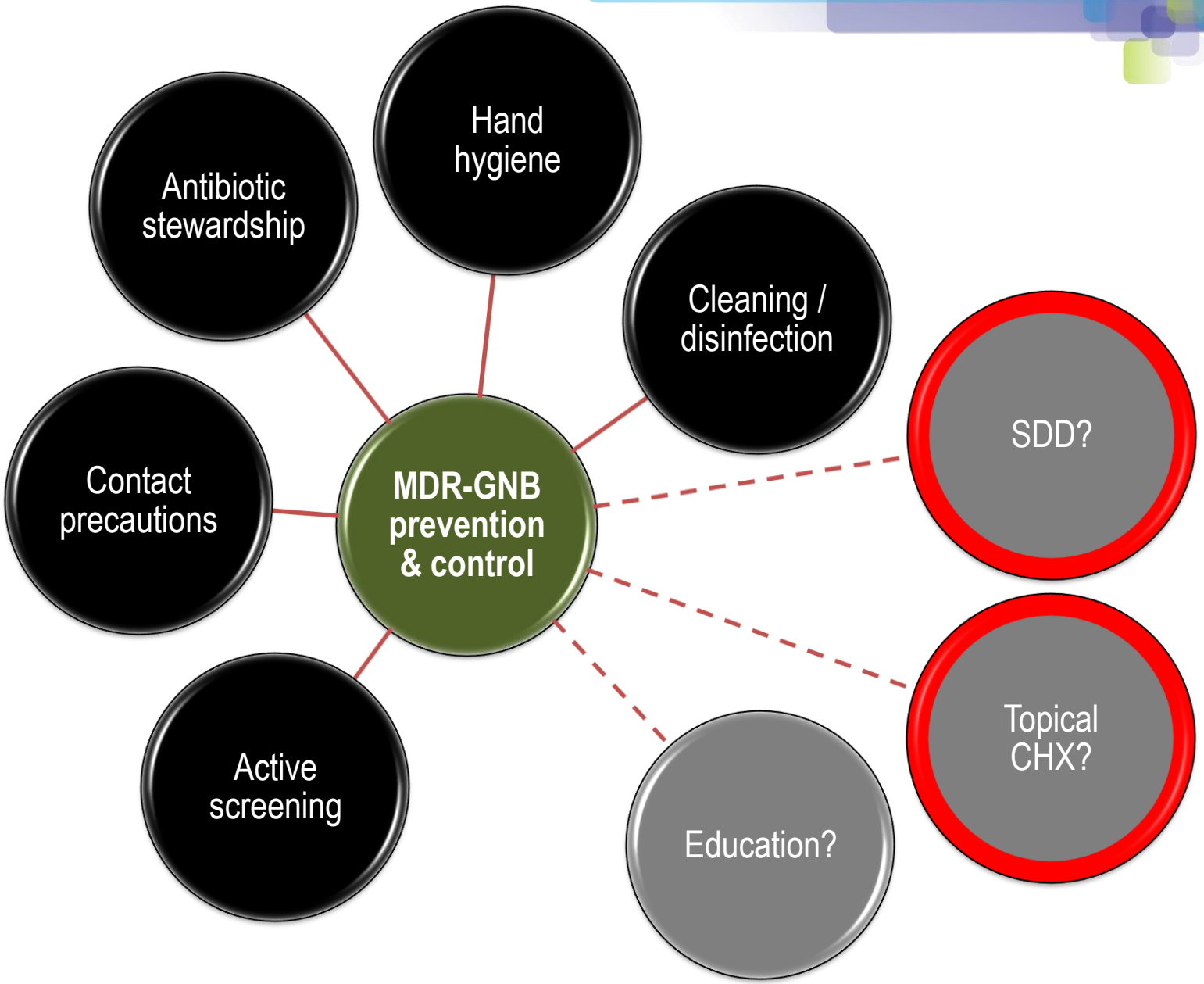

ECDC point prevalence survey 2013.

# 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.



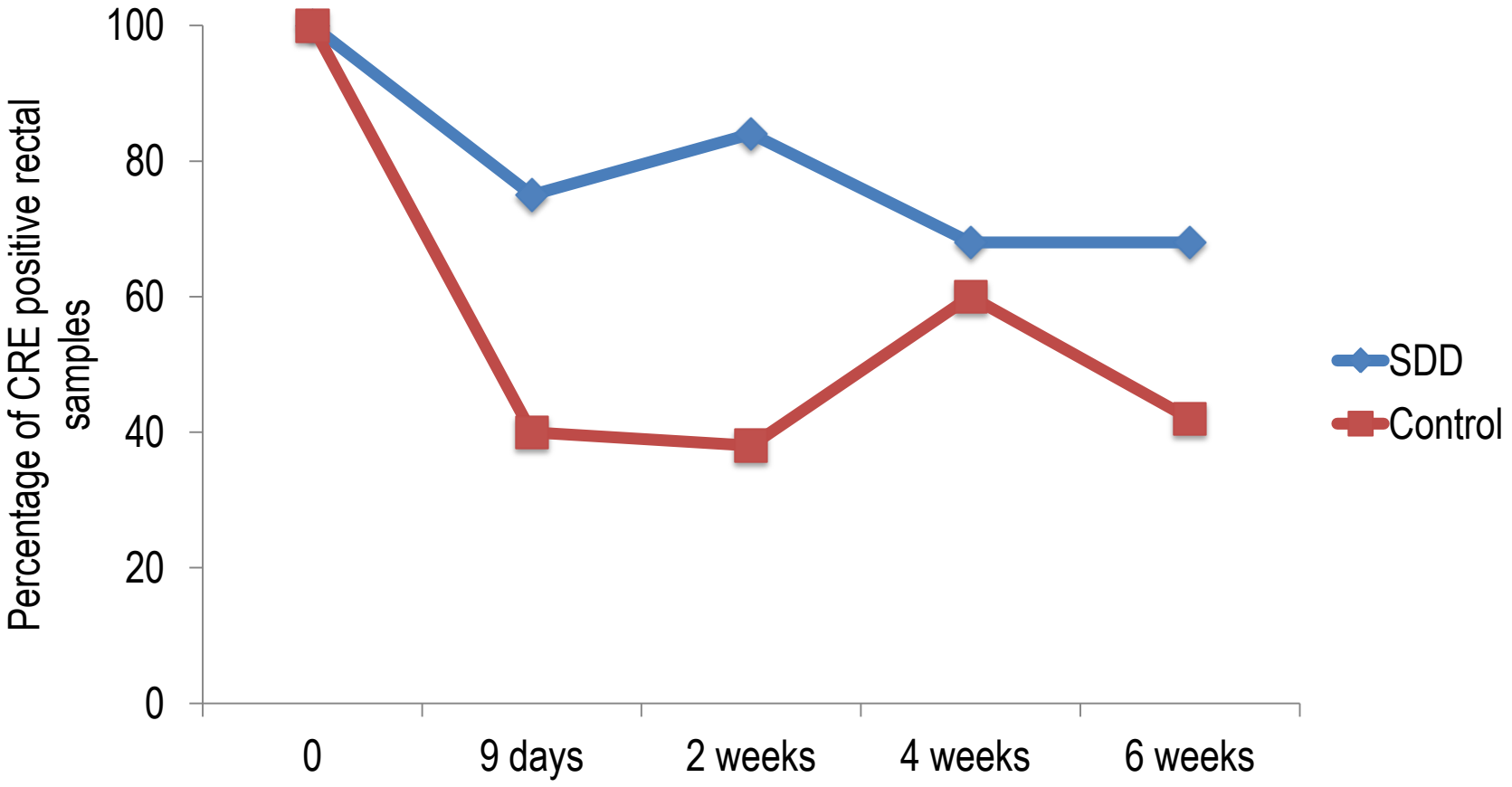

Hou *et al. PLoS ONE* 2014;9:e101447; * = significant difference before vs. after.




Tacconelli *et al. Clin Microbiol Infect* 2014;20 Suppl 1:1-55

# ‘Selective’ digestive decontamination

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




Saidel-Odes *et al. Infect Control Hosp Epidemiol* 2012;33:14-19.

# ‘Selective’ digestive decontamination

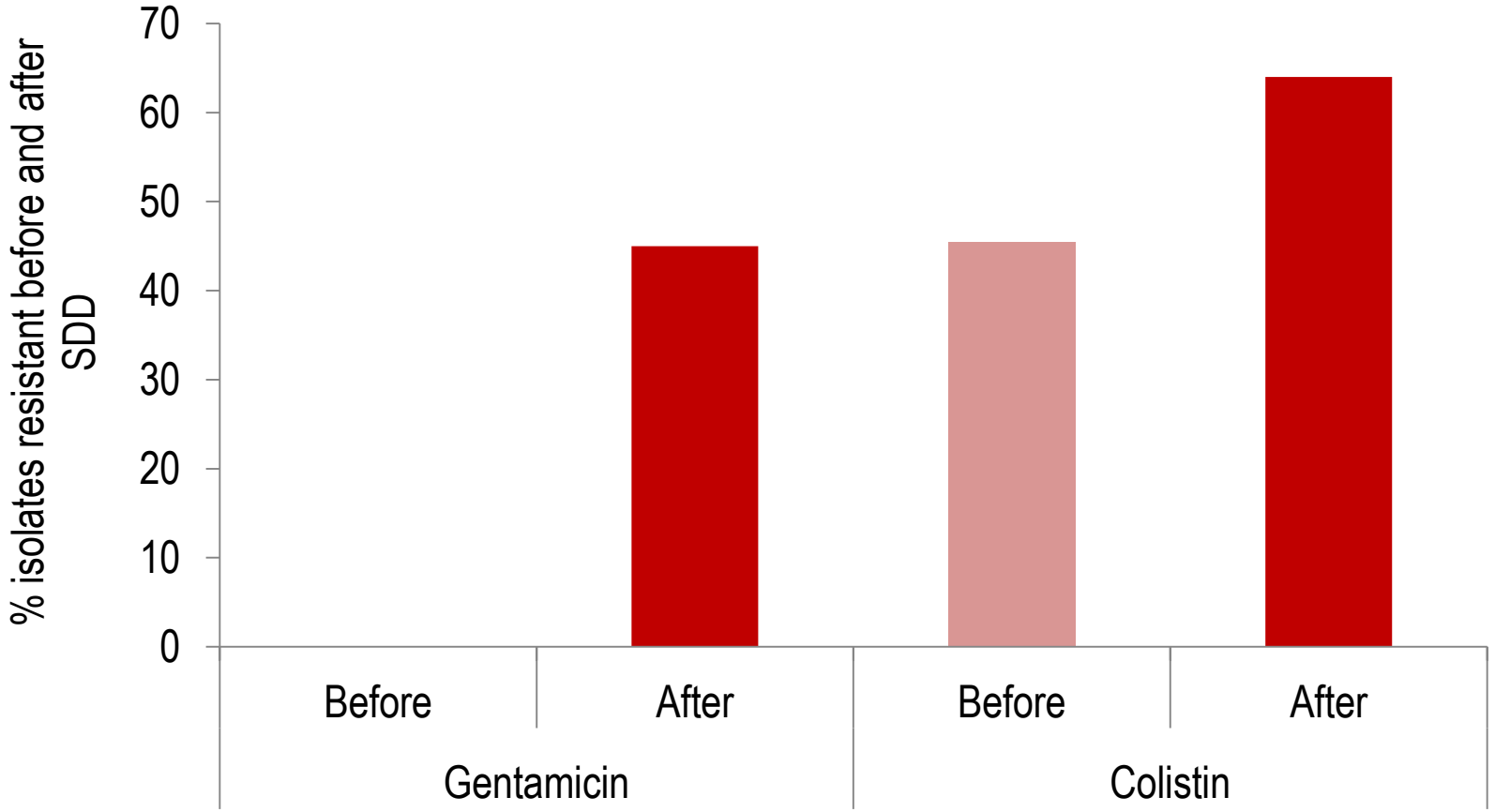
*‘…fighting antimicrobial resistance with more antimicrobials, although a necessary short-term strategy, is a long-term strategy destined to fail.’*

*Tosh & McDonald. Clin Infect Dis 2012;54:707-713.*

**ANTIBIOTICS ARE THE PROBLEM, NOT THE SOLUTION**

# ‘Selective’ digestive decontamination

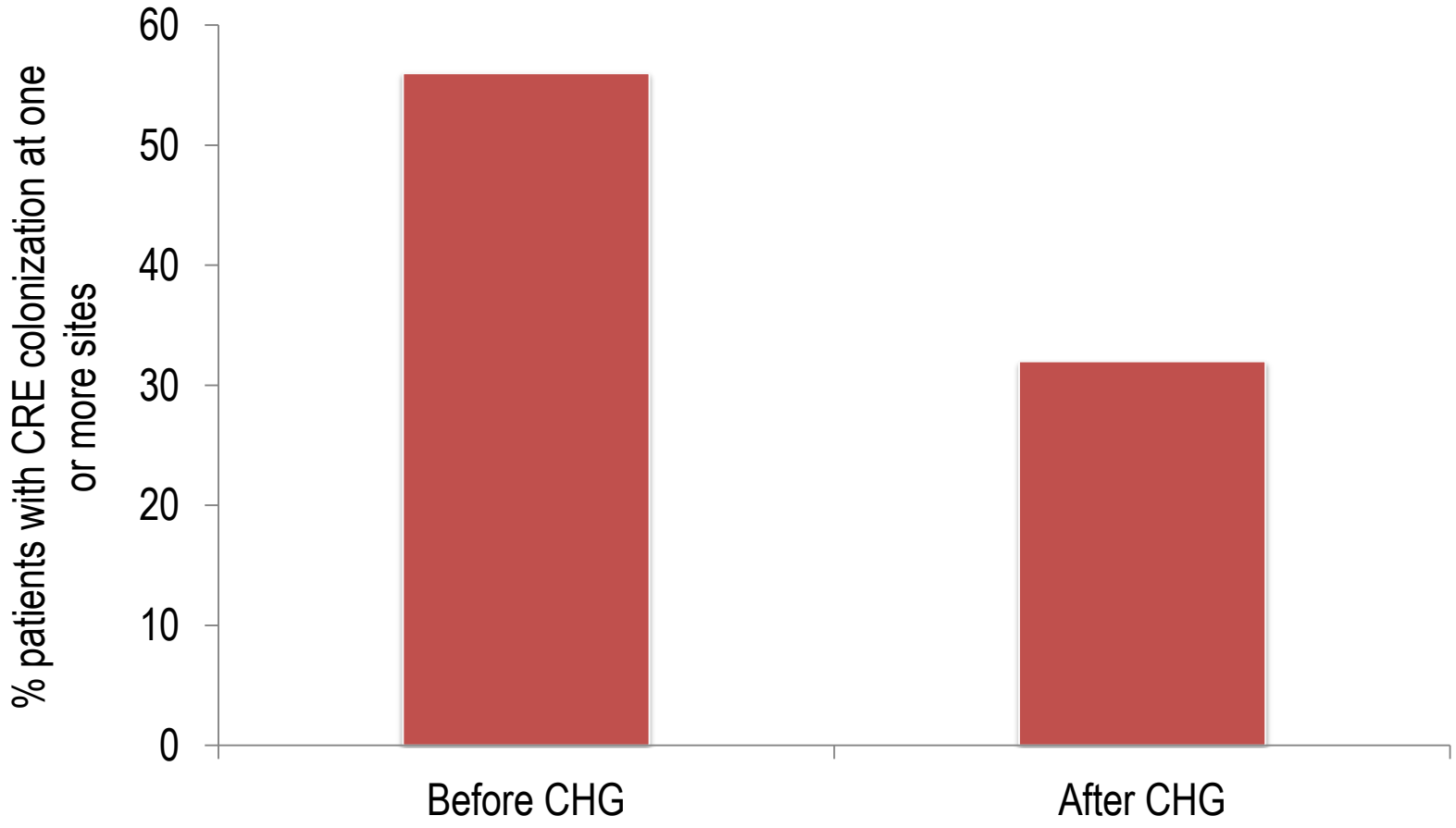
14 SDD patients compared with 76 non-SDD patients; all CRE colonized.




Lubbert *et al. Int J Antimicrob Agents* 2013;42:565-570.

# Chlorhexidine – efficacy

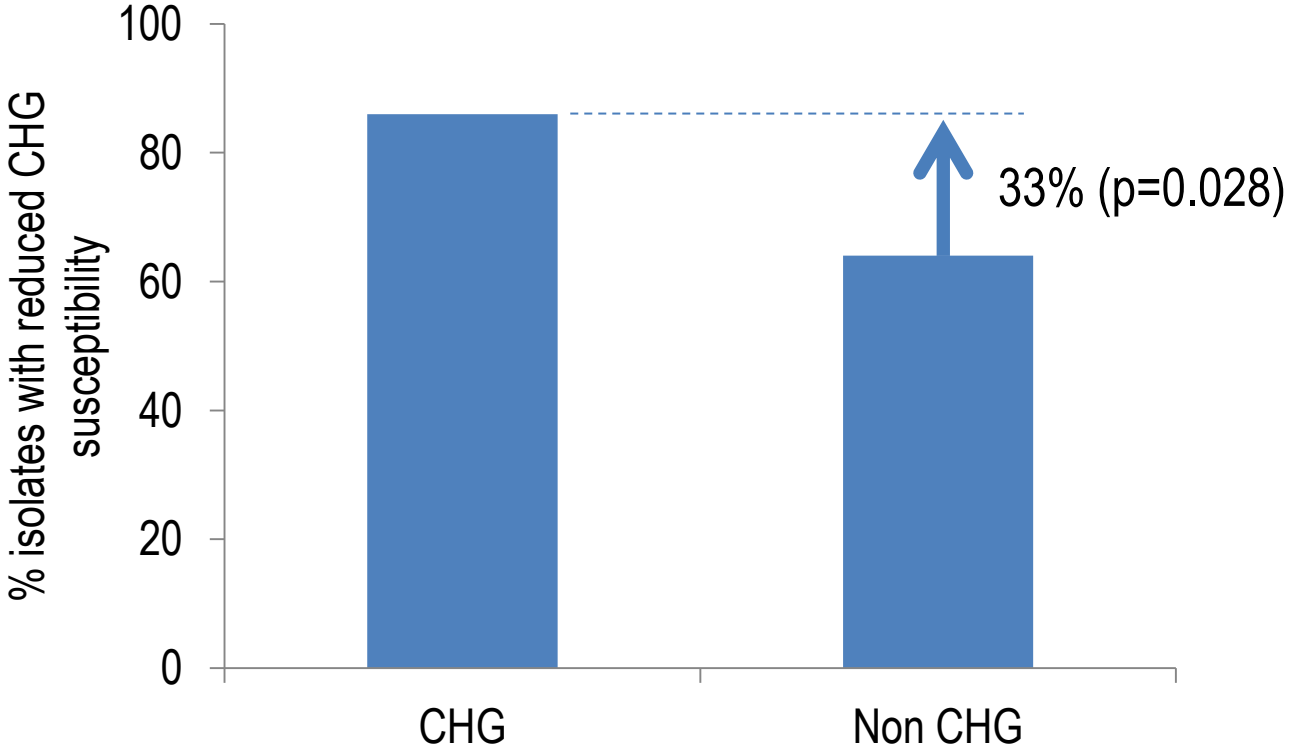
Impact of chlorhexidine gluconate (CHG) daily bathing on skin colonization with KPC-producing *K. pneumoniae* in 64 long-term acute care patients.




Lin *et al. Infect Control Hosp Epidemiol* 2014; 35:440-442.

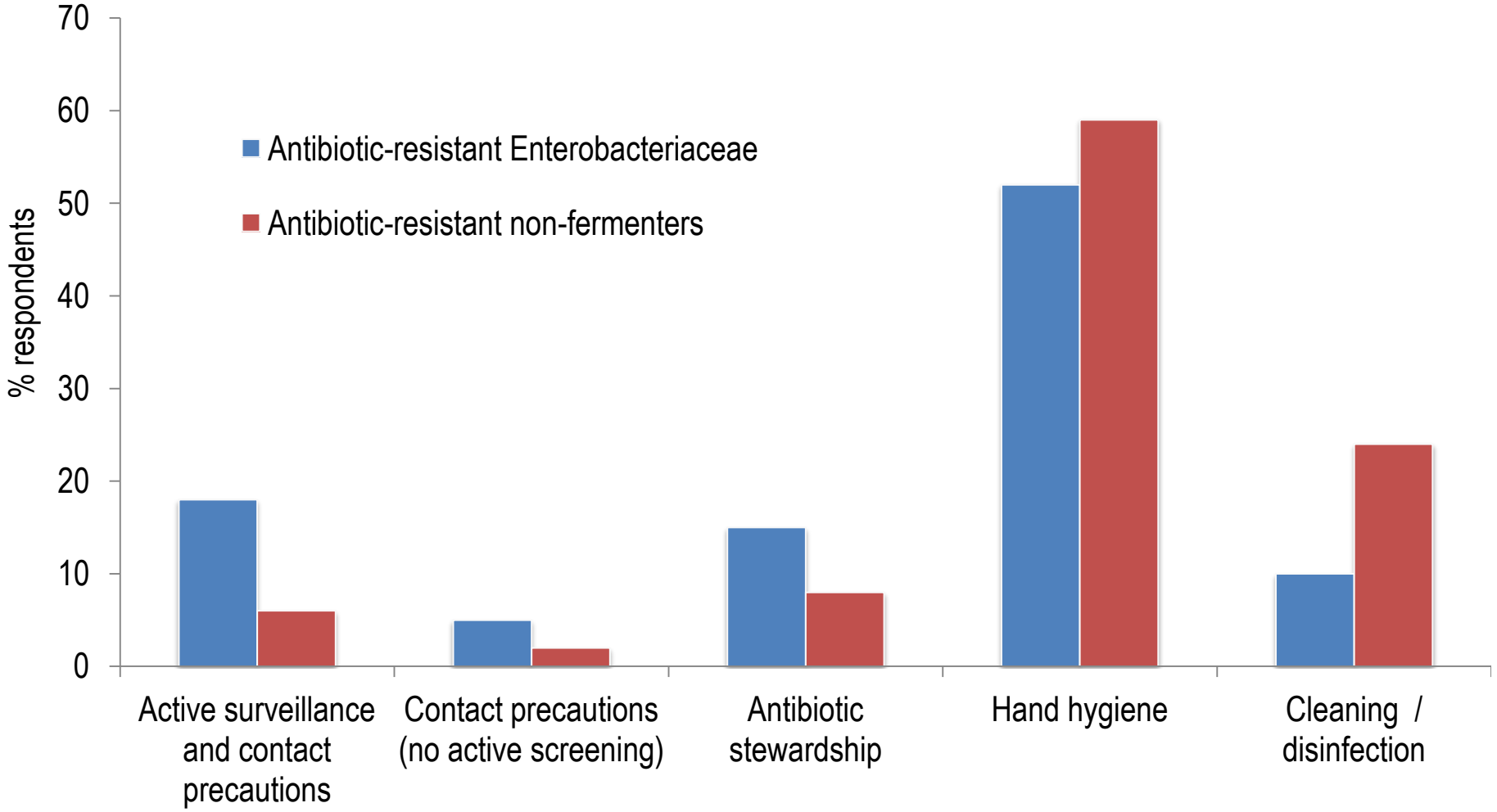
# Chlorhexidine – reduced susceptibility

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

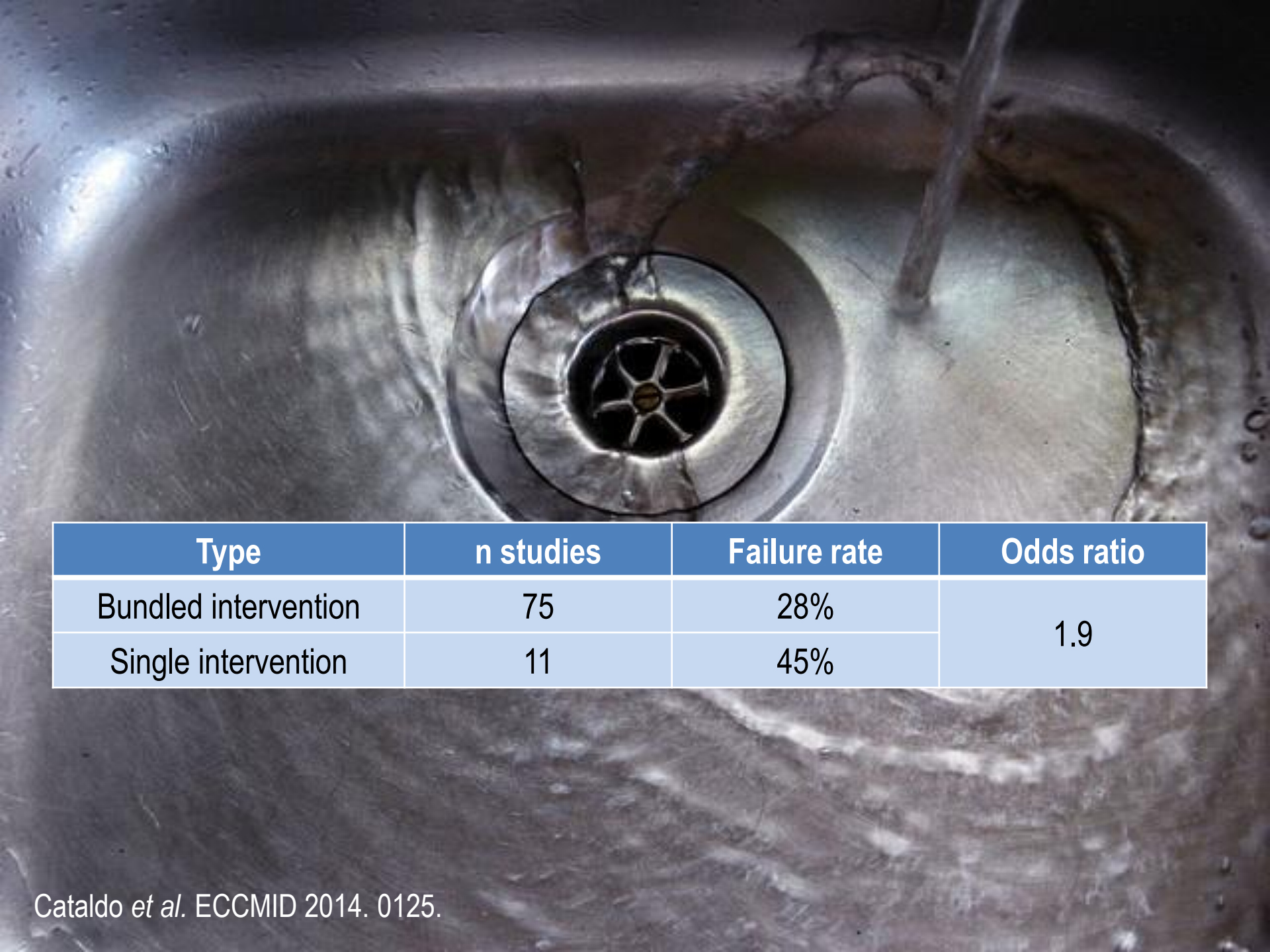



Suwantarat *et al. Infect Control Hosp Epidemiol* 2014;35:1183-1186.

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




Data from around 150 webinar participants, mainly in the US.



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

Cataldo *et al.* ECCMID 2014. 0125.

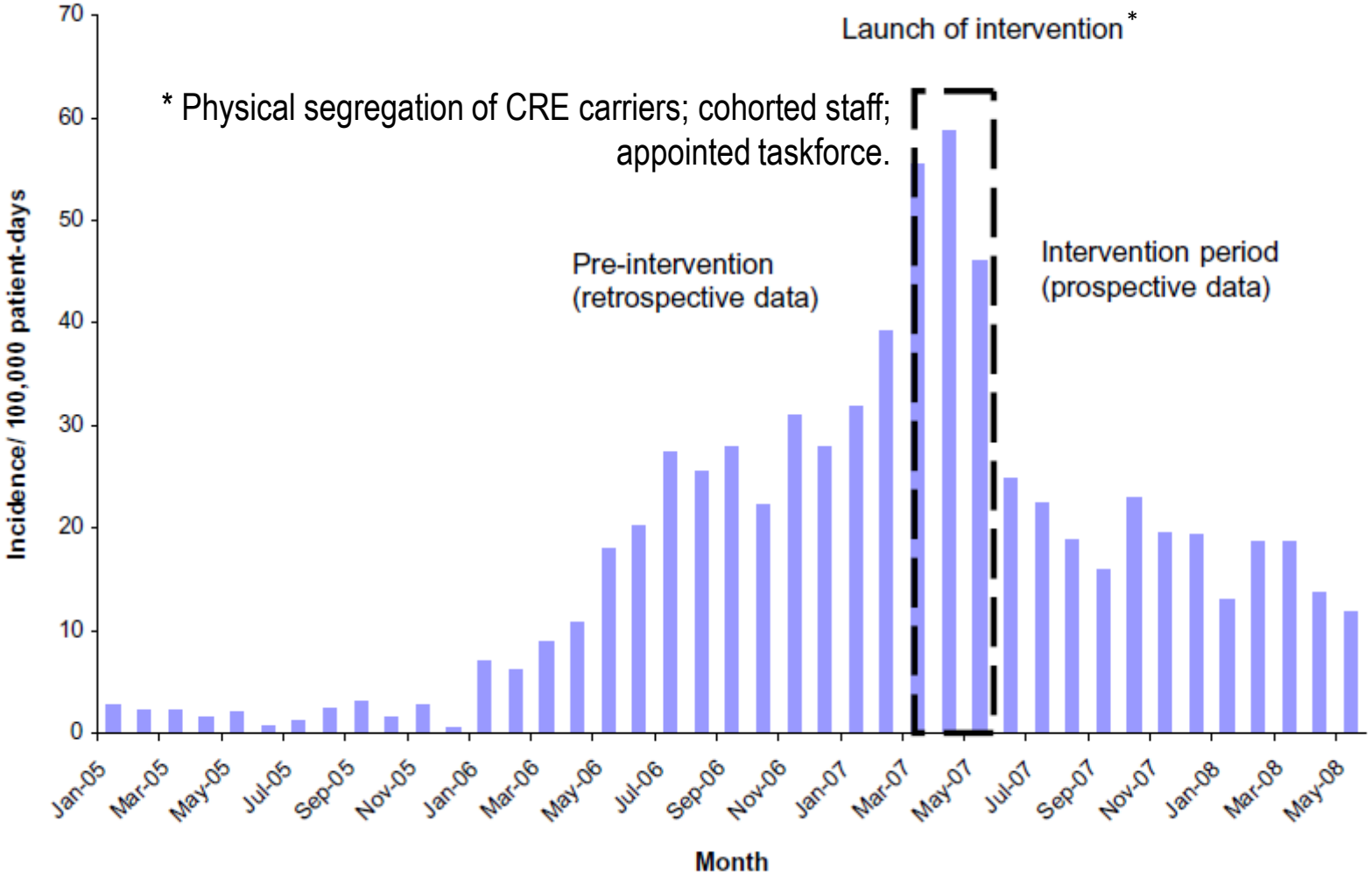
# What works? NIH


Also:

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

Palmore. *Clin Infect Dis* 2013;57:1593-9.

# What works? Israel




Schwaber *et al. Clin Infect Dis* 2011;52:848-855.

# 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-GNB.

3. A "kitchen sink" approach (aka bundle) should be deployed!

4. Effective strategies should cover:
   - Hand hygiene
   - Screening & contact precautions
   - Antimicrobial stewardship
   - Cleaning & disinfection

# Learner objectives

1. Provide an overview of the available guidelines to control CRE and other resistant Gram-negative bacteria.

2. Identify gaps in the guidelines, in terms of definitions of standard precautions, outbreak epidemiology and who should be on the guidelines writing dream team.

3. Discuss controversial areas in terms of effective interventions: patient isolation, staff cohorting and selective digestive decontamination.

# Questions?


3M.com/IPEd

# Resources (not exhaustive!)

- US CDC CRE Toolkit.
- US AHRQ CRE Tookit.
- UK Public Health England CPE Tookit.
- UK ESBL guidelines.
- ECDC risk assessment on the spread of spreading (CPE).
- Canadian guidelines for carbapenem resistant GNB.
- Australian recommendations for CRE control.
- ESCMID MDR-GNR control guidelines.

# Acknowledgements

Pat Cattini and Evonne Curran for slides.

Image credits:

‘Apples and oranges’

Kitchen sink

WHO 5 moments