VUmc

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Amsterdam

Preventing emergence and spread of antibiotic resistance

Role of antibiotic stewardship and infection control

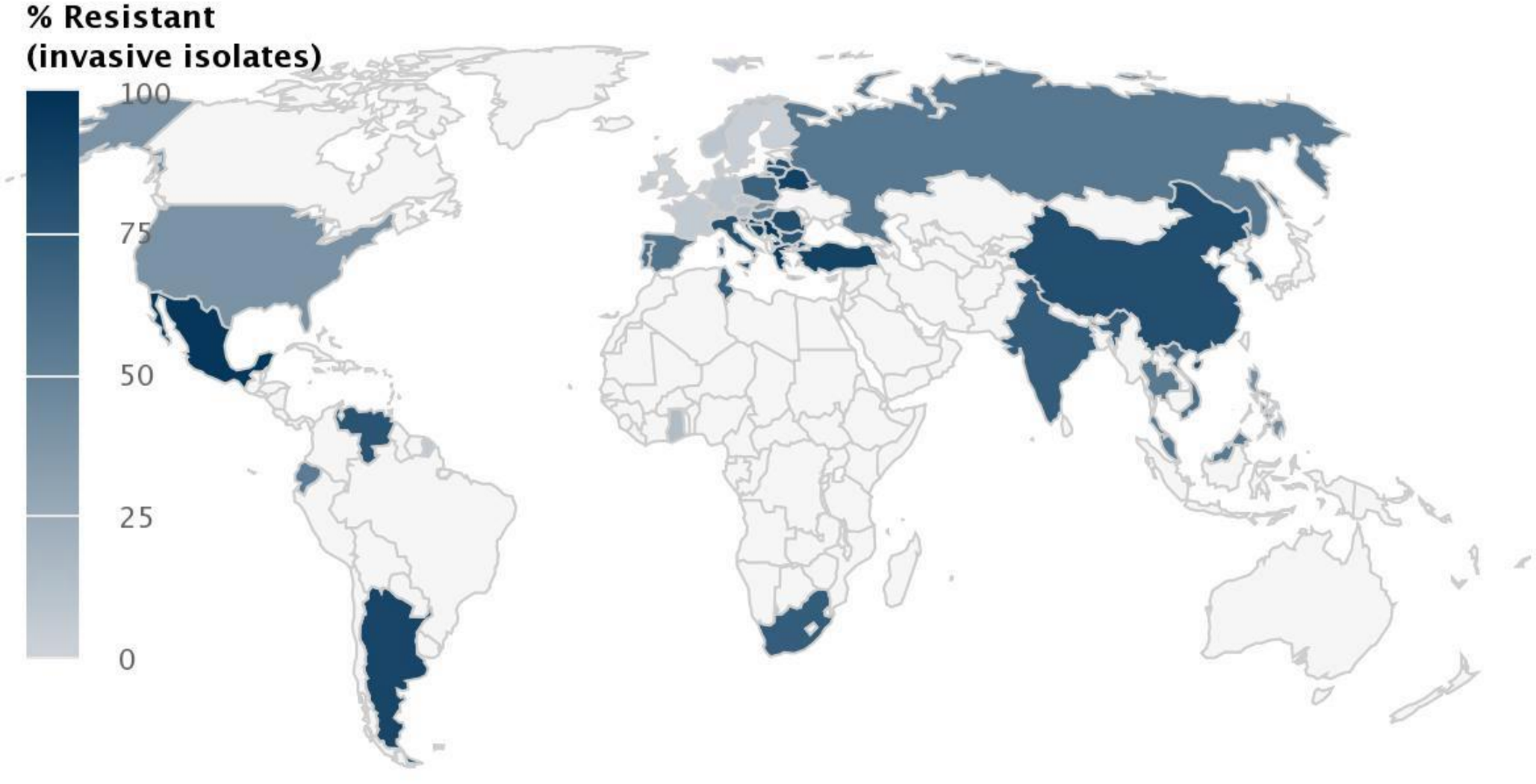
Christina Vandenbroucke-Grauls

http://resistancemap.cddep.org/

ResistanceMap

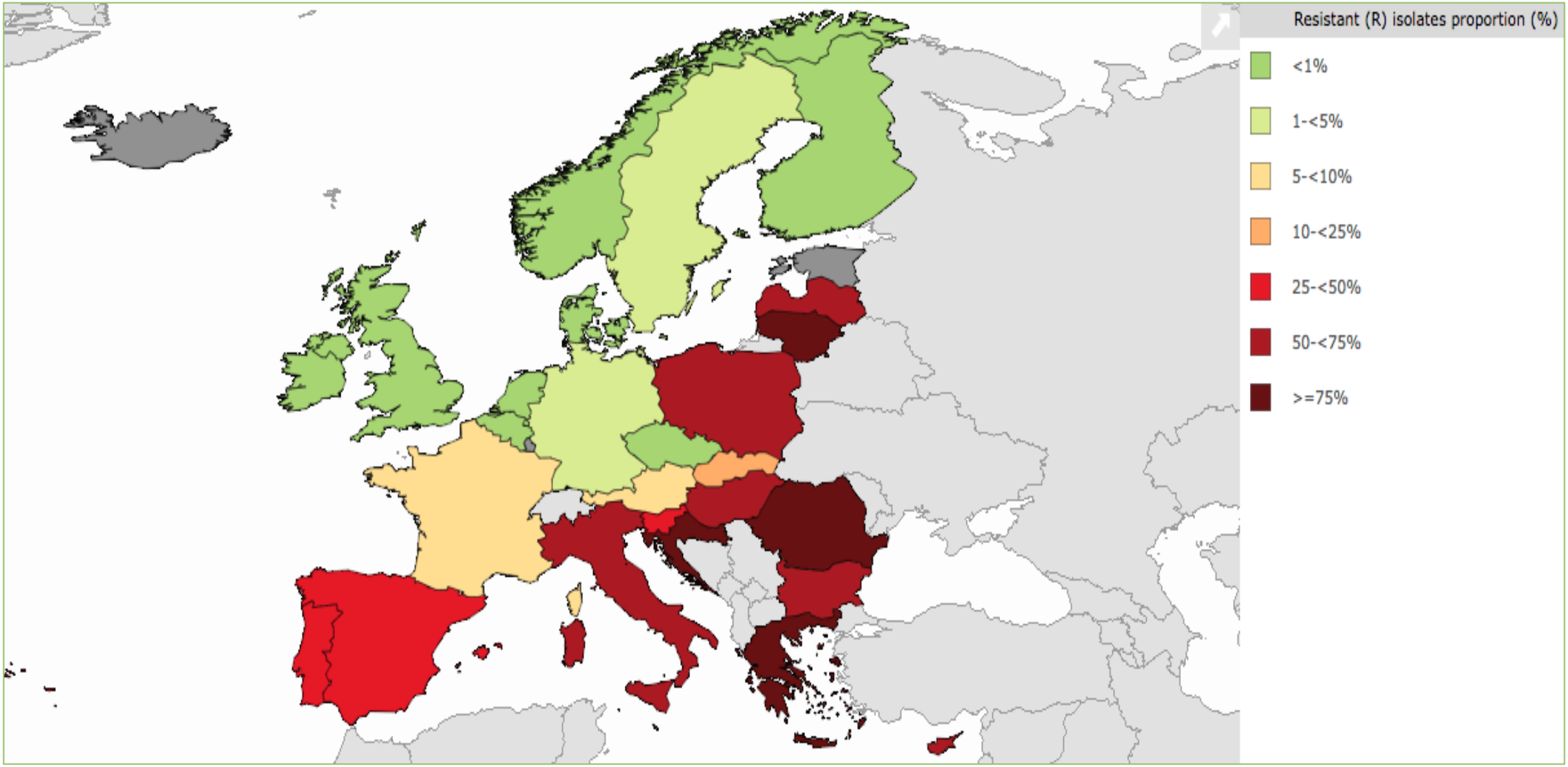
CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Resistance of *Acinetobacter baumannii* to Carbapenems



Surveillance Atlas of Infectious Diseases

2016, *Acinetobacter* spp., blood isolates, resistant to carbapenems, fluoroquinolones, aminoglycosides



http://atlas.ecdc.europa.eu/public/index.aspx

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ResistanceMap

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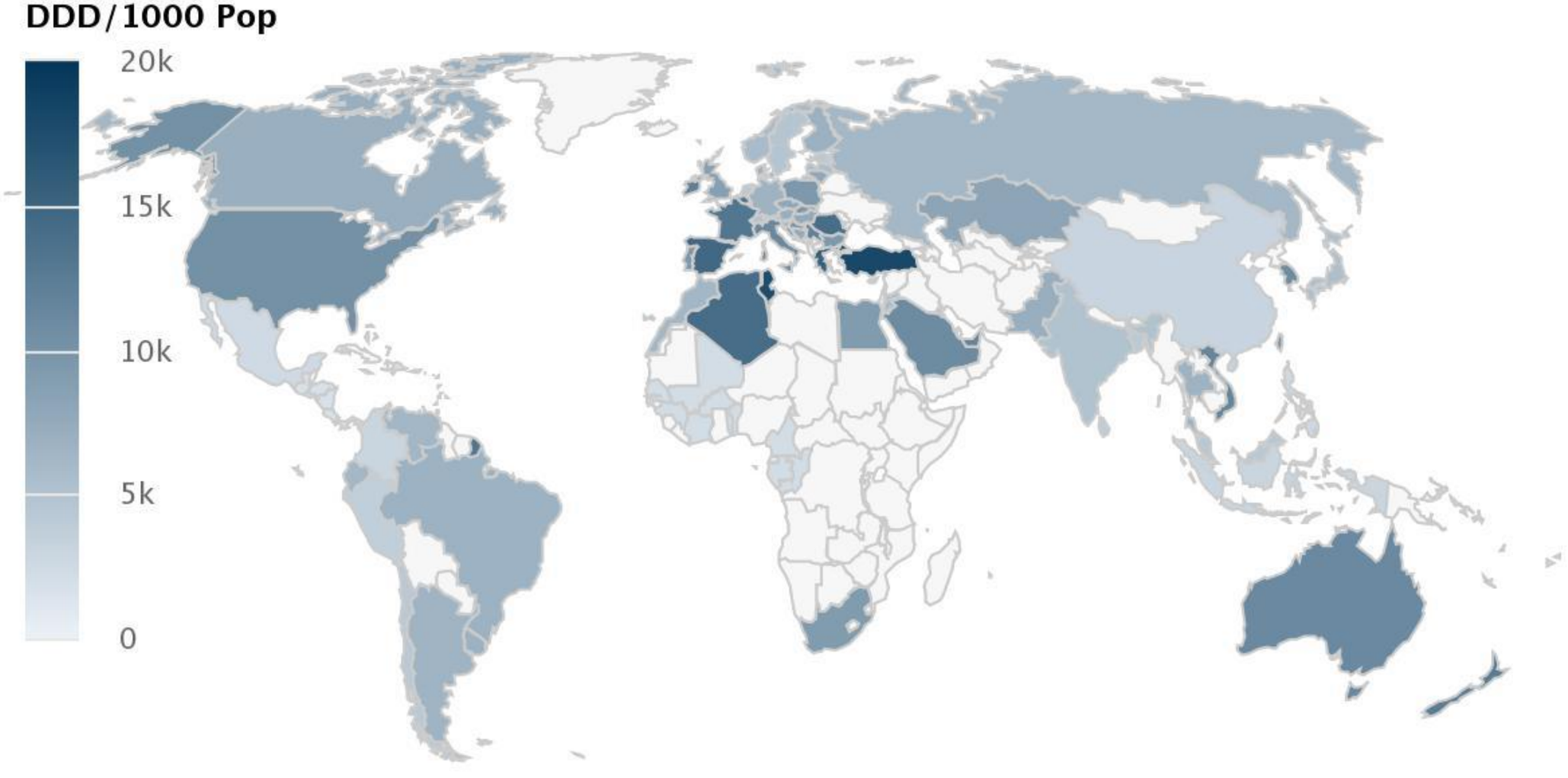
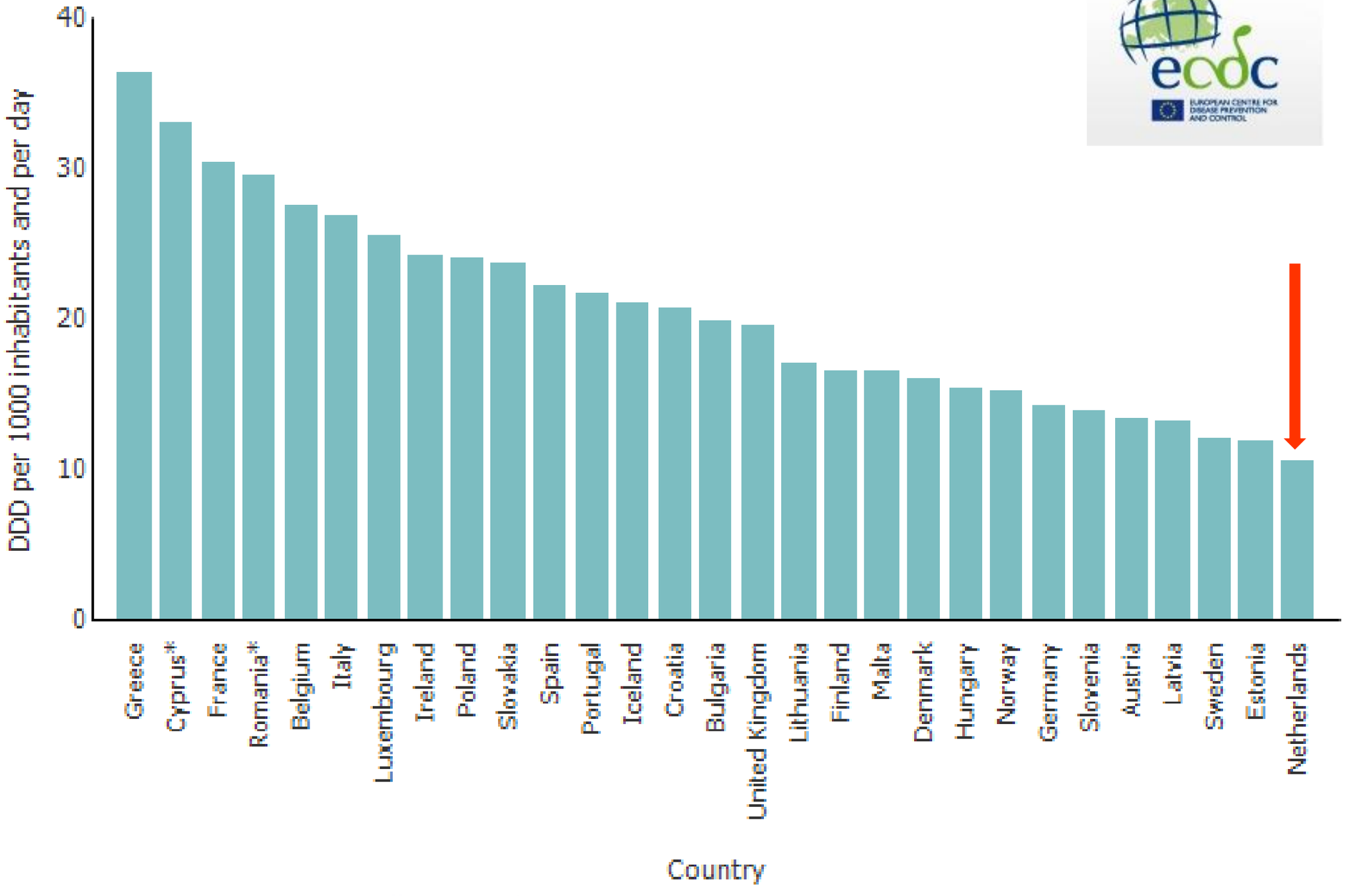
Use of All Antibiotics in 2015

Source: IMS Health



Consumption of Antibacterials for systemic use (ATC group J01) in the community (primary care sector) in Europe, reporting year 2016



European Surveillance of Antibiotic Consumption Network ESAC-Net

Outline

- Antimicrobial stewardship
  - What is it
  - Methods
  - Effective?
- Infection control
  - Focus on hospitals
  - Basic infection control: hand hygiene
  - Special measures for multidrug-resistant strains

Antimicrobial Stewardship
What is it?

- Use of appropriate antibiotics when needed and no unnecessary use
- Optimal selection, dose, and duration of antimicrobial therapy for best clinical outcome with minimal toxicity to the patient and minimal impact on subsequent resistance
- Good antimicrobial stewardship is akin to "motherhood and apple pie" *Gerding, Jt Comm J Qual Improv 2001;27:403*

Antimicrobial Stewardship
How to do it

- Simplest form: written guidelines for antibiotic therapy

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

CID 2007:44 (15 January) • 159

- Team work (infectious disease specialist, pharmacist, clinical microbiologist)
- Strategies:
  - Persuasive: advice how to prescribe and feedback about how prescribed
  - Restrictive: formulary restriction and preauthorization
- Additional elements: written guidelines, education, de-escalation of therapy, dose optimization, change from parenteral to oral antibiotics
- Clinical microbiology laboratory: critical role

JAMA Internal Medicine | Original Investigation

Behavioral Approach to Appropriate Antimicrobial Prescribing in Hospitals

The Dutch Unique Method for Antimicrobial Stewardship (DUMAS) Participatory Intervention Study

Jonne J. Sikkens, MD, MSc; Michiel A. van Agtmael, MD, PhD; Edgar J. G. Peters, MD, PhD; Kamilla D. Lettinga, MD, PhD; Martijn van der Kuip, MD, PhD; Christina M. J. E. Vandenbroucke-Grauls, MD, PhD; Cordula Wagner, PhD; Mark H. H. Kramer, MD, PhD

JAMA Intern Med. 2017;177(8):1130-1138.
Published online May 1, 2017.

- Can antimicrobial prescribing be improved by focusing on prescriber autonomy and participation?
- Participatory intervention study

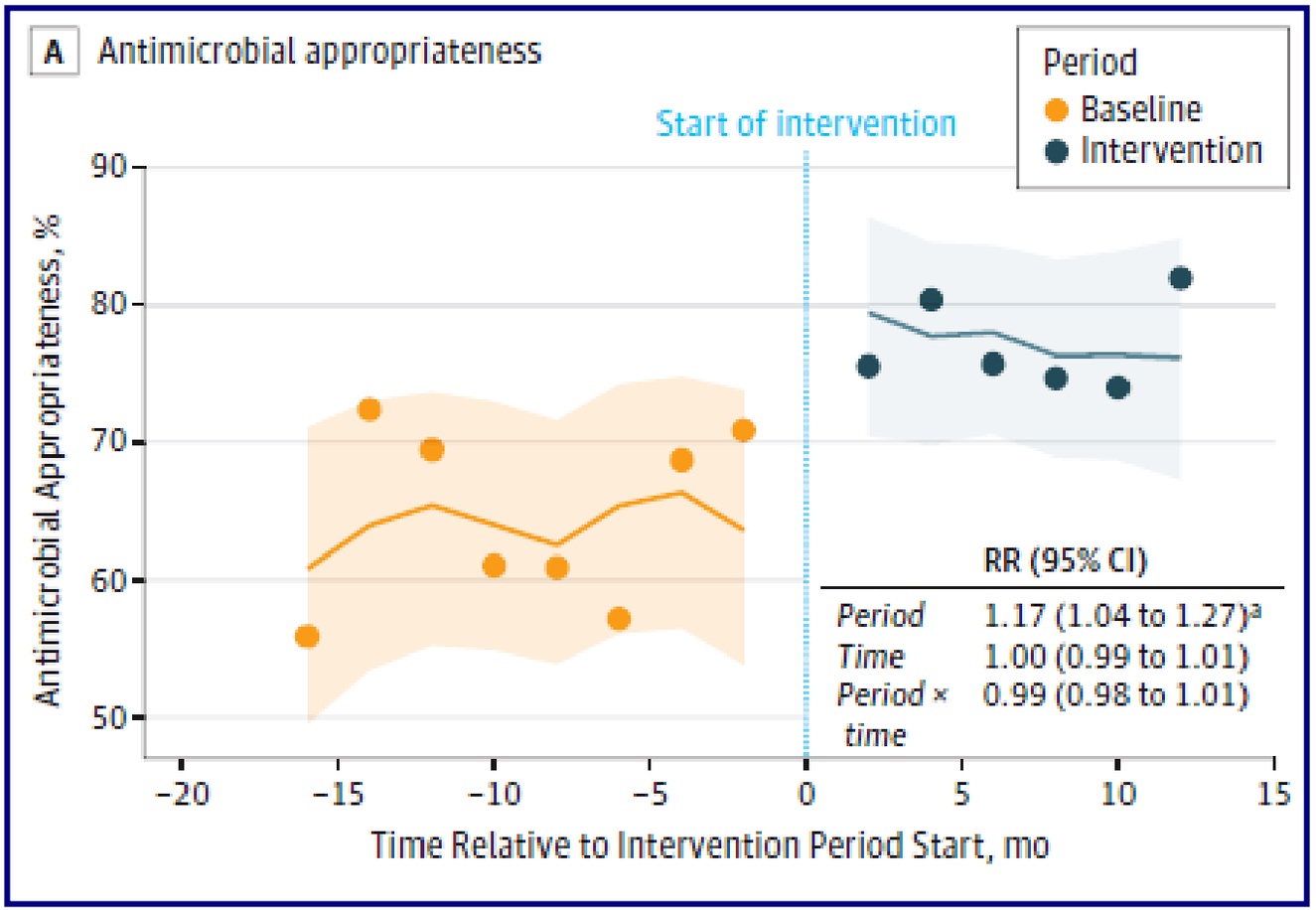
- Repeated point prevalence surveys to measure antibiotic use: amount and appropriateness (= according to the guidelines of the hospital)
- Interviews to analyse causes of inappropriate or high use

- Intervention: departments offered free choice on how to improve antimicrobial prescribing
  Examples: more consultation with experts, daily education rounds, quizzes, development of department-specific guidelines

- Outcomes: appropriateness of use and antimicrobial consumption (also measured by repeated point prevalence surveys)

Sikkens et al, JAMA Internal Med 2017;177:1135

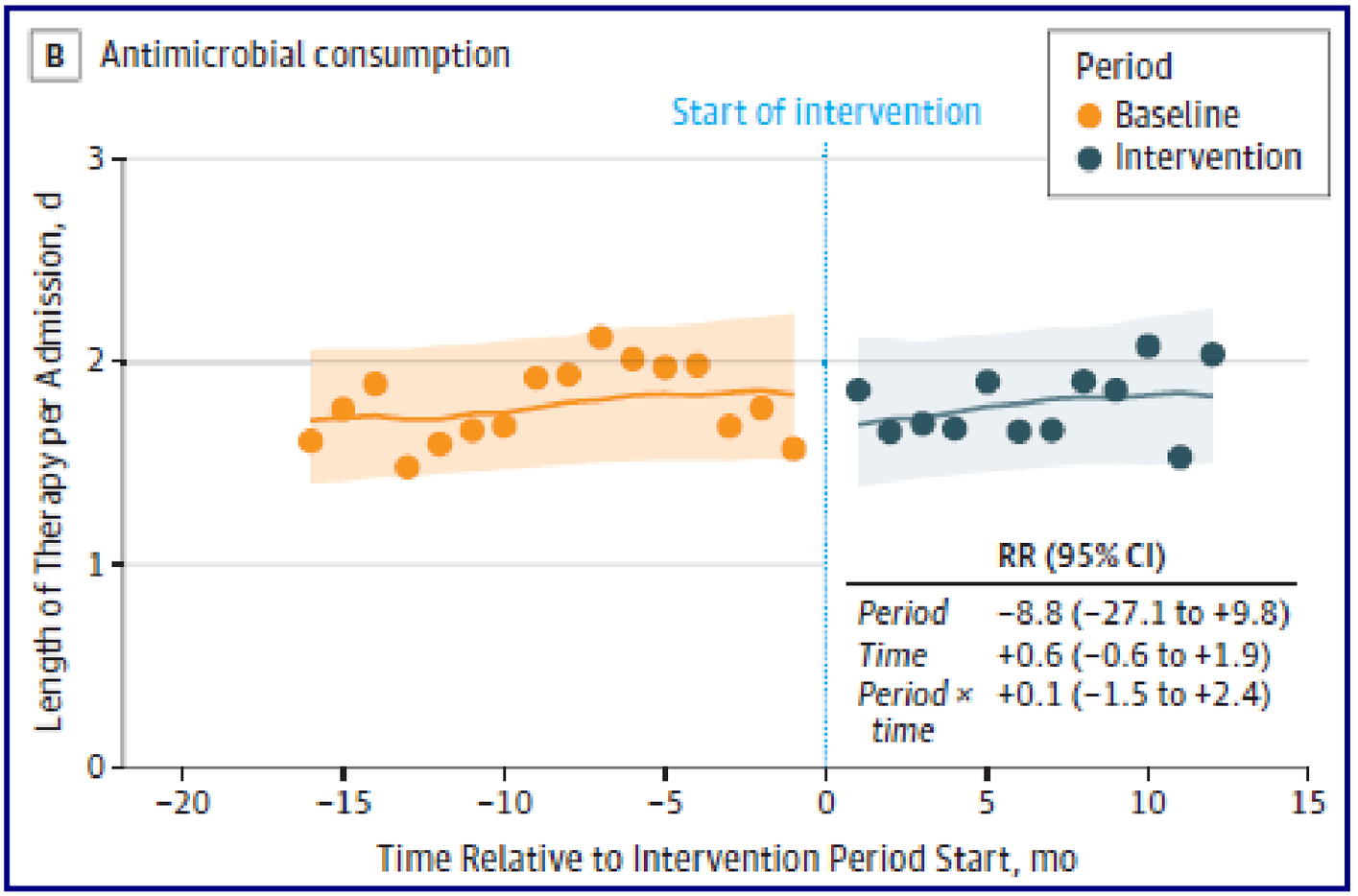
DUMAS Study: results



Optimal selection and dosing

less broad spectrum antibiotics, more small spectrum antibiotics

DUMAS Study: results



Overall consumption

Overall consumption: non-specific measure? (remember: Netherlands is lowest antibiotic user in Europe)

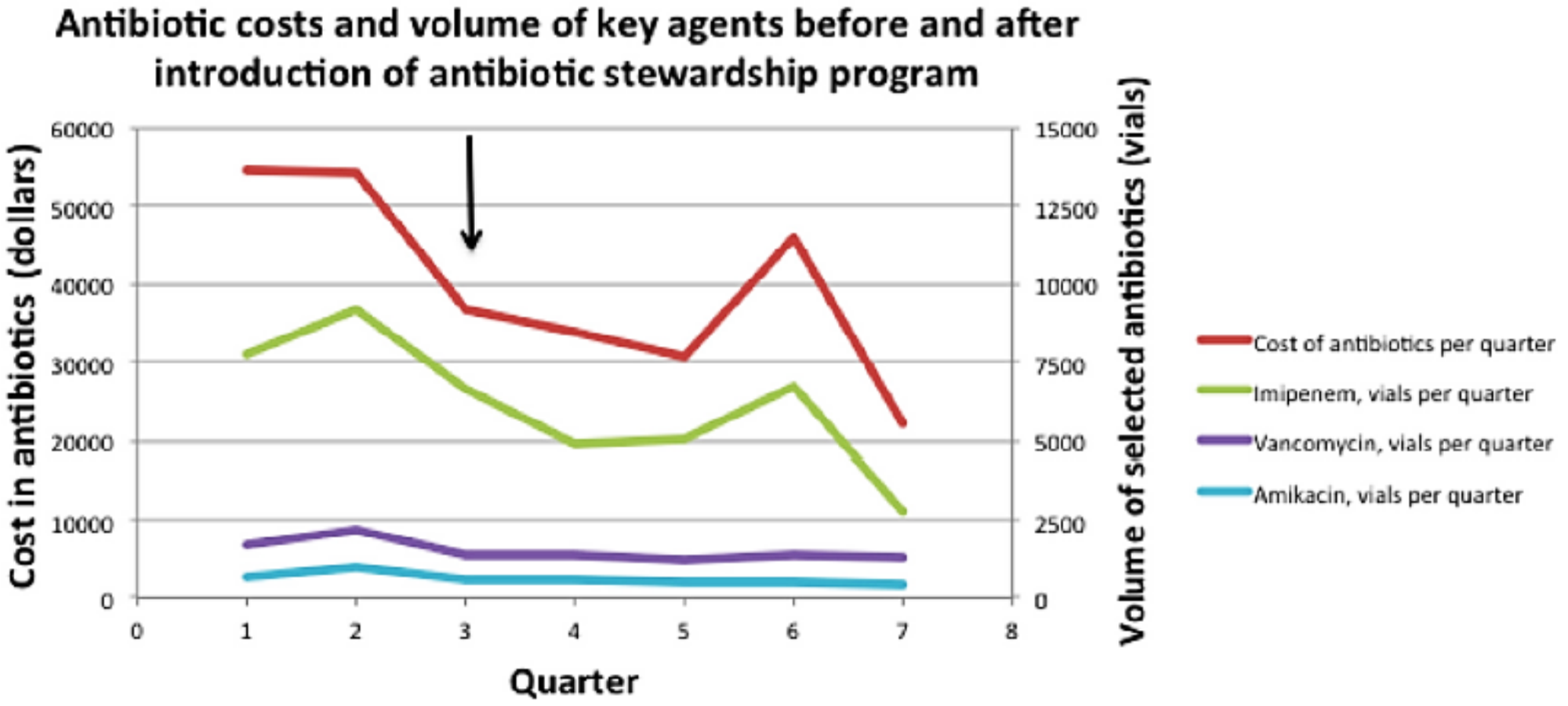
Sikkens et al, JAMA Internal Med 2017;177:1135

Introducing an antibiotic stewardship program in a humanitarian surgical hospital

Naina Bhalla MD [a], Nagham Hussein MD [b], Maha Atari BSc [b], Rasheed M. Fakhri MD [b], Chiara Lepora MD [a], Nadia Walsh RN [a], Sara E. Cosgrove MD [c], Richard A. Murphy MD, MPH [d,*]

Am J Infect Cont 2016;44:1381

- 2013: Médecins Sans Frontières (MSF): AMS program in a surgical unit in Amman, Jordan
  patients from Iraq, Syria, Yemen (+/- 220 at any time)
- Led by experienced MSF physician with a pharmacist, both under supervision of the hospital manager
- Review new hospital antibiotic prescriptions, make real-time recommendations to optimize antibiotic therapy, based on MSF treatment protocols and microbiology results



Bhalla et al, Am J Infec Cont 2016;44:1381

Trends and correlation of antibacterial usage and bacterial resistance: time series analysis for antibacterial stewardship in a Chinese teaching hospital (2009–2013)

Y. M. Zou · Y. Ma · J. H. Liu · J. Shi · T. Fan · Y. Y. Shan · H. P. Yao · Y. L. Dong

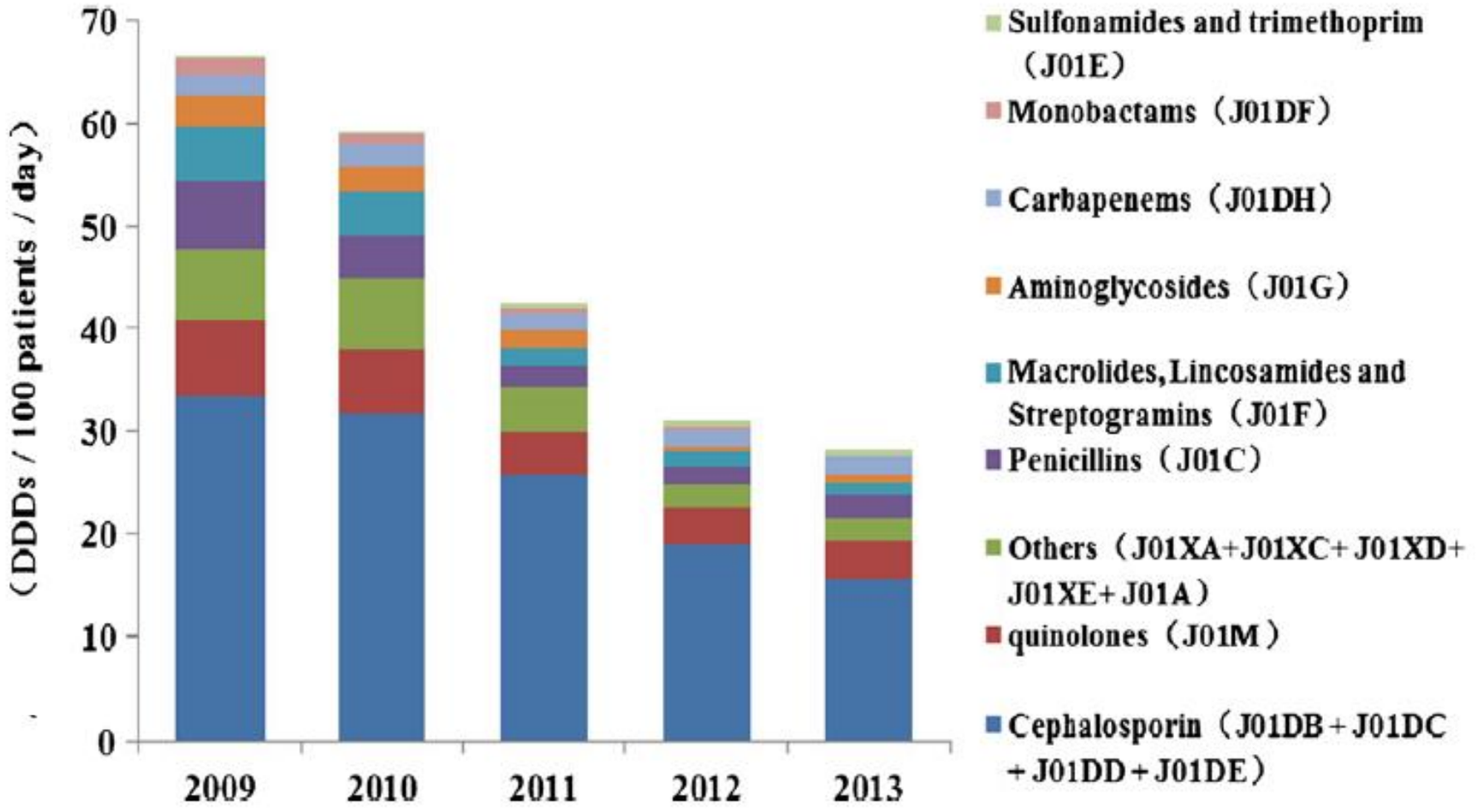
Eur J Clin Microbiol Infect Dis 2015;34:795

First Affiliated Hospital of Xi'an Jiaotong University

- Large, general tertiary-care teaching hospital with 2,341 beds
- AMS program started 2009
- Activities: analysis of trends in antimicrobial resistance and consumption, limitation of antibiotic consumption and antibiotic varieties, and multidisciplinary consultation with qualified individuals

Zou et al, Eur J Clin Microbiol Infect Dis 2015;34:795

Antimicrobial use 2009-2013



Zou et al, Eur J Clin Microbiol Infect Dis 2015;34:795

Antimicrobial Stewardship

Are ASM programs effective to reduce antimicrobial resistance?

Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis

David Baur*, Beryl Primrose Gladstone*, Francesco Burkert, Elena Carrara, Federico Foschi, Stefanie Döbele, Evelina Tacconelli

Lancet Infect Dis 2017;
17: 990–1001

- 32 studies in hospitals
- Main outcome:
  - Incidence ratios of infections by resistant bacteria before/after interventions

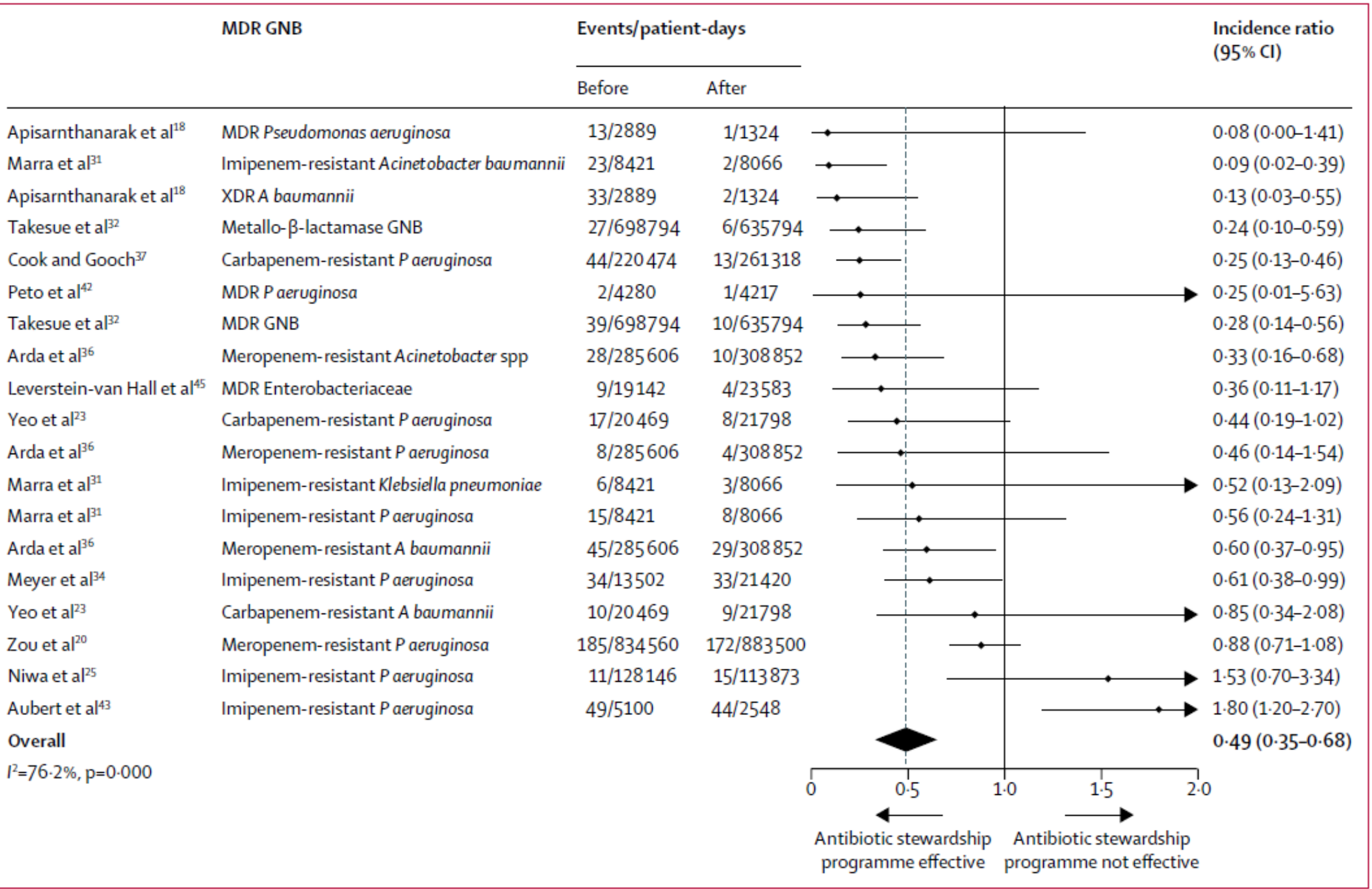
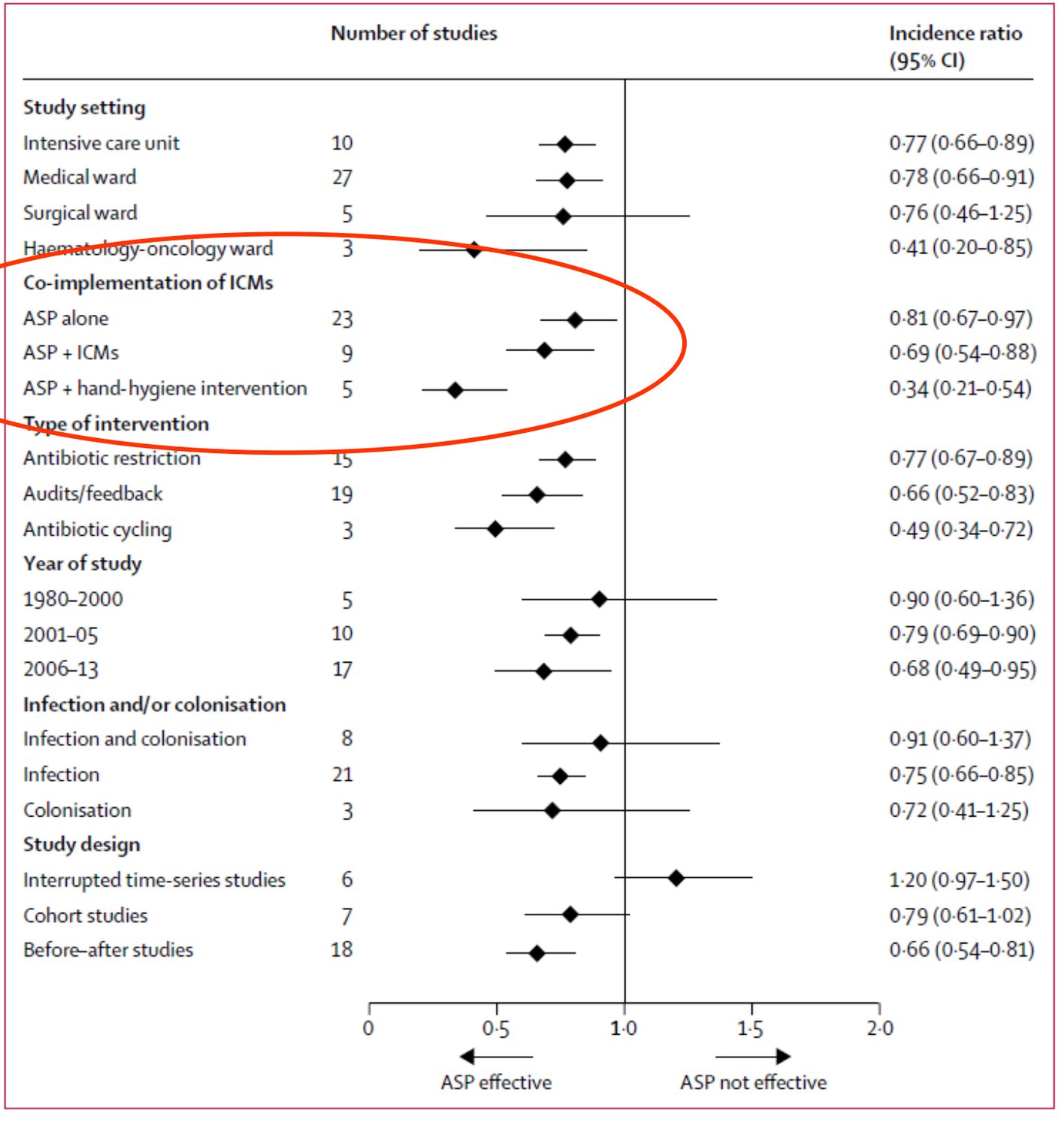


Figure 2: **Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of MDR GNB**

GNB=Gram-negative bacteria. MDR=multidrug-resistant. XDR=extensively drug-resistant.



Baur et al, Lancet Inf Dis 2017;17:990

Antimicrobial Stewardship Conclusion

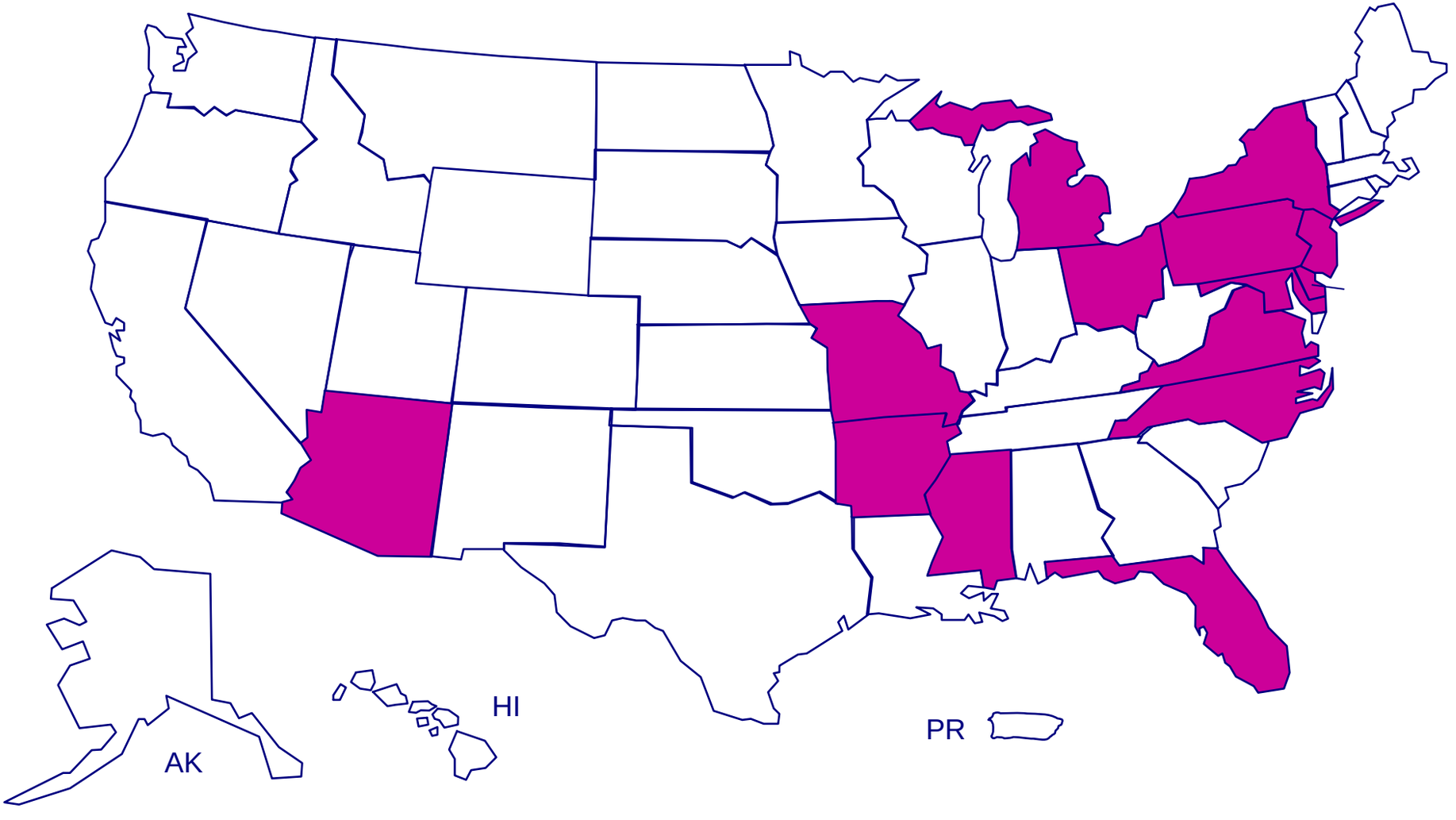
- Antibiotic stewardship programmes can reduce antibiotic use
- Antibiotic stewardship programmes can reduce antibiotic resistance rates
- Co-implementation of infection control measures, in particular hand-hygiene, has a synergistic effect.

Infection Control

- Focus on hospitals
  - Concentration of people and antibiotic use
  - Many contacts between persons

  →Can lead to rapid spread of microorganisms not only within hospitals but also between hospitals

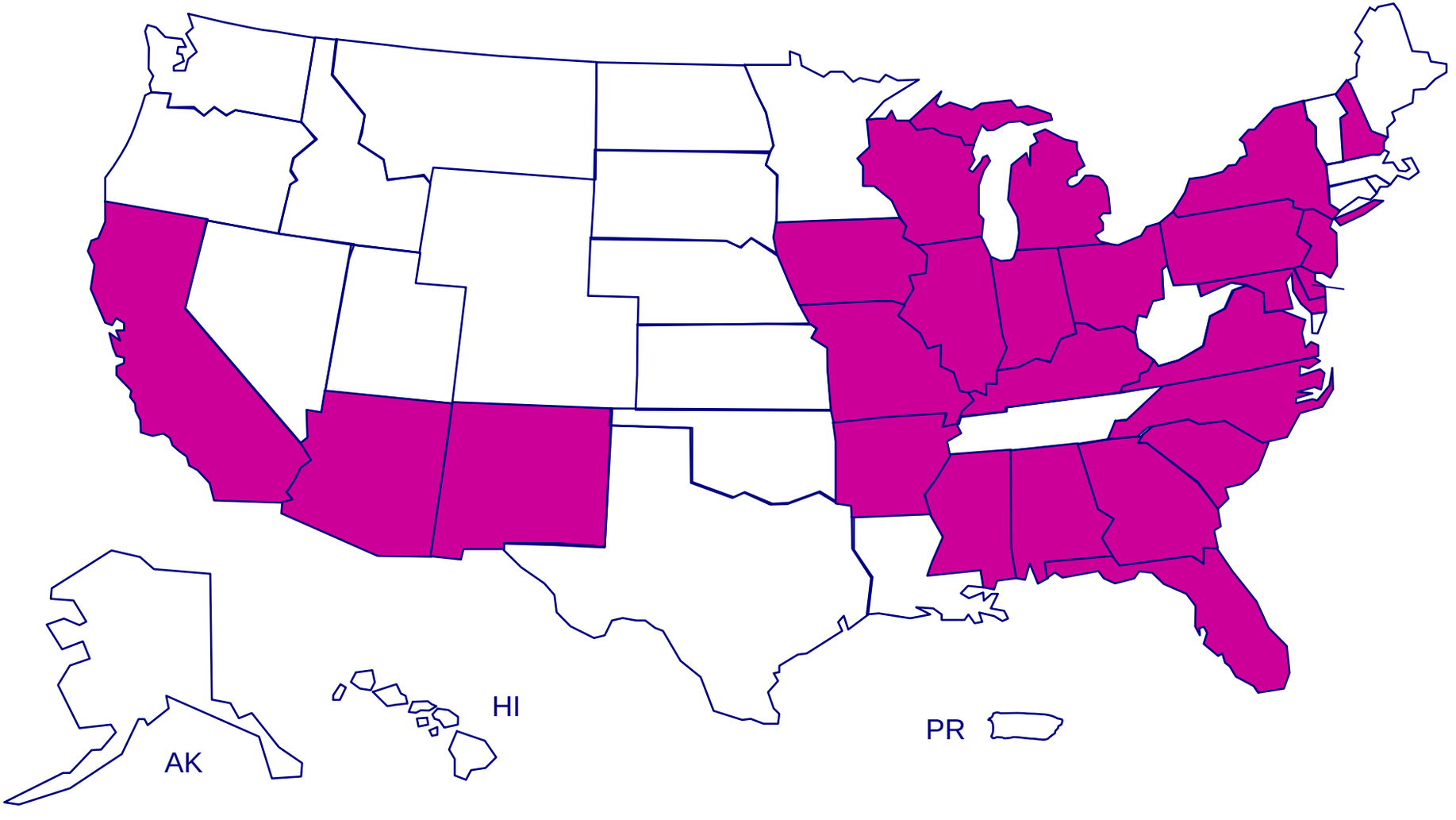
Carbapenem-resistant Enterobacteriaceae in the United states – November 2006



- Patel, Rasheed, Kitchel. 2009. Clin Micro News
- CDC, unpublished data

Courtesy of Arjun Srinivasan, CDC

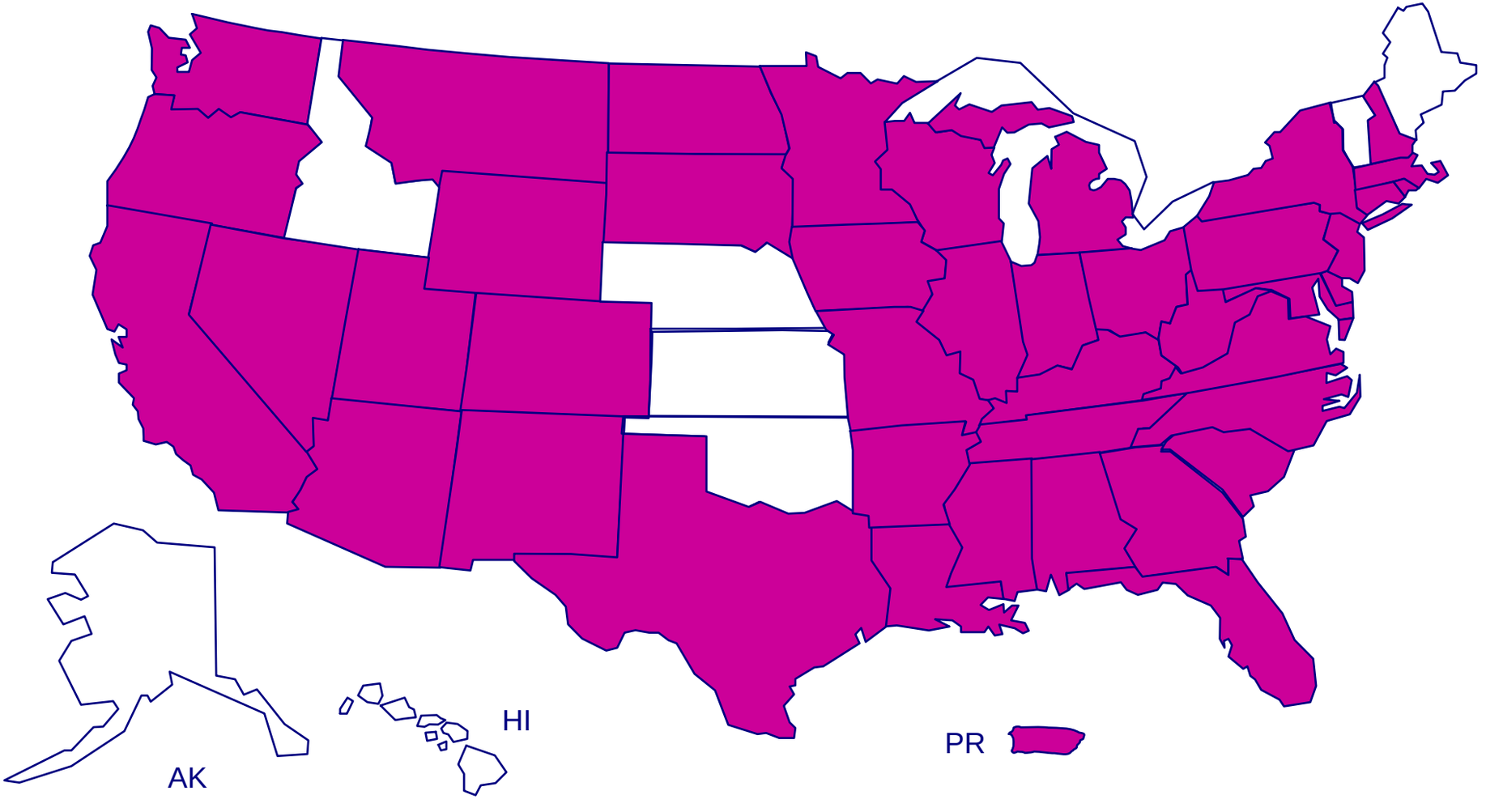
Carbapenem-resistant Enterobacteriaceae in the United states – November 2008



- Patel, Rasheed, Kitchel. 2009. Clin Micro News
- CDC, unpublished data

Courtesy of Arjun Srinivasan, CDC

Carbapenem-resistant Enterobacteriaceae in the United states – November 2012



- Patel, Rasheed, Kitchel. 2009. Clin Micro News
- MMWR. 2010 Jun 25;59(24):750 and MMWR. 2010 Sep 24;59(37):1212.
- CDC, unpublished data

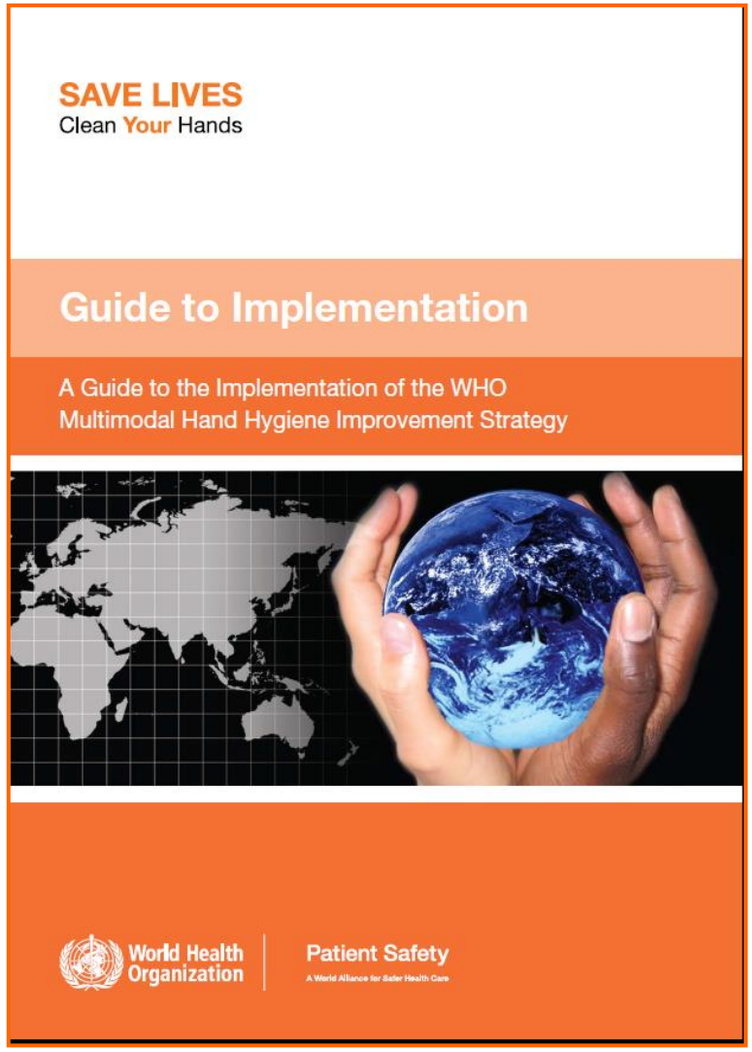
Courtesy of Arjun Srinivasan, CDC

How to control

- Prevention of transmission of microorganisms from one patient to the other:
  - Basic infection control - hand hygiene!
  - Specific precautions for multidrug-resistant strains

To improve Hand hygiene

- 2009: WHO issues an implementation strategy for hand hygiene
  - Provide hand alcohol
  - Safe water, soap and towels
  - Training and education
  - Evaluation and feedback
  - Reminders
  - Institutional safety climate



The Australian National Hand Hygiene Initiative

M. Lindsay Grayson, Andrew J. Stewardson, Philip L. Russo, Kate E. Ryan, Karen L. Olsen, Sally M. Havers, Susan Greig, Marilyn Cruickshank

Hand Hygiene Australia
Infectious Diseases Department, Austin Health, Melbourne
University of Technology Sydney Ultimo
Australian Commission on Safety and Quality in Health Care

Start: 2009

Audits HH: 3x/year

Outcomes:
- Hand hygiene compliance
- *S. aureus* bacteraemia (SAB) reported monthly by all Australian hospitals

Australian National Hand Hygiene Initiative

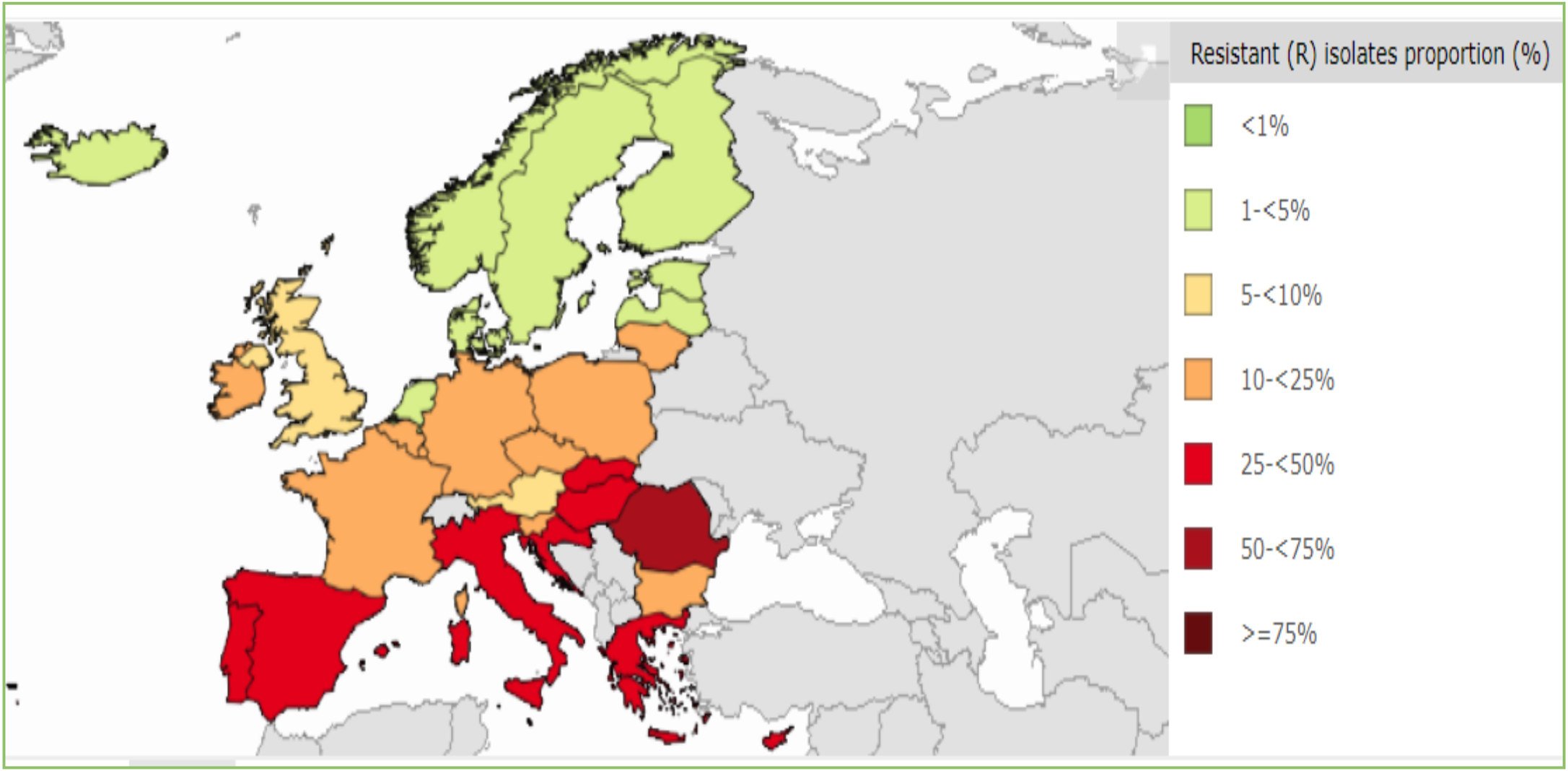
- Large and successful program running for over 8 years

- Hand hygiene improved considerably
- Marked reduction of *S. aureus* bacteraemia

Examples of specific precautions for antibiotic resistant bacteria

Surveillance Atlas of Infectious Diseases

2016, MRSA, % of *S. aureus* blood isolates

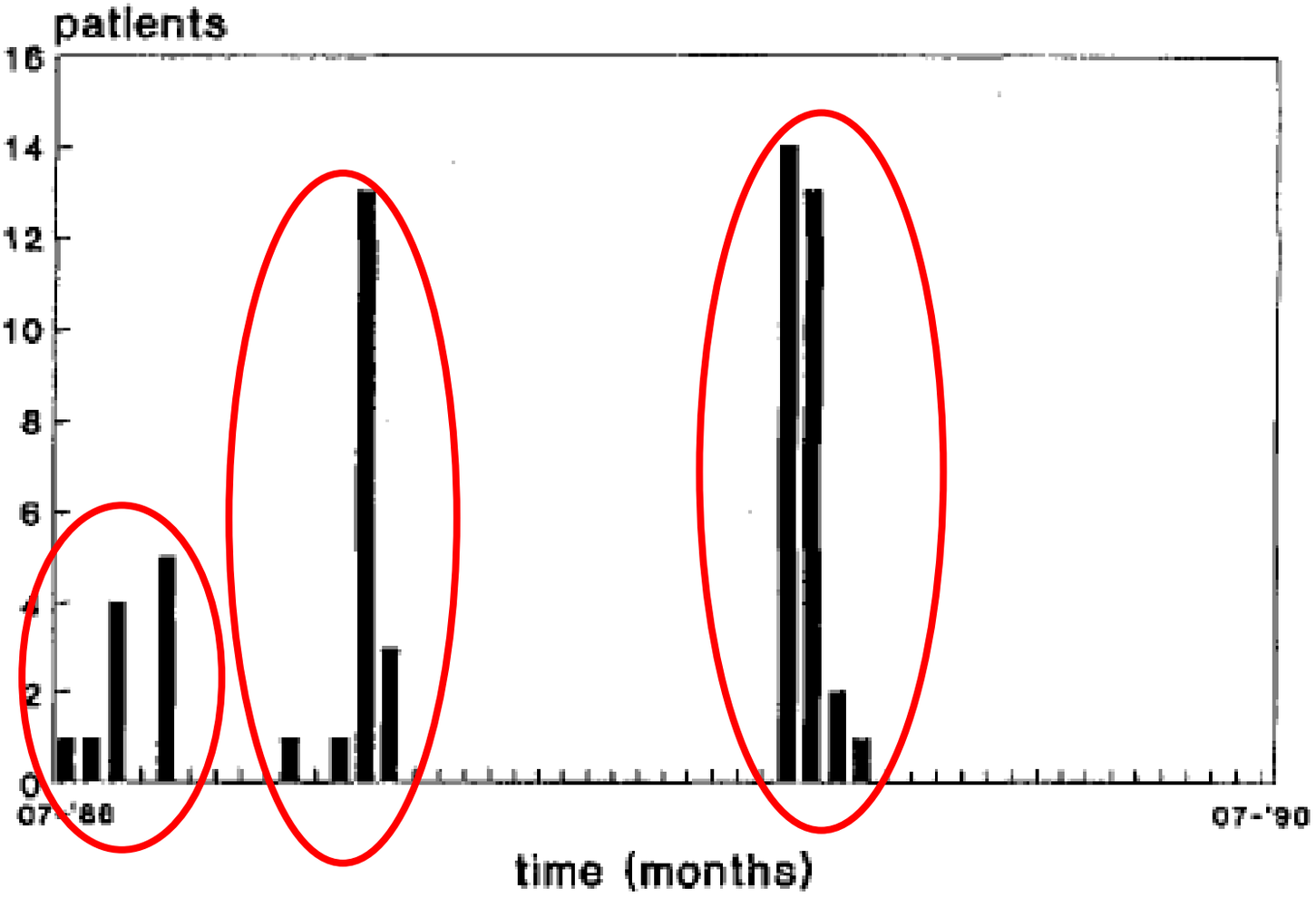


http://atlas.ecdc.europa.eu/public/index.aspx

MRSA in The Netherlands

- Started in the ’80s when the first MRSA strains were noticed in a few hospitals (Utrecht, Amsterdam, Rotterdam)
- Utrecht, July 1986: first MRSA in a patient repatriated from an Italian hospital

Three consecutive outbreaks of MRSA



Vandenbroucke-Grauls et al, Eur J Clin Microbiol Inf Dis 1991;10:6

MRSA in The Netherlands

- Strategy: "Search and Destroy"
  - Strict isolation of all MRSA positive patients (colonized or infected)
  - Search for carriers among contact patients and health care workers
  - Treatment of carriers (patients and HCW) with nasal mupirocin and chlorhexidine bathing
  - Pre-emptive isolation of patients transferred from foreign hospitals or high-risk settings

MRSA in The Netherlands

- "Search and Destroy"
  - National policy by 1989, endorsed by the Health Inspectorate
  - National surveillance by the National Institute for Public Health and the Environment
  - Mandatory notification of all new cases since 10 years

Vandenbroucke-Grauls Rev Med Microbiol 9: 109-116

- Numbers increased slowly over 30 years from 300/year to 3500/year (colonizations and infections) (total inhabitants of The Netherlands: 17 million)

INVITED ARTICLE ANTIMICROBIAL RESISTANCE

George M. Eliopoulos, Section Editor

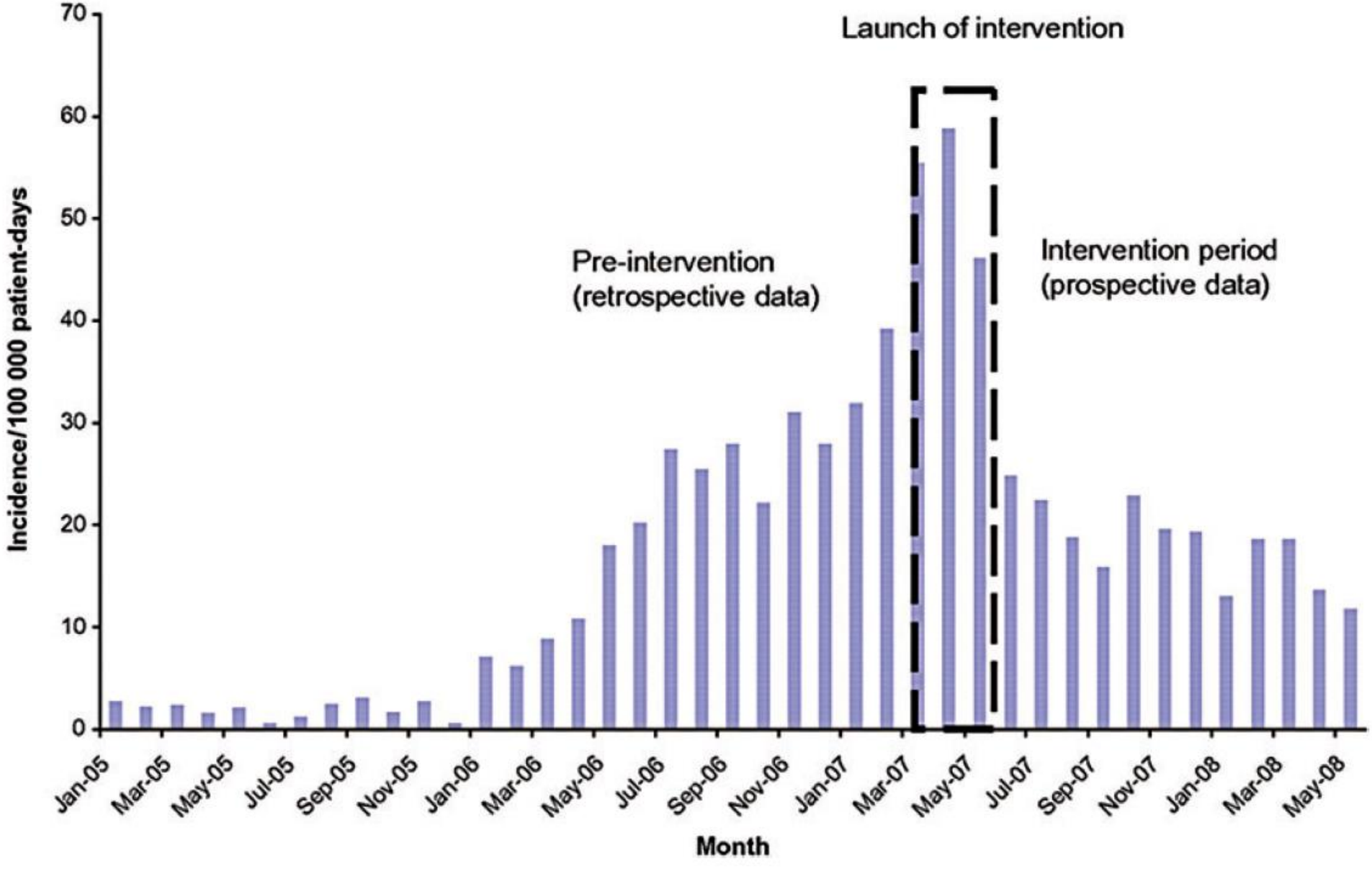
An Ongoing National Intervention to Contain the Spread of Carbapenem-Resistant Enterobacteriaceae

Mitchell J. Schwaber and Yehuda Carmeli

National Center for Infection Control, Tel Aviv, Israel

CID 2014:58 (1 March) • 697

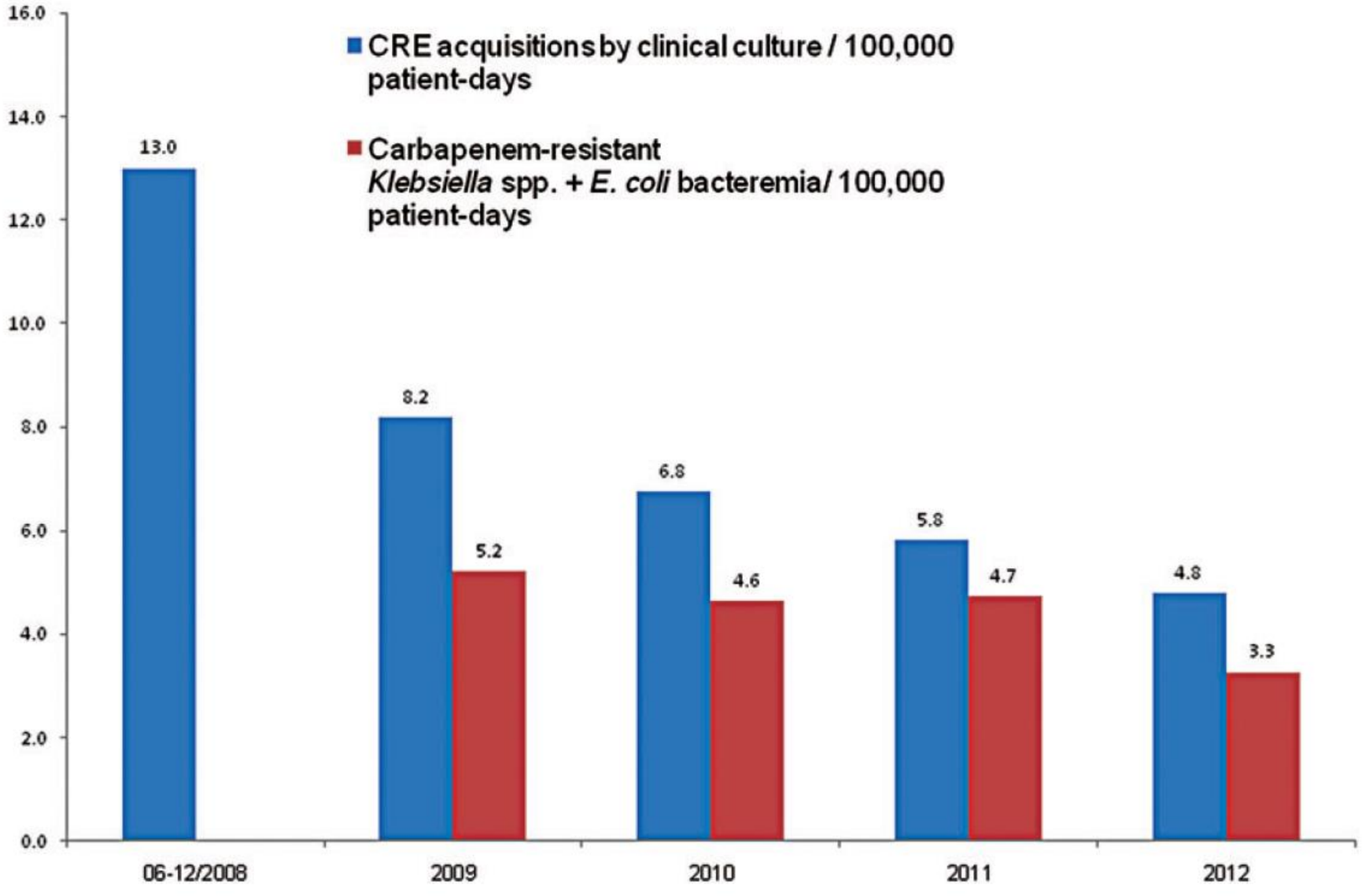
- 2006: nationwide spread of CRE (*K. pneum* ST-258)
- March 2007: Ministry of Health → guidelines
  - Isolation, cohorting, proactive screening
  - Dedicated nursing
  - Specific guidelines for long term care facilities and post-acute care facilities
  - Guidelines for laboratory detection



Monthly incidence (clinical cultures)

Mitchell J. Schwaber and Yehuda Carmeli

National Center for Infection Control, Tel Aviv, Israel



Annual incidence (clinical cultures) and annual incidence of bacteraemia

Mitchell J. Schwaber and Yehuda Carmeli

National Center for Infection Control, Tel Aviv, Israel

- MRSA in The Netherlands shows that a fast reaction and a concerted national action at the first appearance of resistant strains helps in preventing increase to high numbers
- CRE in Israel shows that a concerted national action can reduce high numbers to more acceptable levels

- The MRSA success in The Netherlands is also due to the traditionally low antibiotic use
- Israel started a national program for antibiotic stewardship in 2012

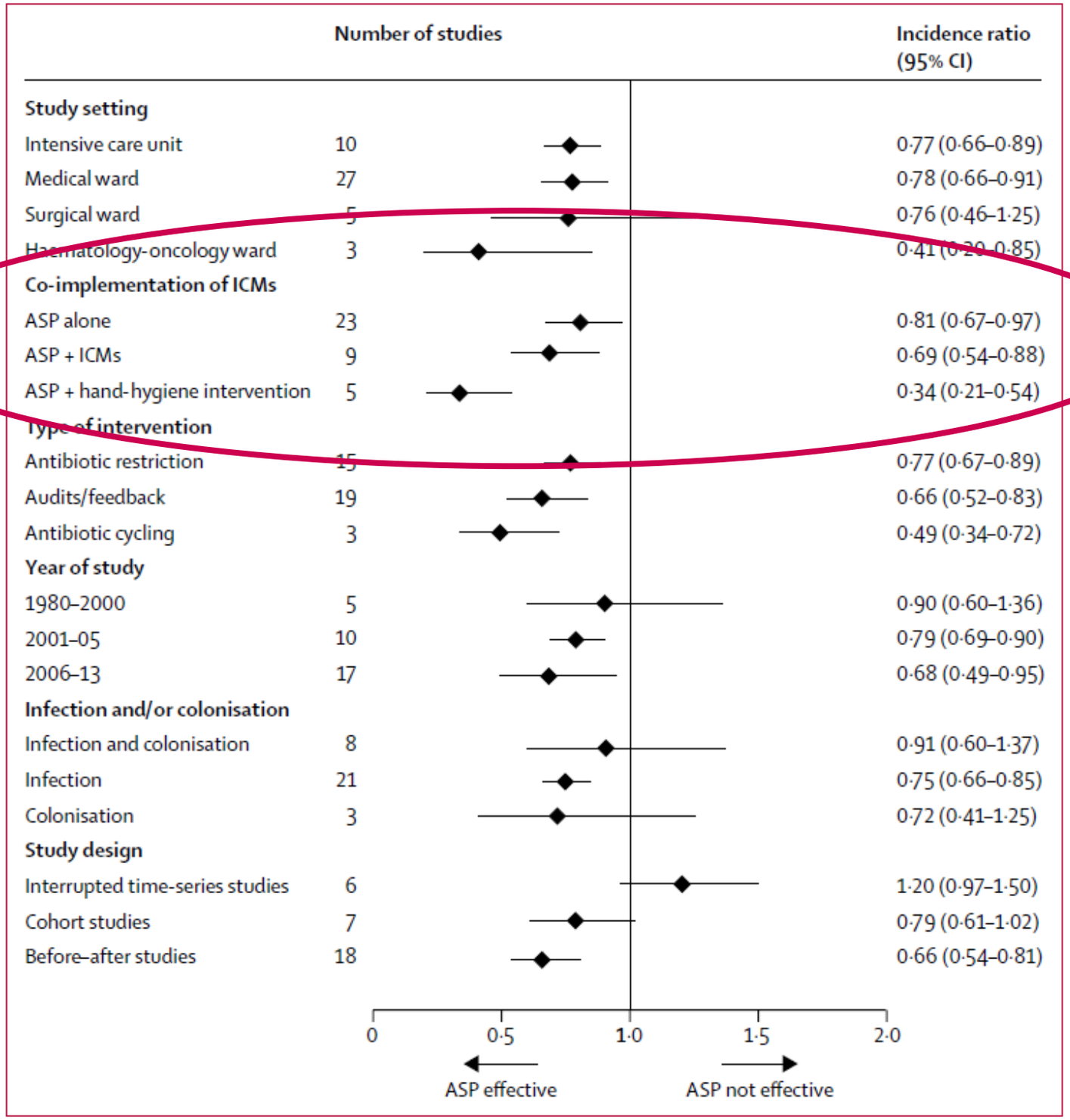


Figure 5: **Summary forest plot of the incidence ratios for studies investigating the effect of ASPs on antibiotic resistance, according to study characteristics**

ICM=infection control measure. ASP=antibiotic stewardship programme.

Baur et al, Lancet Inf Dis 2017;17:990

Conclusion

- Slowing down the emergence of resistant strains and countering their spread is possible
- Requires wise antibiotic use combined with good infection control