Emerging Antimicrobial Resistance

A View (and response) from

Down-Under

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Infectious Diseases & Microbiology Department, Austin Health
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Hosted by Claire Kilpatrick
WHO Infection Control Global Unit

Sponsored by the World Health Organization
Infection Control Global Unit - www.who.int/gpsc/en

Conflict of Interest Disclosures

Funding:

- Australian Commission on Safety & Quality in Health Care
- Australian National Health & Medical Research Council (NHMRC)
- Dept. of Health, Victoria, Australia
- Director, Hand Hygiene Australia

Overview

- The view from Mars
- Antimicrobial Resistance
  - Setting the scene for Australia
  - Current status – politics, resistance and prescribing
  - What is missing?
- New approaches
  - Building an IPC "fire-break"
  - New approaches to AMS
  - Re-assessing older agents
- The daunting future for Australia
  - What we can do about it

A brief summary of the problem

A view from Mars

A brief summary of the problem

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A view from Mars

- Pre-1940s – no Antibiotics
- Wonder drugs invented
- Within 70 years (2-3 human generations) – antibiotics misused
- Rapidly emerging multi-drug resistance
  - Gram+ves – MRSA, VISA, VRE, L-VRE
  - Gram-ves – CREs, colistin-resistant, etc
  - XDR-TB
  - Hypervirulent *C. difficile*

A brief summary of the problem

A view from Mars

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This can't be right!

No-one could be so completely stupid!

A brief summary of the problem

A view from Mars

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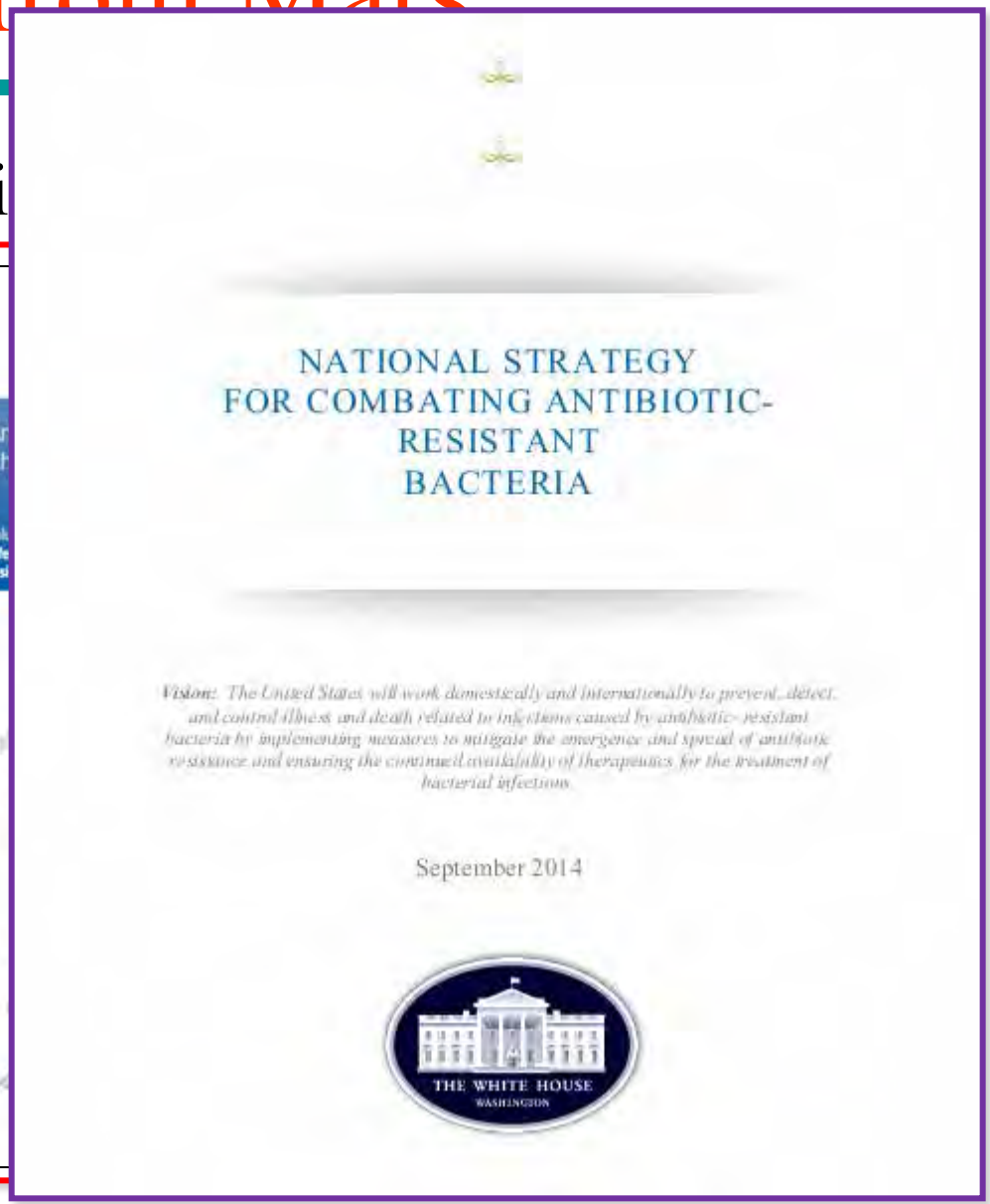

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Figure 1.1. **World Health Organization regions**

5. WHO European Region

Regional facts

- Number of Member States: 53
- Number of Member States for which information was available for the analysis: 49 (92%)
- Regional population: 902 million
- Life expectancy for region: average: 77 years; range: 63–83 years

4. WHO Eastern Mediterranean Region

Regional facts

- Number of Member States: 21
- Number of Member States for which information was available for the analysis: 13 (62%)
- Regional population: 583 million
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7. WHO Western Pacific Region

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Figure 1.1. World Health Organization regions

6. WHO South-East Asia Region

Regional facts

- Number of Member States: 11
- Number of Member States for which information was available for the analysis: 11 (100%)
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- Life expectancy for region: average: 70 years; range: 66–77 years

3. WHO Region of the Americas

Regional facts

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2. WHO African Region

Regional facts

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Key problems - worldwide

- Weak regulatory systems & inability to enforce laws
- Ready availability of antibiotics
  - Over the counter sales
  - Internet sales
- Market and salary distortions for prescribers (MDs)
- Counterfeit drugs
- Poor laboratory diagnostic intrastructure
- Ready dissemination of MDR clones
  - Poor sanitation infrastructure in populous regions
  - Ready access to air travel

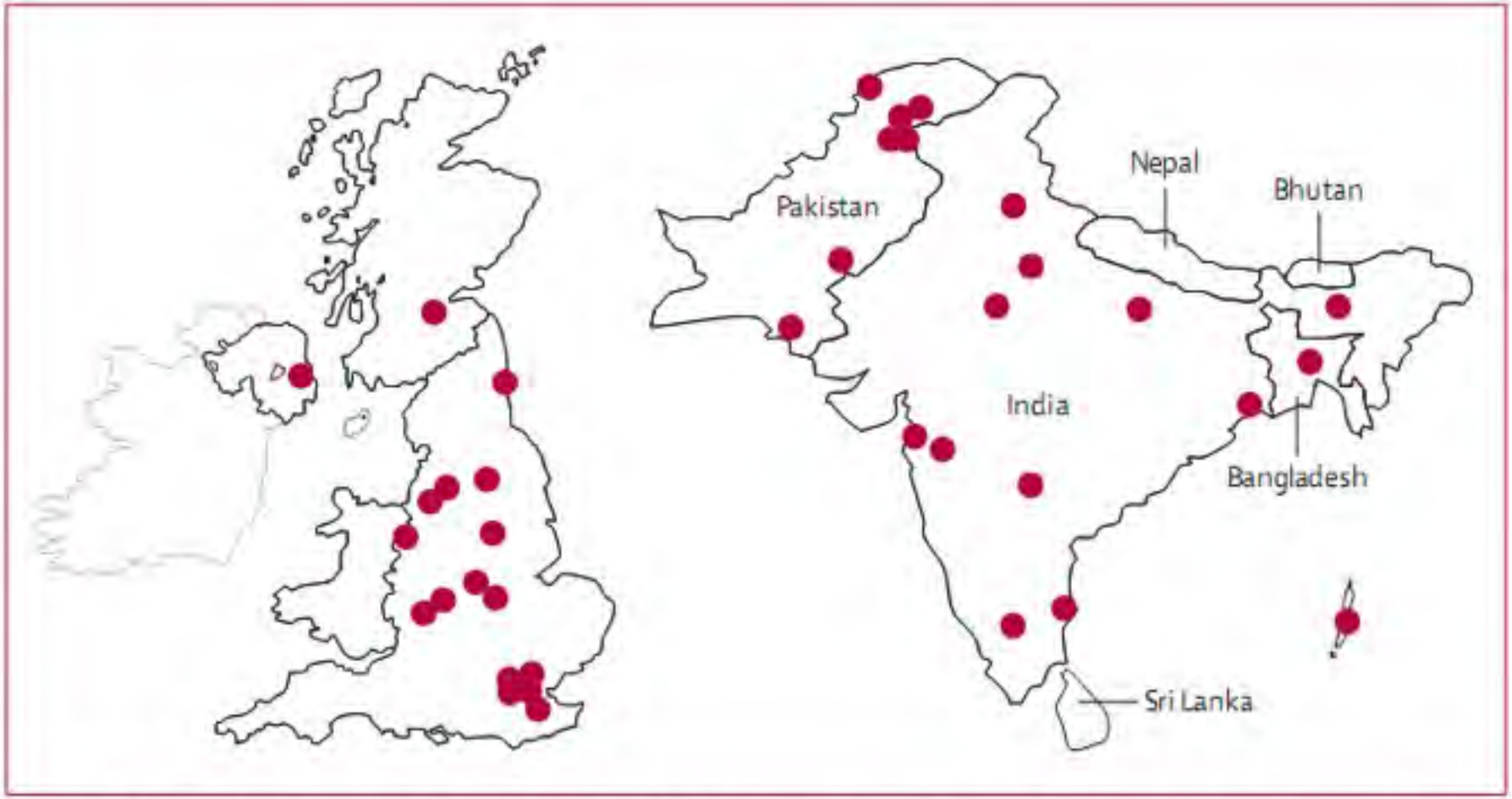

Figure 5: Distribution of NDM-1-producing Enterobacteriaceae strains in Bangladesh, Indian, Pakistan, and the UK

Figure 1: Map of NDM-1-positive samples from New Delhi centre and surrounding areas

Hospitals Overseas travel raises risk levels

Alarm on superbug spread

Kate Hagan
Health Reporter

Australians are increasingly returning from overseas with multi-drug-resistant "superbugs", prompting warnings for hospitals to isolate high-risk patients to stop their spread.

Austin Hospital infectious diseases director Lindsay Grayson *of Australia*, doctors from the Austin said they had treated 10 patients infected with superbugs after overseas travel between December 2011 and February 2013.

In one case, a 66-year-old man developed a ruptured bowel that became infected with superbugs

him in a single room with a dedicated bathroom, cleaning his room daily with bleach, avoiding use of shared equipment and enforcing contact precautions, including the use of gowns and gloves. Professor Grayson said healthy bacteria in people's bowels were being

The Age

Monday 3rd Feb 2014

Case reports

Lessons from practice

The growing burden of multidrug-resistant infections among returned Australian travellers

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doi: 10.5694/mja13.10592

Clinical record

A previously well 66-year-old man was repatriated from Athens, Greece, to the Austin Hospital for ongoing management after a protracted hospital admission for an ischiorectal abscess secondary to perforated diverticulitis. This was complicated by faeculent peritonitis, multiple intra-abdominal abscesses and necrotising fasciitis of the abdominal wall. These complex problems required multiple laparotomies to drain and debride the abscesses, management of an open abdomen with vacuum-assisted closure dressings, and the formation of a loop sigmoidostomy. He also developed a grade IV sacral pressure ulcer with underlying sacral osteomyelitis. Organisms isolated from the intra-abdominal collections included carbapenem-resistant *Pseudomonas aeruginosa* and a carbapenemase-producing *Klebsiella pneumoniae* (bla_{KPC}). Due to the complexity of the patient's illness, he had spent 93 days in hospital in Greece, predominantly in intensive care, with three interhospital transfers within Greece before repatriation to Australia. Antibiotics administered in Greece included tigecycline, colistin, fosfomycin, vancomycin, clindamycin and anidulafungin.

As the patient had multiple resistant organisms, detailed infection control plans were made before his arrival at the Austin Hospital. This included placement in a single room with a dedicated ensuite bathroom, daily bleach cleaning of the room,[1] no use of shared equipment, enforcement of strict contact precautions including gowns and gloves, and hand hygiene. Patient movement was severely restricted and only two visitors were allowed at any one time.

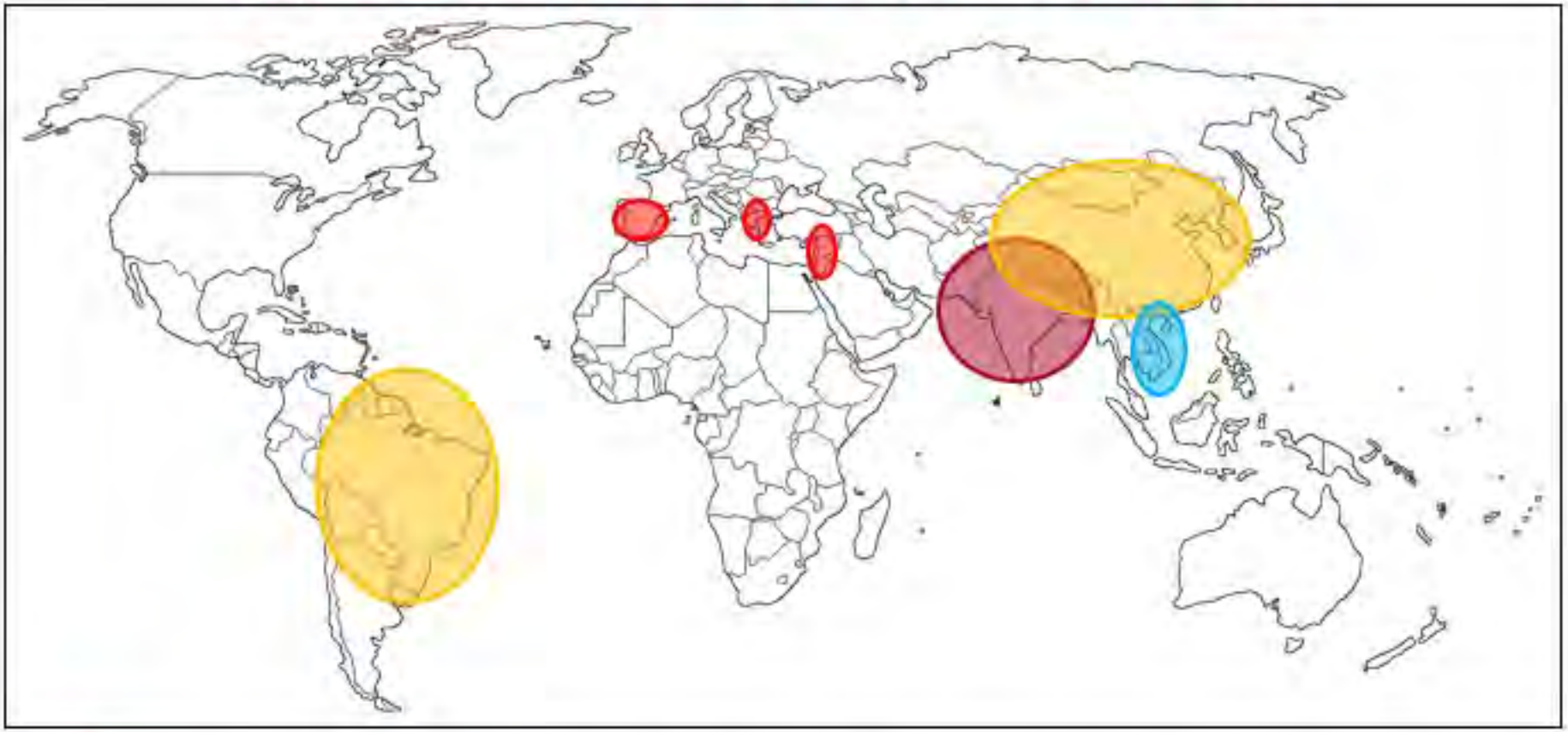
Unfortunately, the patient developed a new intra-abdominal collection, bowel obstruction and abdominal sepsis. This required surgical intervention, including extensive division of adhesions, resection of the sigmoid and part of the descending colon, retroperitoneal enteric fistula repair and retroperitoneal abscess drainage. An end colostomy and loop ileostomy were formed. This procedure resulted in faecal continence and therefore control of the perianal source of multidrug-resistant organisms. Culture of the intra-abdominal abscess grew mixed enteric flora including *Enterococcus faecium*, *Escherichia coli*, *Citrobacter* spp, *Candida glabrata* and *K pneumoniae*. The latter organism was resistant to multiple drugs, including meropenem, due to the production of *K pneumoniae* carbapenemase-2 (bla_{KPC-2}) (Patient 1, Box). The same organism was found in his faeces.

A bla_{KPC-2}-producing *K. pneumoniae* was also isolated from a sacral ulcer swab, but the susceptibility profile was slightly different. This isolate was also resistant to all aminoglycosides, including gentamicin and amikacin, and demonstrated an increased minimum inhibitory concentration to colistin (Box). The patient's antibiotic treatment included meropenem, tigecycline, colistin and caspofungin for 6 weeks, and his sacral ulcer was treated with a vacuum-assisted closure dressing. He stayed at the Austin Hospital for 101 days before being discharged home.

Six months later, the patient re-presented to the Austin Hospital with urosepsis. The causative organism, isolated in both urine and blood, was *E coli* (Box). Strikingly, the organism was found to be a bla_{KPC-2}-producing strain, suggesting interspecies transfer of this mobile genetic element between *K. pneumoniae* and *E. coli*. Unlike the *K. pneumoniae*, this isolate was susceptible to ciprofloxacin, and the patient was successfully treated with this antibiotic. During this second admission, the same infection control measures were enforced.

At follow-up 6 months later, the patient remained well. There was no documented inhospital transmission of bla_{KPC-2}, suggesting the infection control measures employed were successful.

High rate areas for MDR Gram-negatives and Key Australian traveller destinations - 2012



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- High risk – ESBL Gram-negatives – mainly healthcare acquired
- Rapidly emerging high risk – ESBL Gram-negatives – contaminated food suspected
- Suspected risk – ESBL Gram-negatives – source uncertain

Australian Bureau of Statistics - http://www.abs.gov.au/ausstats

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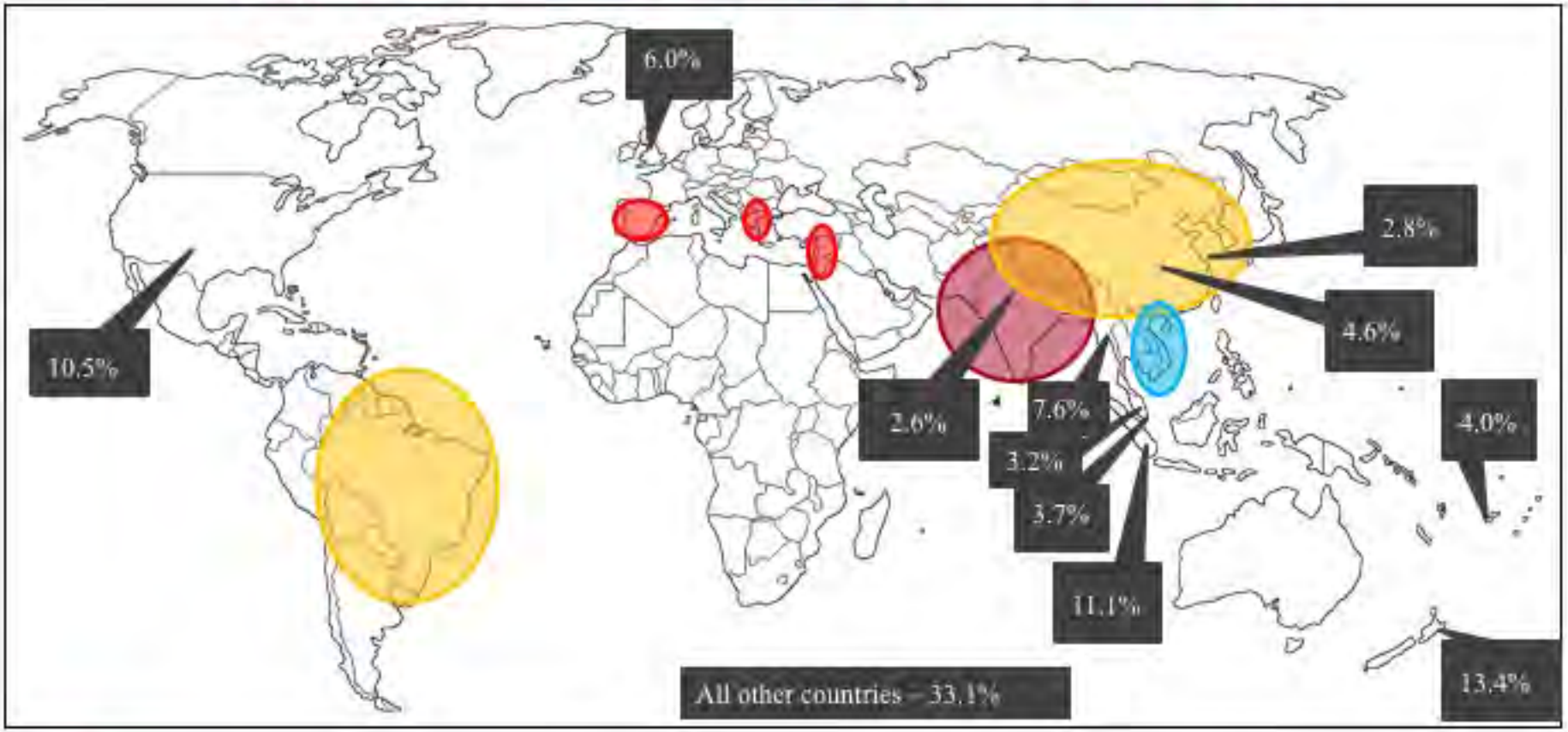

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1999

The use of antibiotics in food-producing animals:

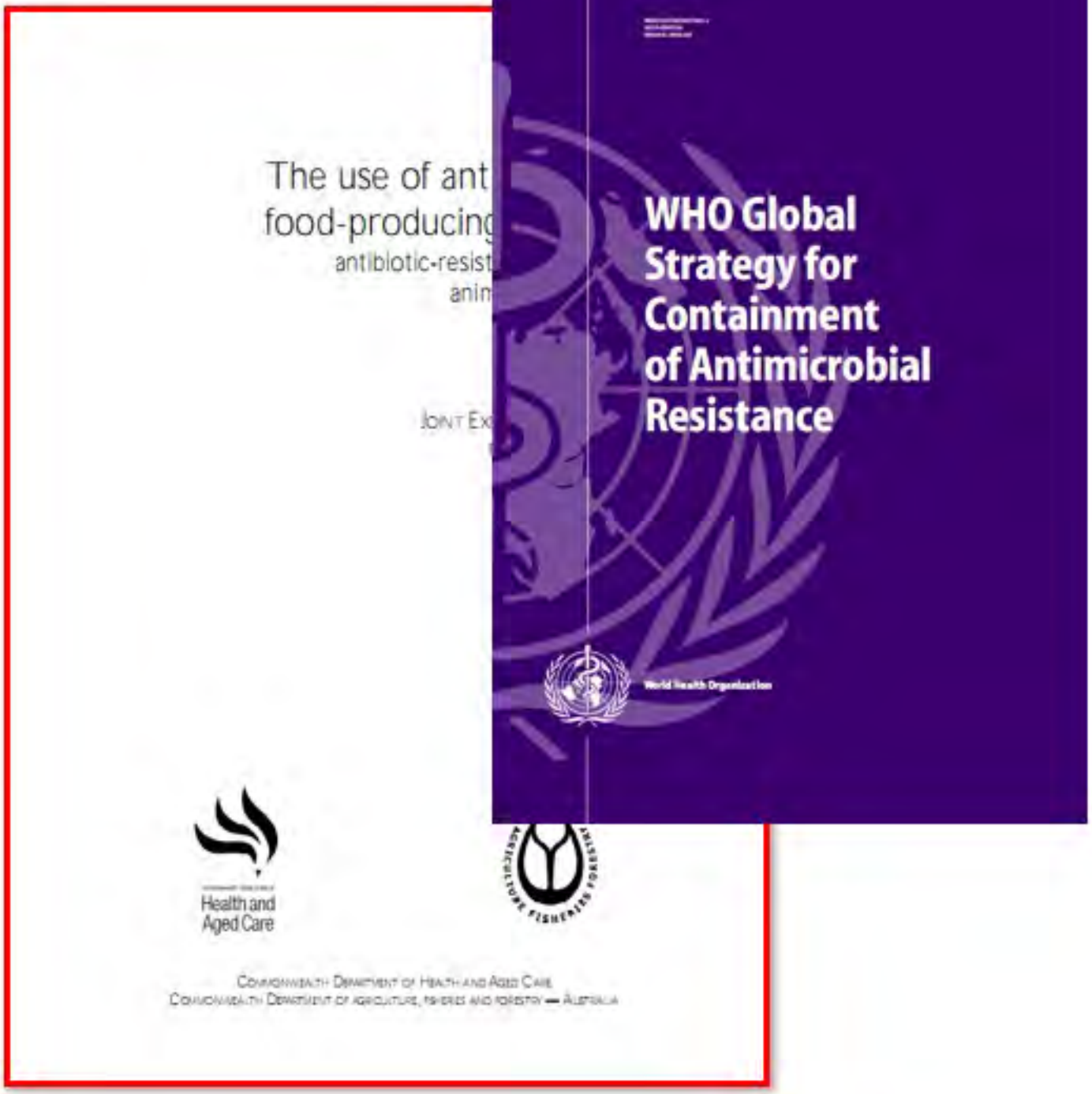
antibiotic-resistant bacteria in animals and humans

Report of the
Joint Expert Advisory Committee
on Antibiotic Resistance
(JETACAR)

Health and Aged Care

Agriculture Fisheries Forestry

Commonwealth Department of Health and Aged Care
Commonwealth Department of Agriculture, Fisheries and Forestry — Australia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CONSULTATIONS AND WORKSHOPS
Critically Important Antimicrobials for Human Medicine:
Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use
Report of the Second WHO Expert Meeting
Copenhagen, 29–31 May 2007
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DEPARTMENT OF FOOD SAFETY, ZOONOSES AND FOODBORNE DISEASES

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The evolving threat of antimicrobial resistance

Options for action

World Health Organization | Patient Safety

Austin Health

2013

Finance and Public Administration References Committee

Progress in the implementation of the recommendations of the 1999 Joint Expert Technical Advisory Committee on Antibiotic Resistance

June 2013

Finance and Public Administration

Members

Senator Scott Ryan, Chair	LP, Victoria
Senator Helen Polley, Deputy Chair	ALP, Tasmania
Senator Richard Di Natale	AG, Victoria
Senator Anne McEwen	ALP, South Australia
Senator Arthur Sinodinos	LP, New South Wales
Senator John Williams	NAT, New South Wales

Austin Health

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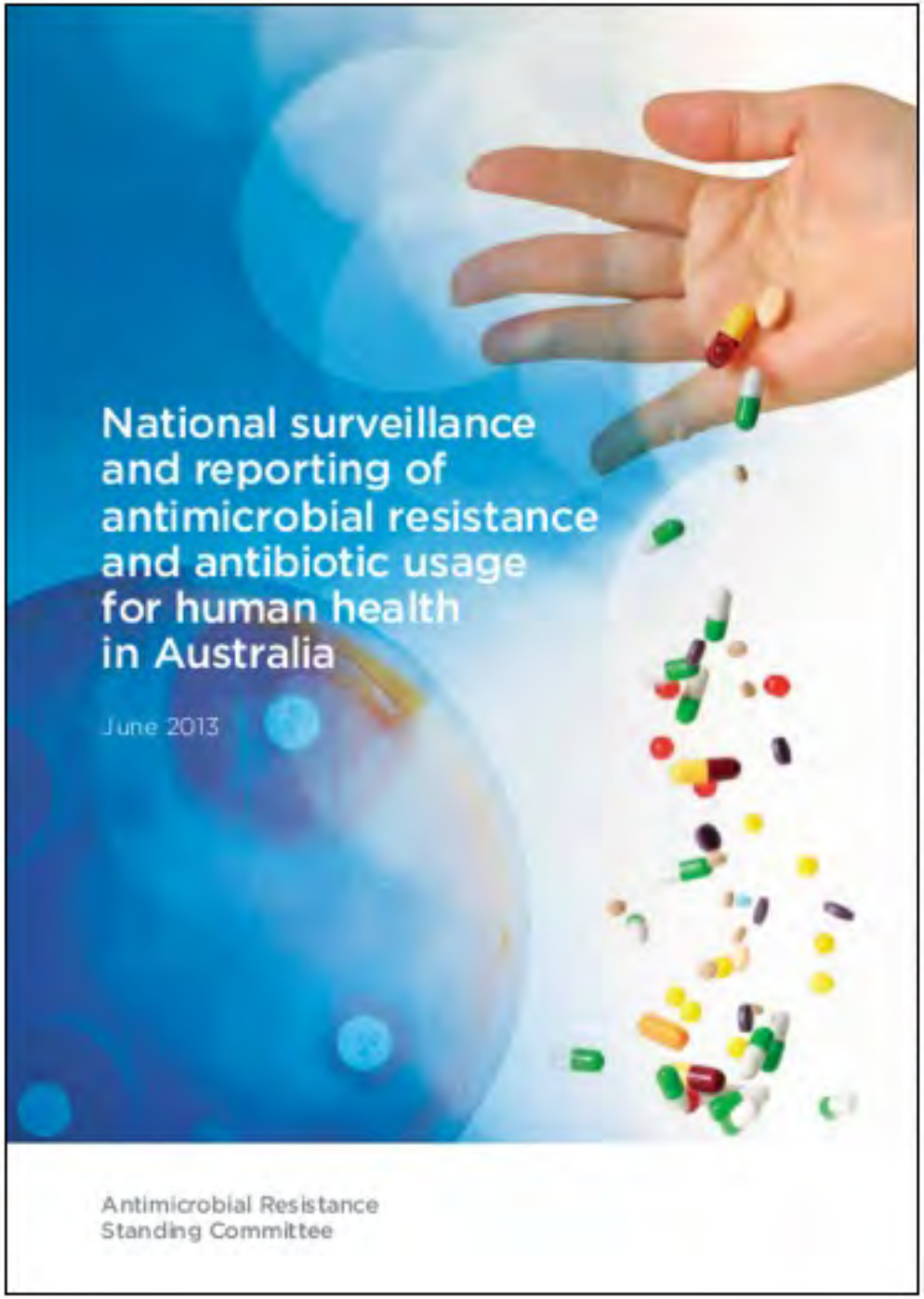
National surveillance and reporting of antimicrobial resistance and antibiotic usage for human health in Australia
June 2013
Antimicrobial Resistance Standing Committee

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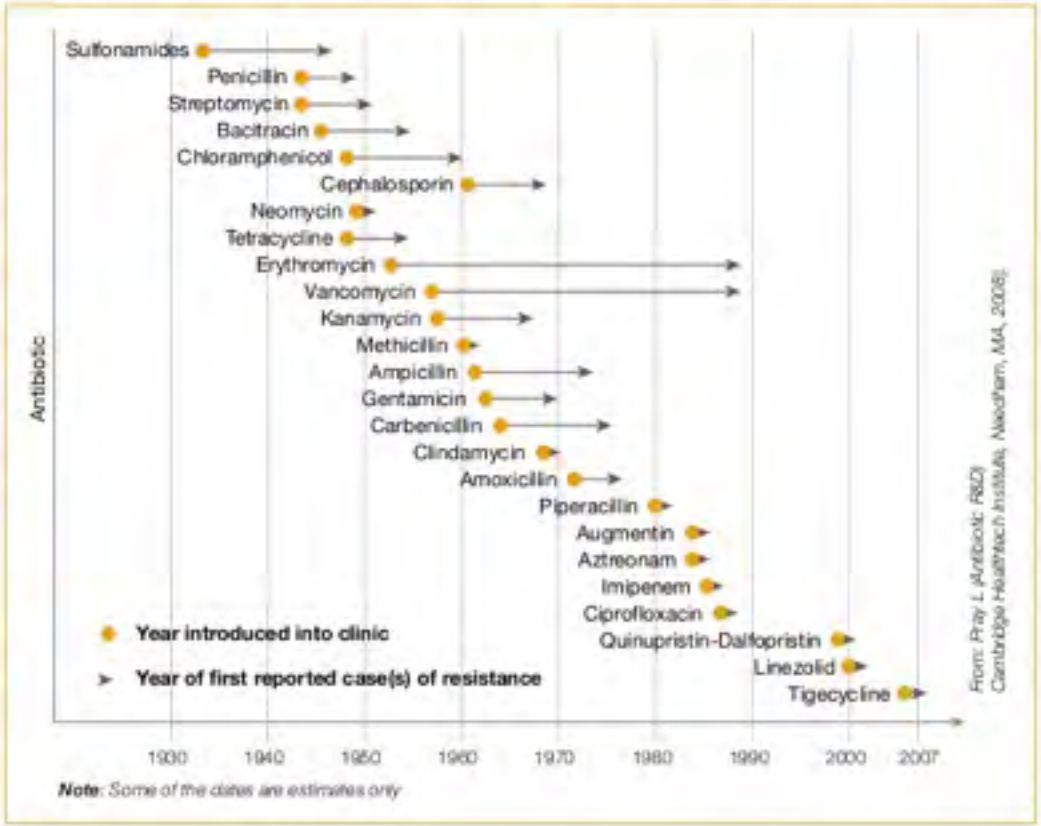
Figure 1: Time lag between an antibiotic being introduced to clinical use and the first appearance of resistance



Note: *Some of the dates are estimates only*

Austin Health

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Antimicrobial Resistance
Standing Committee

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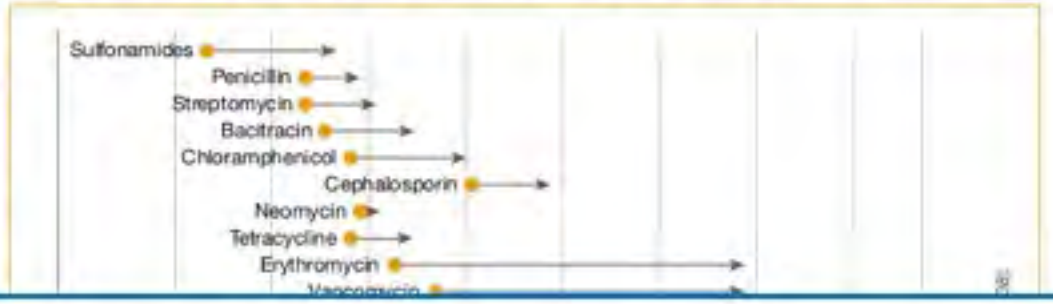
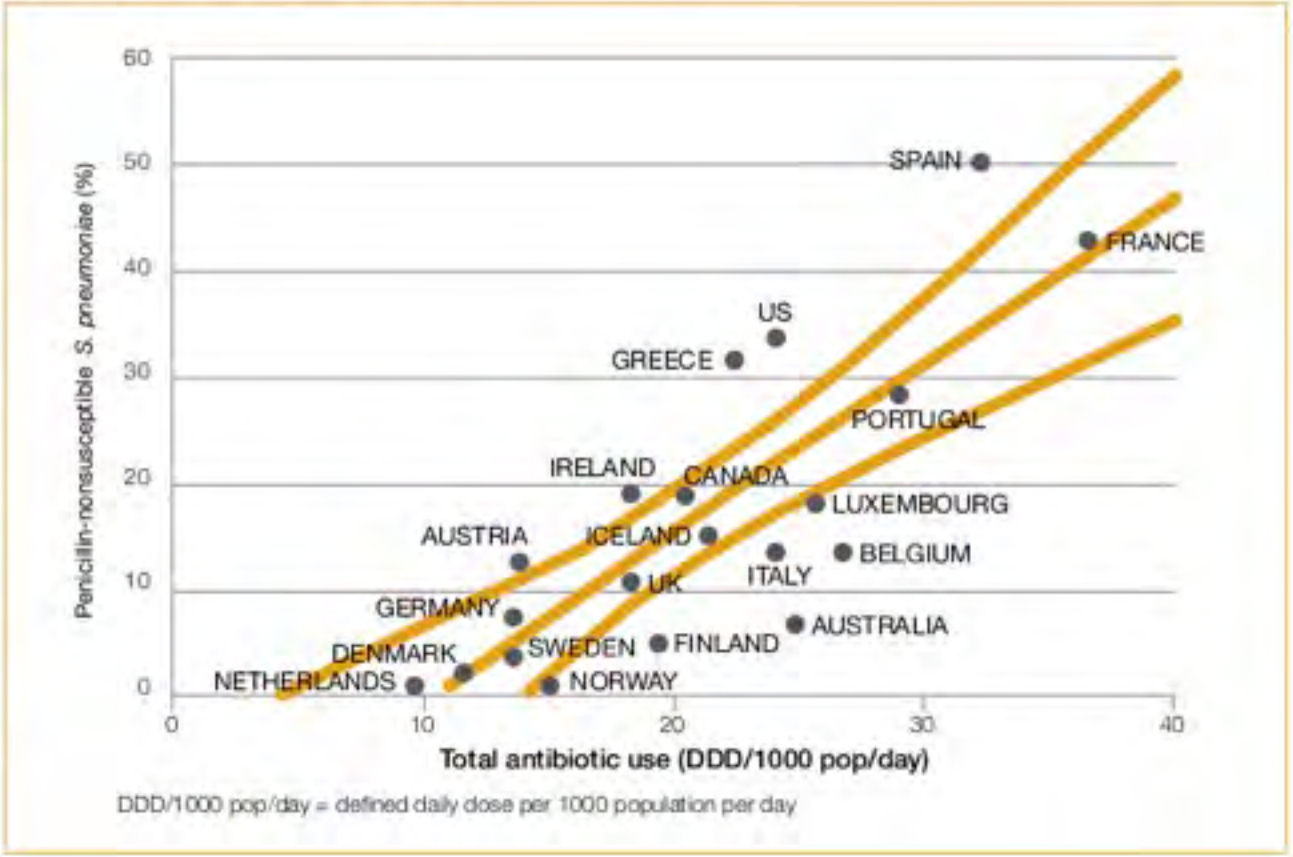


Figure 2: Relationship between total antibiotic consumption and *Streptococcus pneumoniae* resistance to penicillin in 20 industrialised countries



DDD/1000 pop/day = defined daily dose per 1000 population per day

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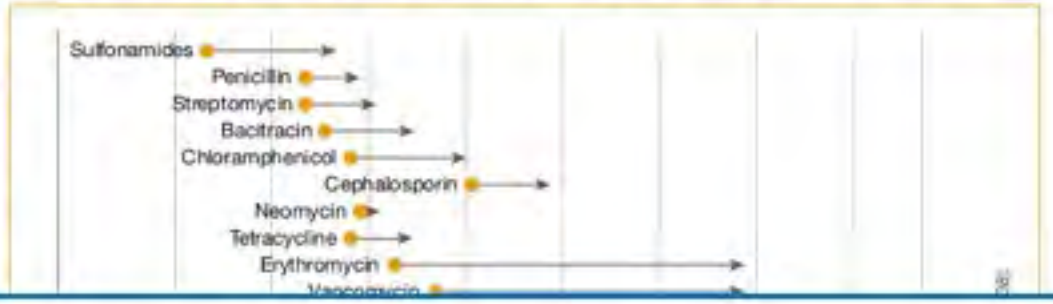

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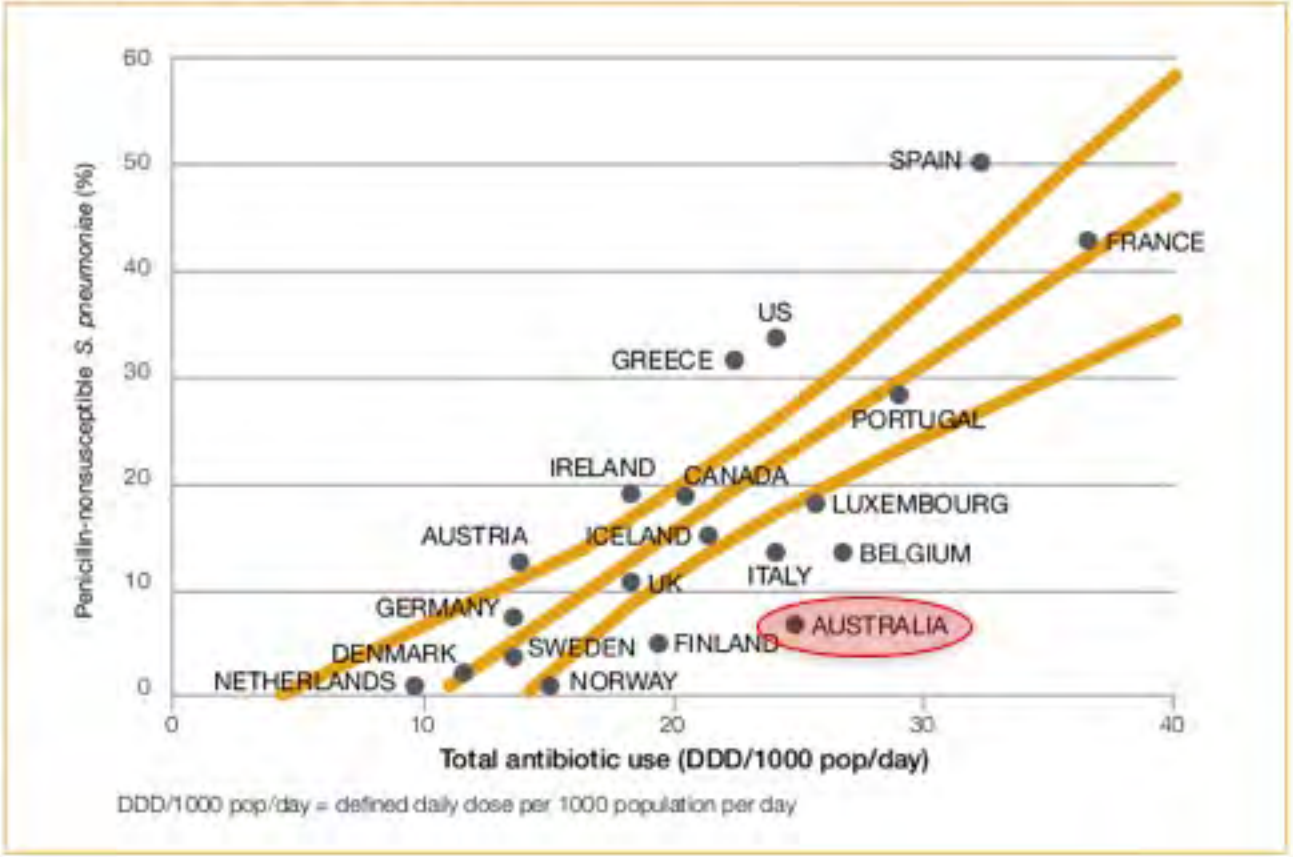

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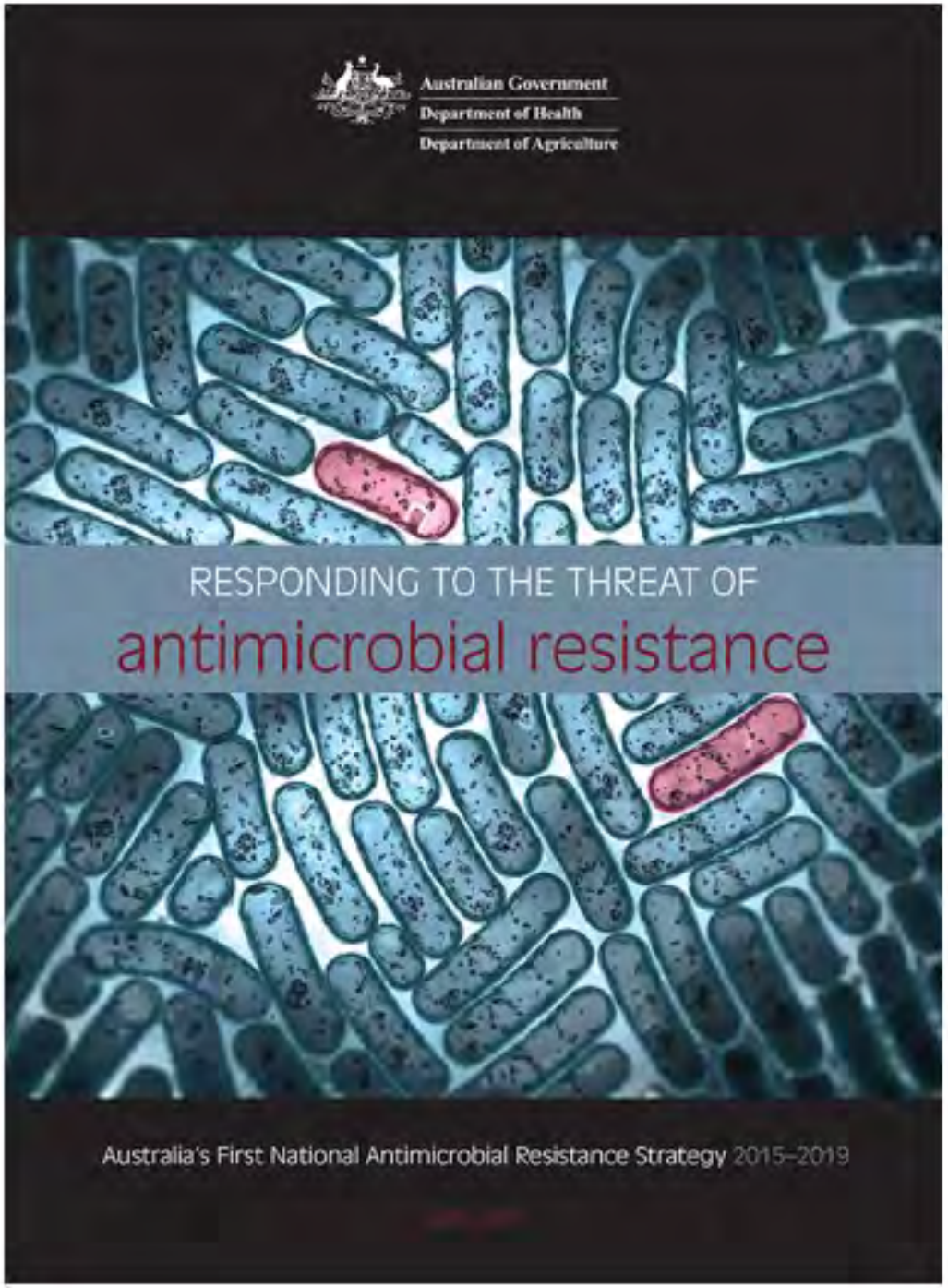
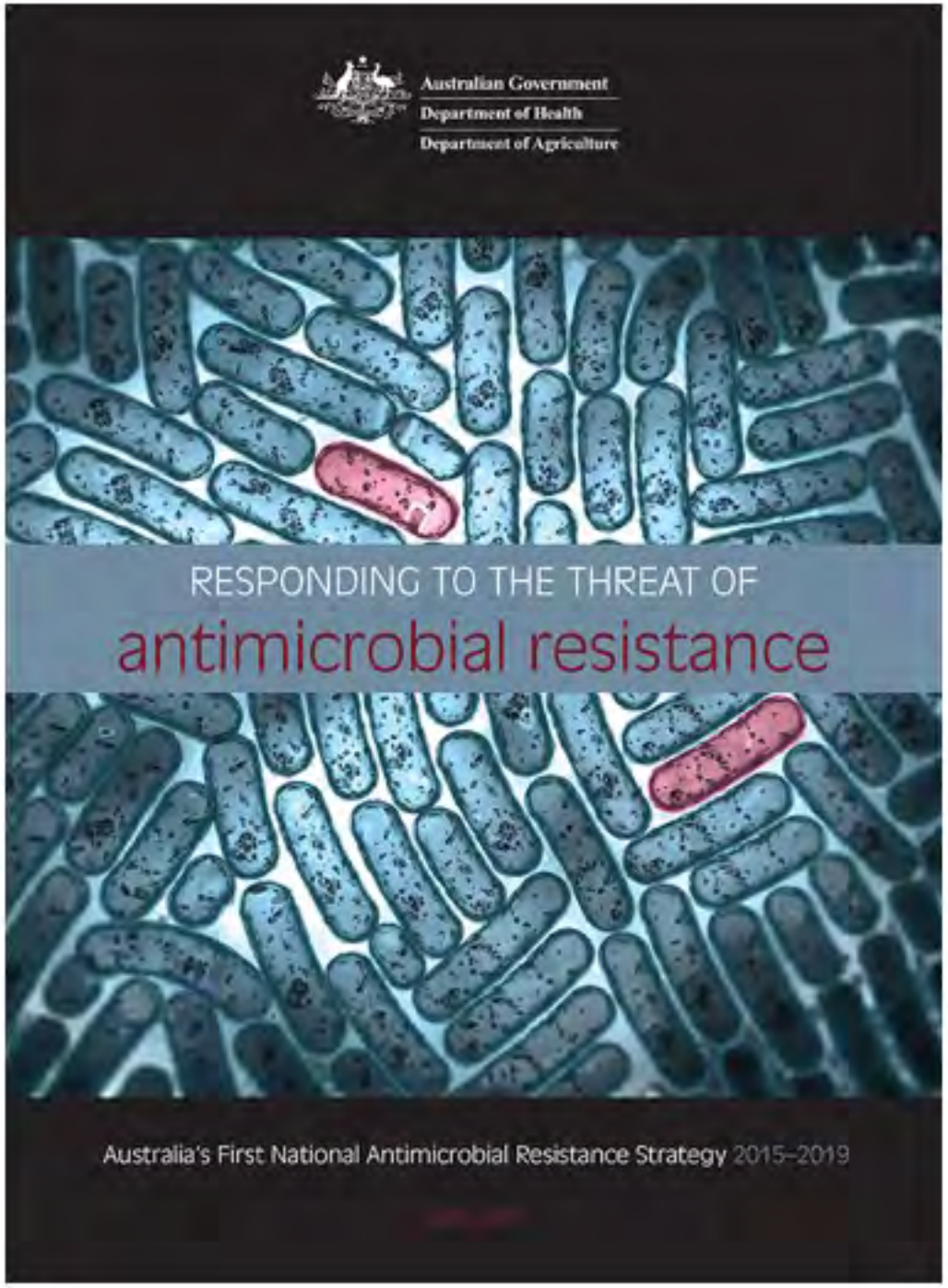

Australian Government
Department of Health
Department of Agriculture
RESPONDING TO THE THREAT OF
antimicrobial resistance
Australia's First National Antimicrobial Resistance Strategy 2015–2019

"One Health" approach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Vision

A society in which antimicrobials are recognised and managed as a valuable shared resource, maintaining their efficacy so that infections in humans and animals remain treatable and communities continue to benefit from the advances that antimicrobials enable.

Goal

Minimise the development and spread of antimicrobial resistance and ensure the continued availability of effective antimicrobials.

Table 1: Australia's list of priority organisms for human health

Rationale	Species
Impact in both hospitals and the community	Enterobacteriaceae (principally *Escherichia coli* and *Klebsiella* species) *Enterococcus* species *Mycobacterium tuberculosis* ***Neisseria gonorrhoeae*** *Neisseria meningitidis* ***Salmonella* species** ***Shigella* species** ***Streptococcus pneumoniae*** ***Staphylococcus aureus***
Impact largely in hospitals	*Acinetobacter baumannii* complex *Enterobacter cloacae/aerogenes* *Pseudomonas aeruginosa*
Epidemiological and/or antimicrobial usage marker	*Campylobacter jejuni/coli*
Monitored through passive surveillance and elevated to targeted surveillance if threshold exceeded	*Clostridium difficile* *Haemophilus influenzae* type b *Streptococcus agalactiae* *Streptococcus pyogenes*

*WHO priority organisms for surveillance are in **red**.

Resistance Surveillance

AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

AURA
Antimicrobial Use and Resistance in Australia

What's missing?

- AMR activities largely focused on surveillance and inappropriate antibiotic use

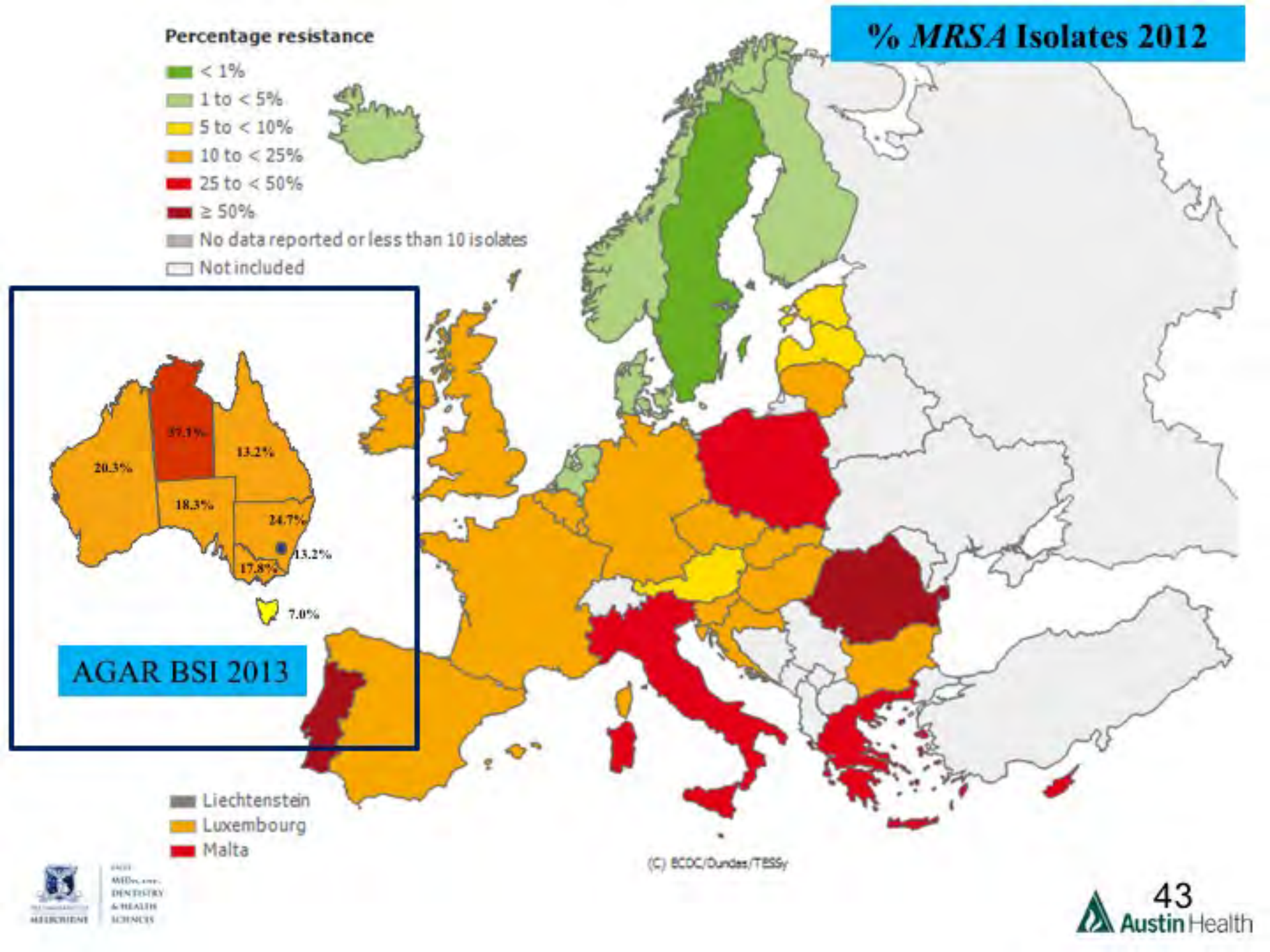
- Numerous effective infection control programs seen as HAI activities rather than as part of an AMR control strategy

Australian AGAR Sepsis Outcome Studies 2013

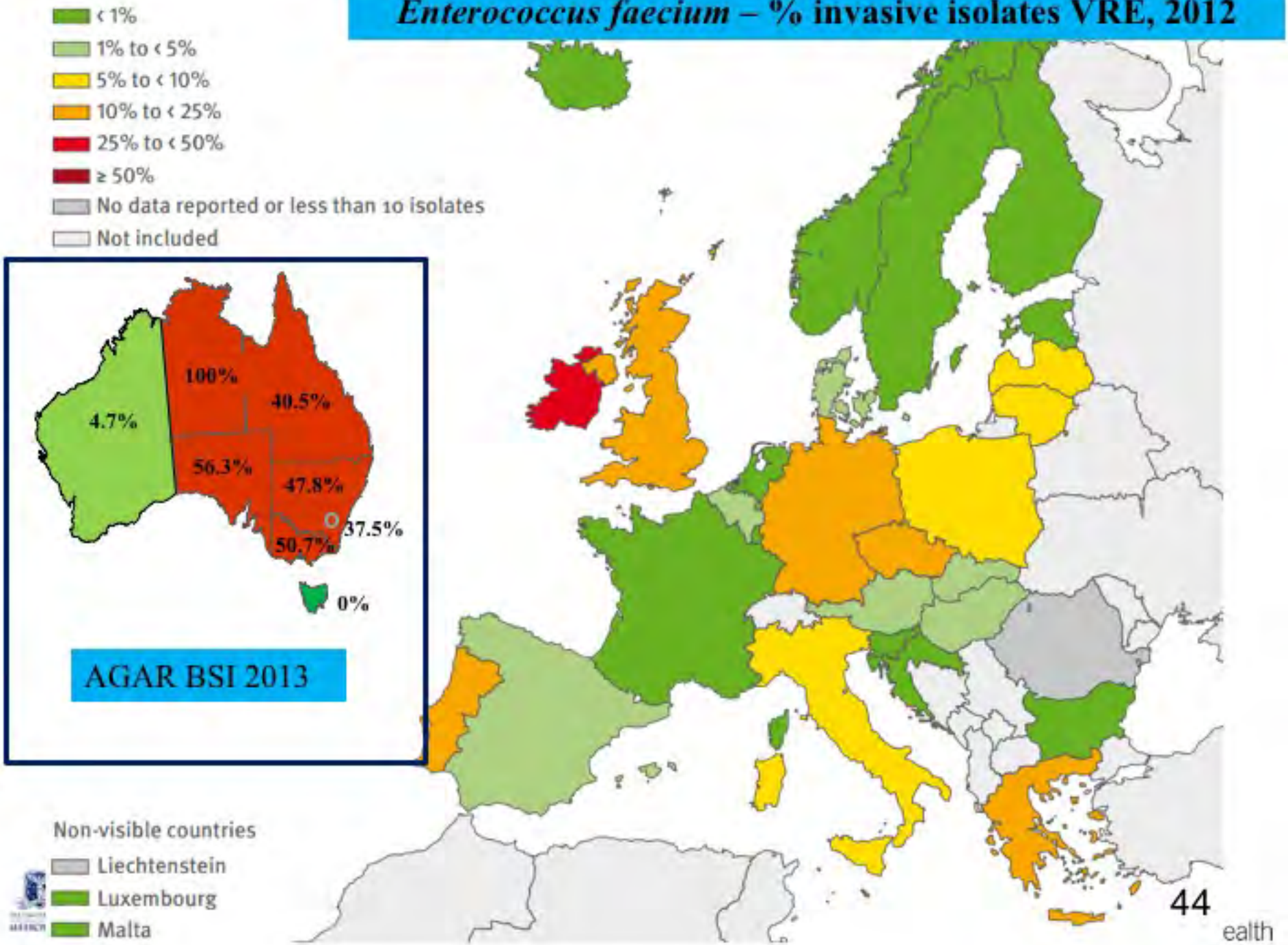
Comparison to EARSS data 2012

Australian Group on Antimicrobial Resistance (AGAR)

% *MRSA* Isolates 2012



Enterococcus faecium – % invasive isolates VRE, 2012



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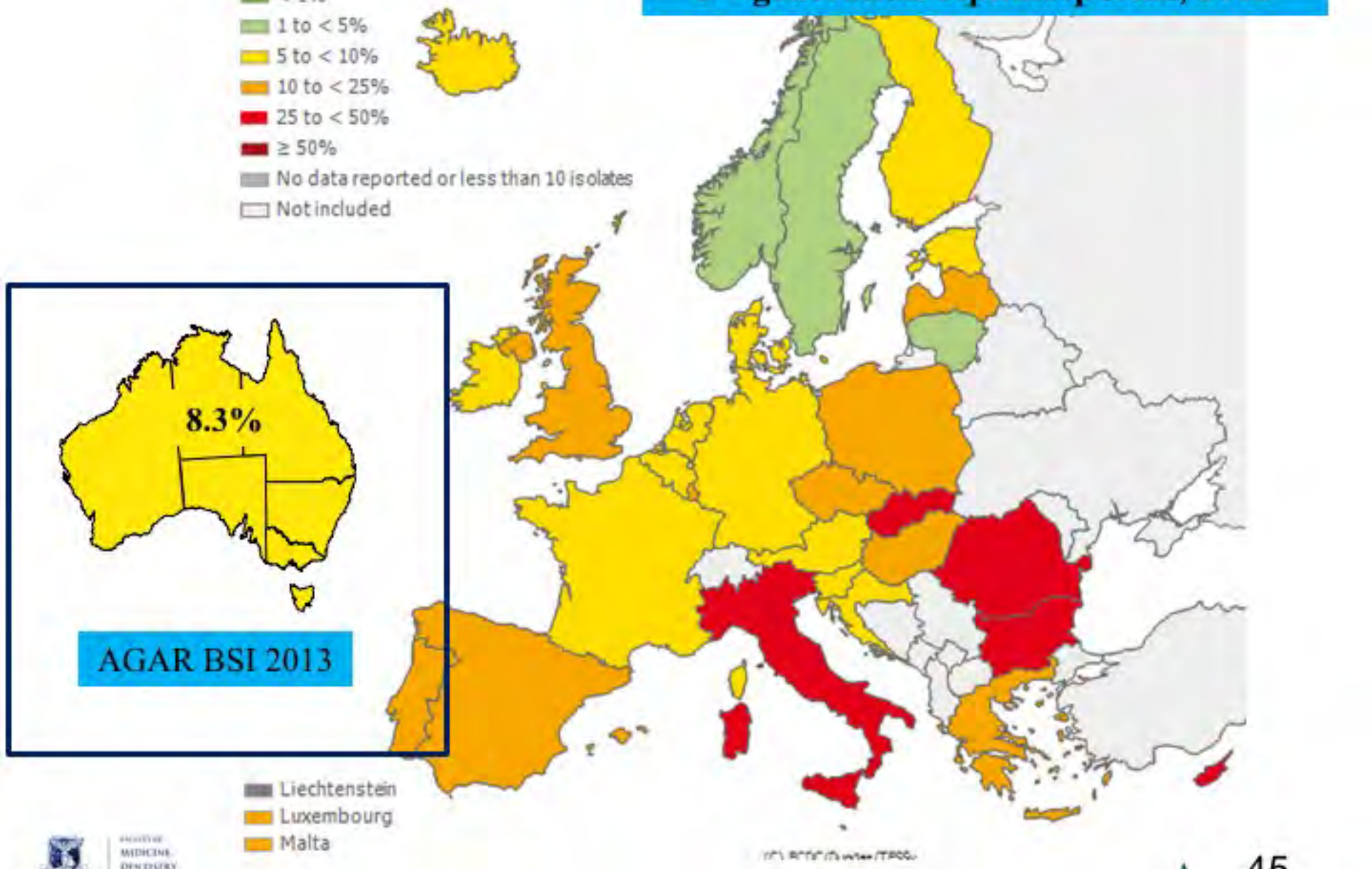
E. coli - % invasive isolates resistant to 3rd generation cephalosporins, 2012



Escherichia coli. % invasive isolates resistant to fluoroquinolones, 2012

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

AGAR BSI 2013

Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

Klebsiella pneumoniae - % invasive isolates resistant to 3rd generation cephalosporins, 2012

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
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- ≥ 50%
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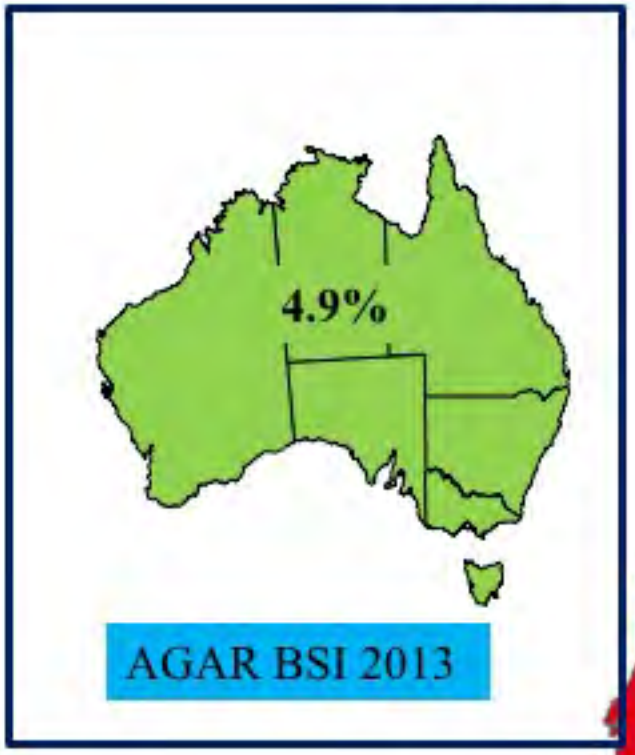
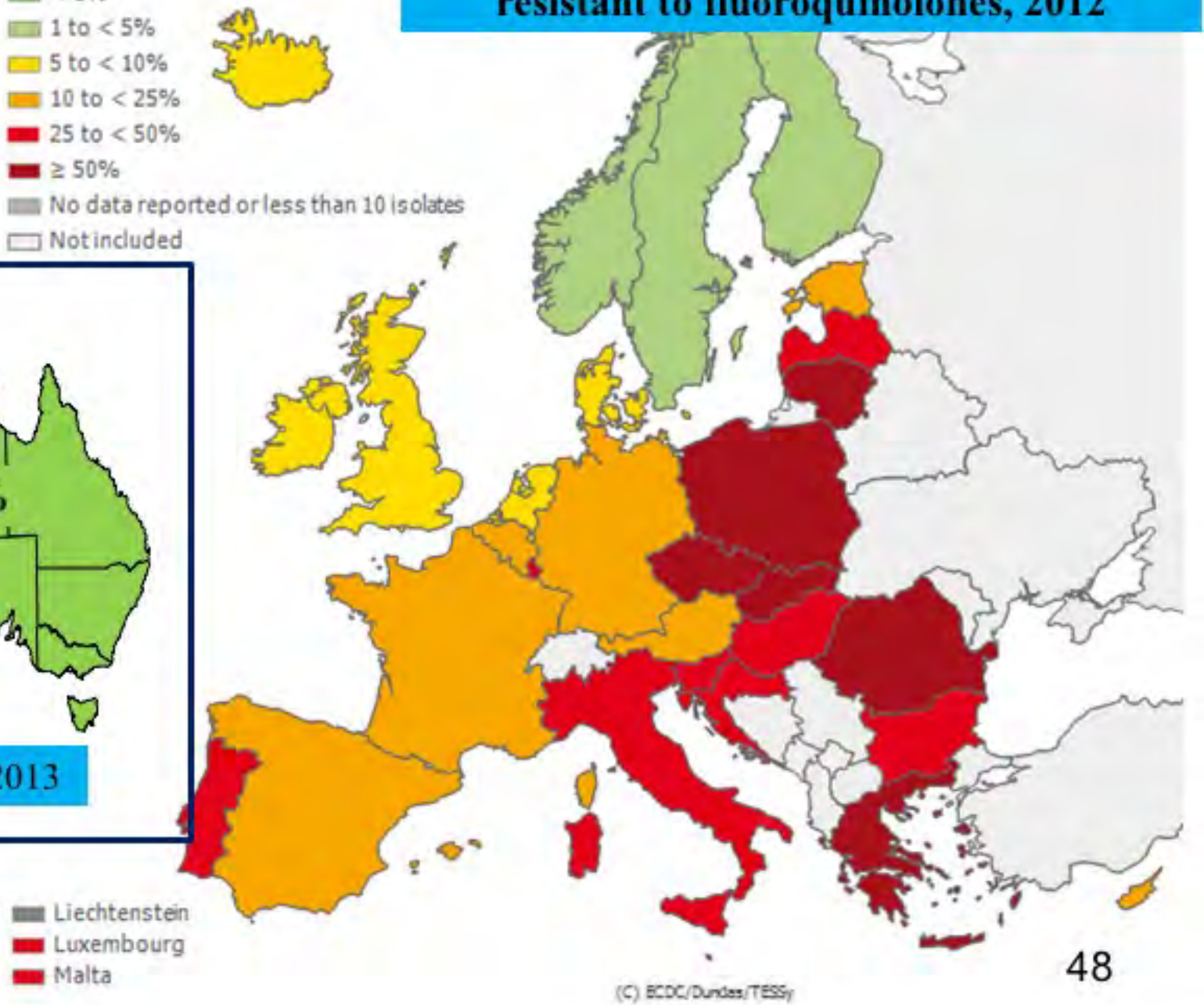
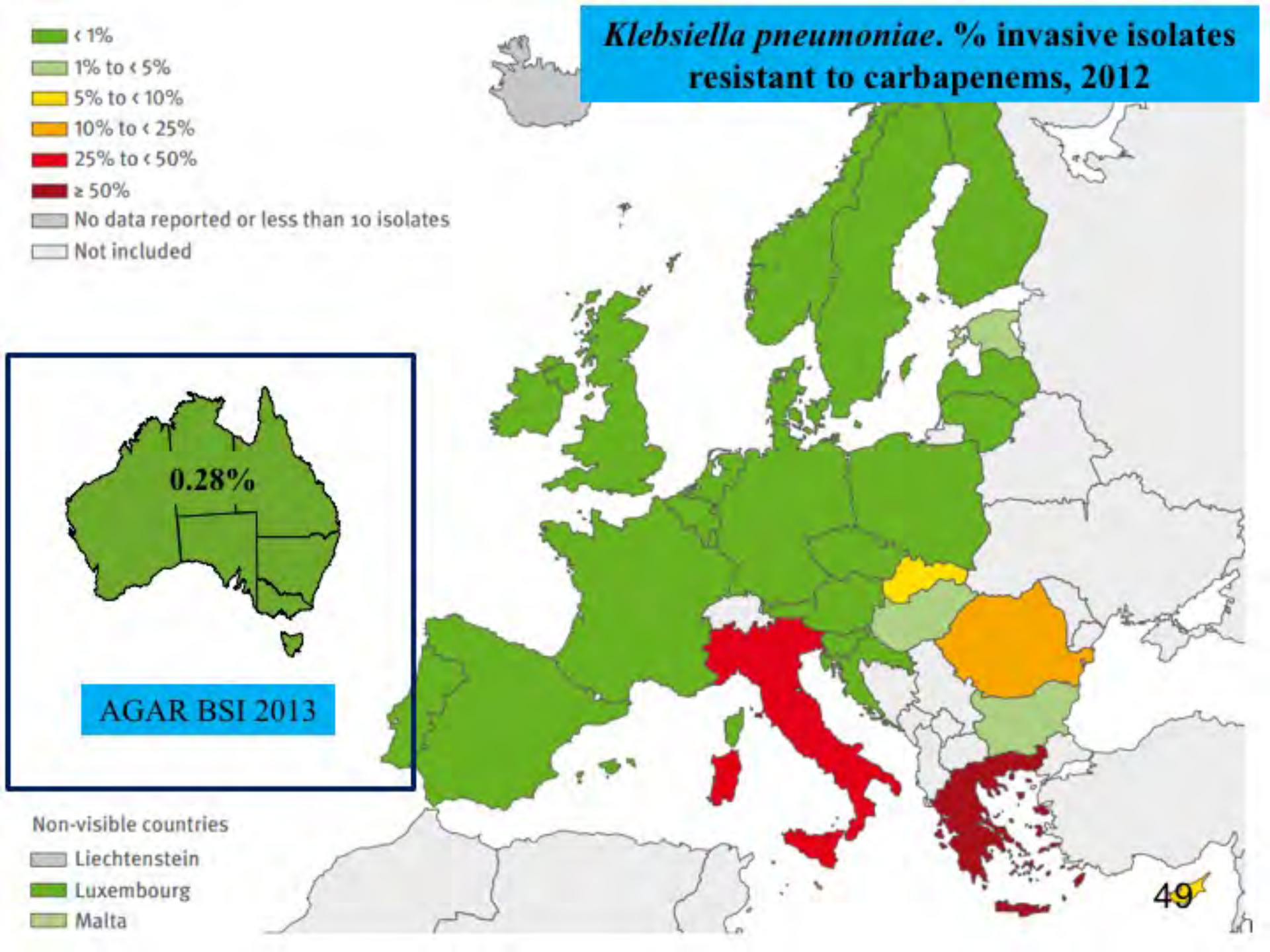




Klebsiella pneumoniae. % invasive isolates resistant to carbapenems, 2012



What's missing?

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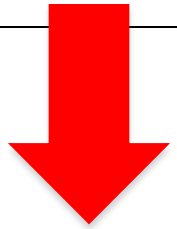

Information regarding the **Clinical impact of AMR**

Necessary to engage prescribers, the public and politicians

Improving Antimicrobial Stewardship

- Community usage – Pharmaceutical Benefits Scheme
- Hospital usage – NAUSP
- Practical stewardship issues

Antibiotics: PBS/RPBS utilisation, Oct 2014 and Feb 2015

Page last updated: 29 May 2015

Drug utilisation sub-committee (DUSC)

October 2014 and February 2015

Data source / methodology:

- Extracted from - Department of Human Services (DHS) Medicare pharmacy claims database and the DUSC database

Key Findings - Calendar year 2013:

- 45% of the Australian population (10,441,015 unique patients) were supplied at least one antibiotic through the PBS
  - 26,436,021 prescriptions supplied for systemic antibiotics
  - 29,227,581 prescriptions supplied for any antibiotic (including systemic & topical antibiotics)
- The most commonly supplied antibiotics were:
  - Amoxycillin (n=5,665,810)
  - Cephalexin (n=5,413,046)
  - Amoxycillin+clavulanic acid (n=4,512,149).
- The defined daily dose was calculated to be 22.8 DDD/1000/day
  - This is higher than the 2009 OECD average of 21.1

OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing

Australian Government Department of Health

PBS Pharmaceutical Benefits Scheme

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October 2014 and February 2015

Data source / methodology:

- Extracted from - Department of Human Services (DHS) Medicare pharmacy claims database and the DUSC database

Key Findings - Calendar year 2013:

- 45% of the Australian population (10,441,015 unique patients) were supplied at least one antibiotic through the PBS
  - 26,436,021 prescriptions supplied for systemic antibiotics
  - 29,227,581 prescriptions supplied for any antibiotic (including systemic & topical antibiotics)
- The most commonly supplied antibiotics were:
  - Amoxycillin (n=5,665,810)
  - Cephalexin (n=5,413,046)
  - Amoxycillin+clavulanic acid (n=4,512,149).
- The defined daily dose was calculated to be 22.8 DDD/1000/day
  - This is higher than the 2009 OECD average of 21.1

OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing

Australian Government Department of Health

PBS The Pharmaceutical Benefits Scheme

Antibiotics: PBS/RPBS utilisation, Oct 2014 and Feb 2015

Page last updated: 29 May 2015

Drug utilisation sub-committee (DUSC)

October 2014 and February 2015

Key Findings - 2013:

- $116.5 million in PBS/RPBS benefits was paid for antibiotics.
- For commonly used systemic antibiotics (amoxycillin, cephalexin, roxithromycin and amoxycillin+clavulanic acid):
  - Repeats were ordered on the majority of prescriptions for cephalexin, amoxycillin+clavulanic acid and roxithromycin.
  - Repeats were written on 40% of amoxycillin original prescriptions
  - The majority of repeats ordered were not dispensed
- Some original prescriptions and repeats were dispensed long after the date the prescription was written
  - This use may not be consistent with the original reason for the prescription

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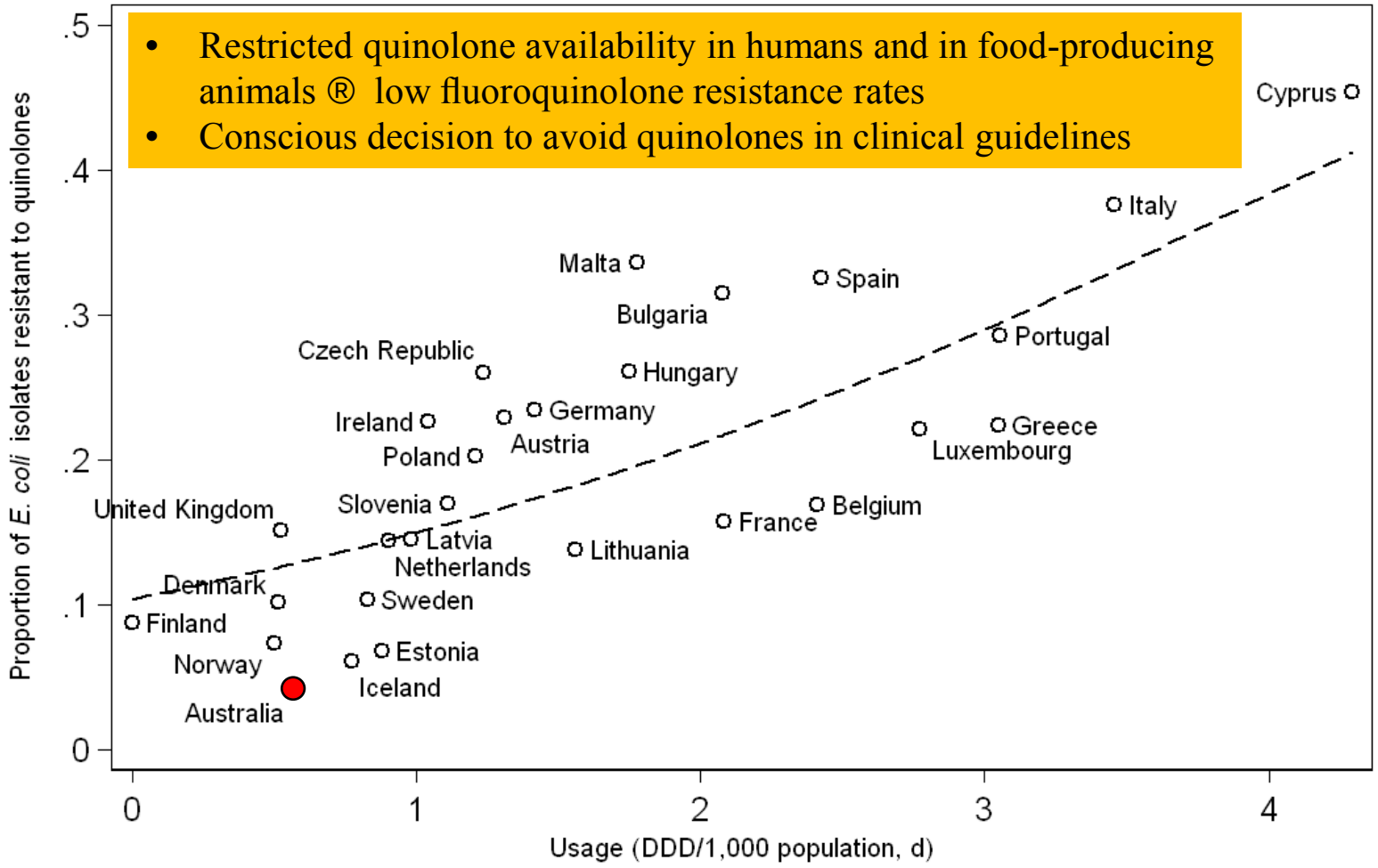
Control of Fluoroquinolone Resistance through Successful Regulation, Australia

Allen C. Cheng, John Turnidge, Peter Collignon, David Looke, Mary Barton, and Thomas Gottlieb

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 18, No. 9, September 2012

- Restricted quinolone availability in humans and in food-producing animals ® low fluoroquinolone resistance rates
- Conscious decision to avoid quinolones in clinical guidelines



Relationship of quinolone consumption and resistance in *E.coli* Durham K. Eur J Clin Microbiol Inf Dis 2010; 29, 353-356

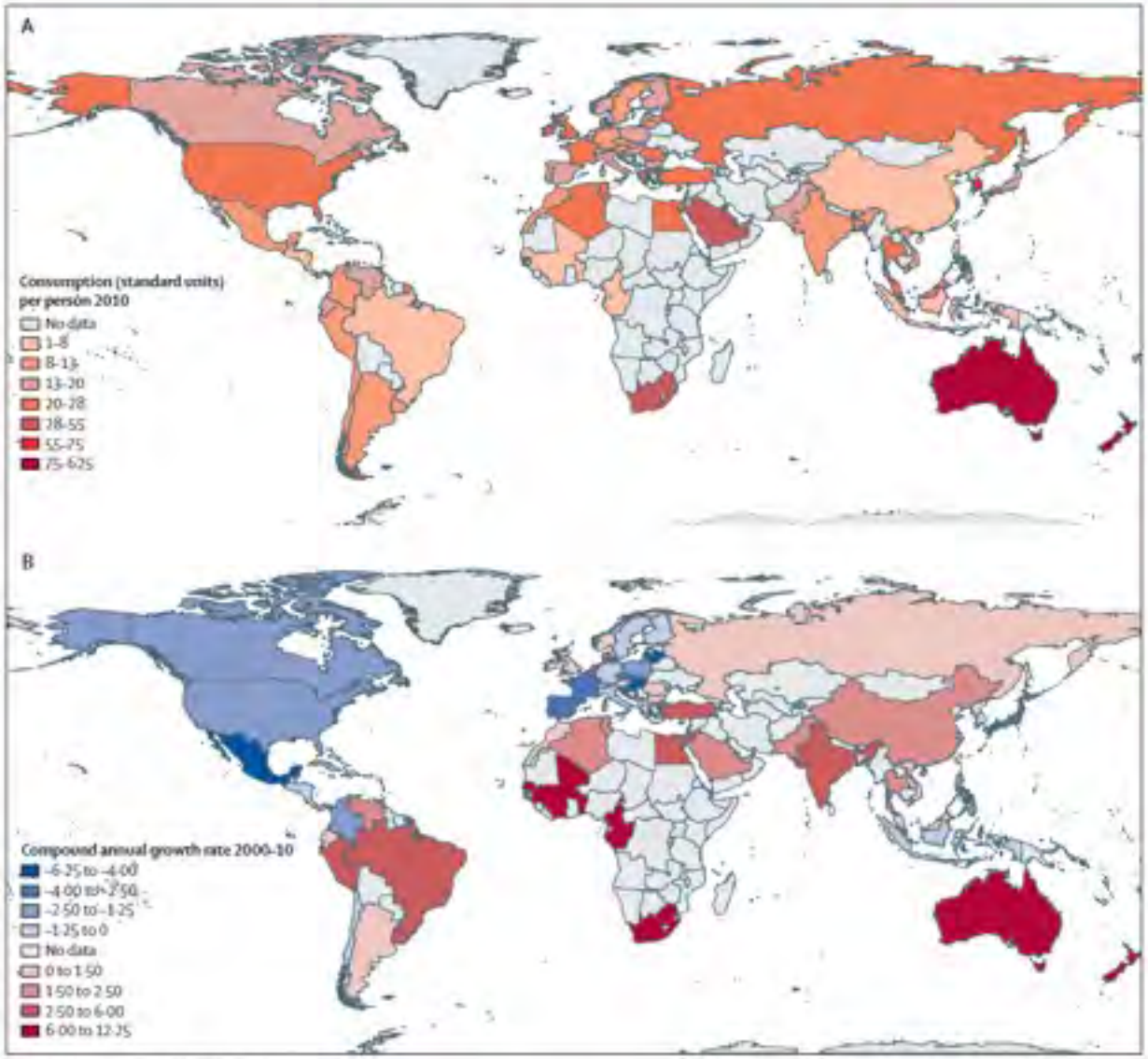


Figure 2: Consumption of antibiotics in 2010
(expressed in standard units (ie, pill, capsule, or ampoule) per person (A), and compound annual growth rate of antibiotic drug consumption between 2000 and 2010 (B))

The Australian Approach

Problem pathogens & impact on prescribing I

S. pneumoniae

- Penicillin resistance rare – clinically unimportant
- CAP – Rx of choice: Benzylpenicillin + doxycycline
- No fluoroquinolone use for CAP

MRSA

- Massive decline with National Hand Hygiene Initiative
- Some cMRSA – mostly sensitive to clindamycin and TMP-SMX
- Persistent MRSA bacteraemias – assessed for hVISA
- Minimal daptomycin use
- National system of SAB reporting – public disclosure

Charles *et al.* Clin Infect Dis 2008; 46:1513-21
Chua *et al.* Clin Infect Dis. 2011; 52: 99-114.

Problem pathogens & impact on prescribing II

VRE

- Mostly *vanB* – susceptible to teicoplanin
- High rates of *vanB* gene carriage in naturally occurring anaerobes
- Most hospitals – faecal carriage screening in high-risk patients - isolation

C. difficile

- Uncommon – national reporting scheme
  - Minimal use of moxifloxacin and other fluoroquinolones; Federal approval required
- Some increase in community rates - ?detection bias (incl PCR)
- Metronidazole > vancomycin >> fidaxomicin
- Rarely - faecal transplantation - problems

Graham et al, 2008 AAC 53:1195-7
Young et al, 2007. JAC 59: 809-10

Problem pathogens & impact on prescribing III

MDR – Gram-negatives

- Main concern = returned travelers, incl. inter-hospital transfers
  - Discussion re. isolation and screening
  - Travelers - MDR salmonella and campylobacter common
- Growing suspicion about contaminated imported foods
  - No. unexplained rural cases
- Major impacts in some elective surgery:
  - Trans-rectal prostate biopsy
  - Colonic surgery
  - Questionnaires and pre-op faecal screening in some centres

Overview

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Creating an Infection Control "Fire-break"

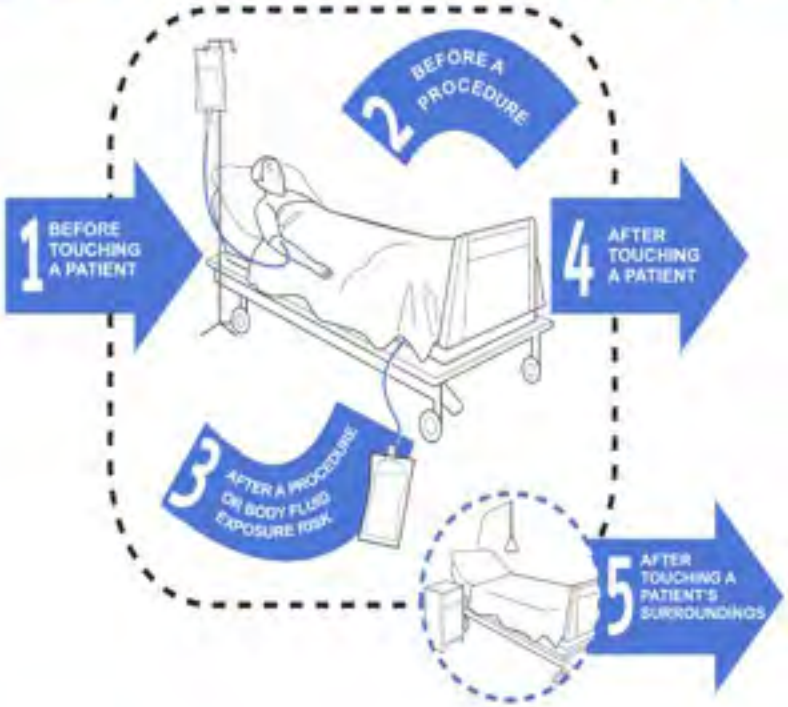
Creating an Infection Control "Fire-break"

WORLD ALLIANCE *for* PATIENT SAFETY

Clean Care is Safer Care

Hand Hygiene Australia

5 Moments for HAND HYGIENE

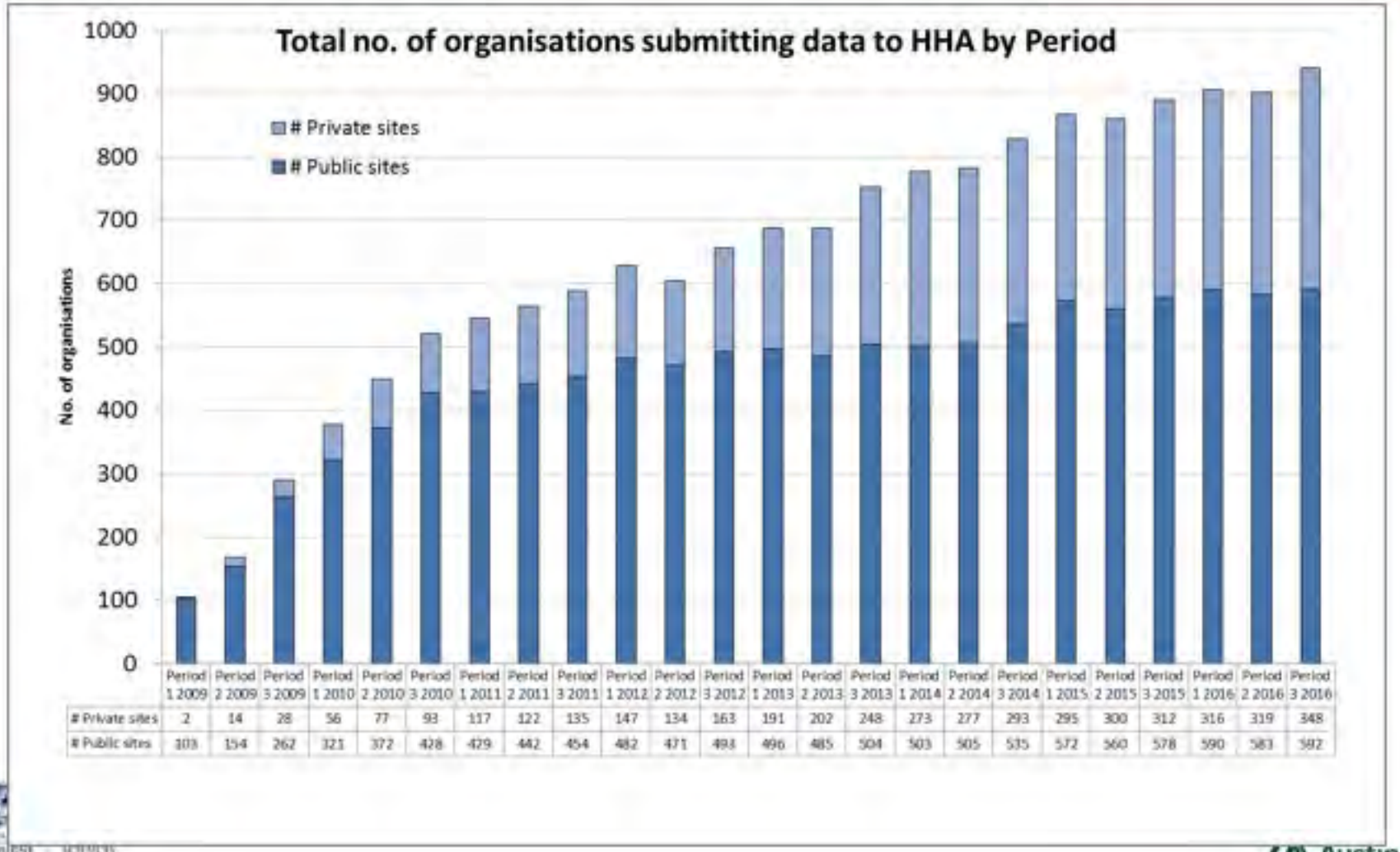


AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

World Health Organization

Australian NHHI participation – Private and Public

Period 1, 2009 – Period 3, 2016 – 940 sites



	Period 1 2009	Period 2 2009	Period 3 2009	Period 1 2010	Period 2 2010	Period 3 2010	Period 1 2011	Period 2 2011	Period 3 2011	Period 1 2012	Period 2 2012	Period 3 2012	Period 1 2013	Period 2 2013	Period 3 2013	Period 1 2014	Period 2 2014	Period 3 2014	Period 1 2015	Period 2 2015	Period 3 2015	Period 1 2016	Period 2 2016	Period 3 2016
# Private sites	2	14	28	56	77	93	117	122	135	147	134	163	191	202	248	273	277	293	295	300	312	316	319	348
# Public sites	103	154	262	321	372	428	429	442	454	482	471	493	496	485	504	503	505	535	572	560	578	590	583	592

Australian NHHI participation – Private and Public

Period 1, 2009 – Period 3, 2016 – 940 sites

99% public & >70% private acute beds

	Period 1 2009	Period 2 2009	Period 3 2009	Period 1 2010	Period 2 2010	Period 3 2010	Period 1 2011	Period 2 2011	Period 3 2011	Period 1 2012	Period 2 2012	Period 3 2012	Period 1 2013	Period 2 2013	Period 3 2013	Period 1 2014	Period 2 2014	Period 3 2014	Period 1 2015	Period 2 2015	Period 3 2015	Period 1 2016	Period 2 2016	Period 3 2016
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Organisation Types Summary

Period 3, 2016

Organisation type	Organisations *N* (%)	Moments *N* (%)	Compliance* % (95% CI)
Hospital	893 (95%)	631529 (98.1%)	83.9 (83.9-84.0)
Dental/oral health clinic	27 (2.9%)	6736 (1%)	94.3 (93.7-94.9)
Community health service	14 (1.5%)	3113 (0.5%)	91.9 (90.9-92.8)
Long-term care facility	2 (0.2%)	466 (0.1%)	97.2 (95.3-98.5)
Other	4 (0.4%)	2094 (0.3%)	86.6 (85.1-88.1)
TOTAL	940	643,938	84.1 (84.0-84.2)

* Aggregate compliance with data from all organisations combined

Hospital Types Summary

Period 3, 2016

Hospital type	Organisations *N* (%)	Moments *N* (%)	Compliance* % (95% CI)
Acute hospitals	634 (71%)	545407 (86.4%)	83.7 (83.6-83.8)
Women's and children's hospitals	15 (1.7%)	22956 (3.6%)	84.2 (83.7-84.6)
Other acute specialised hospitals	13 (1.5%)	2907 (0.5%)	85.3 (84.0-86.6)
Same day hospitals	132 (14.8%)	26513 (4.2%)	85.4 (85.0-85.8)
Psychiatric hospitals	20 (2.2%)	5877 (0.9%)	87.0 (86.1-87.8)
Subacute and non-acute hospitals	49 (5.5%)	12132 (1.9%)	86.7 (86.1-87.3)
Outpatient hospitals	3 (0.3%)	128 (0%)	86.7 (79.6-92.1)
Unpeered hospitals	27 (3%)	15609 (2.5%)	86.5 (86.0-87.1)

* Aggregate compliance with data from all organisations combined

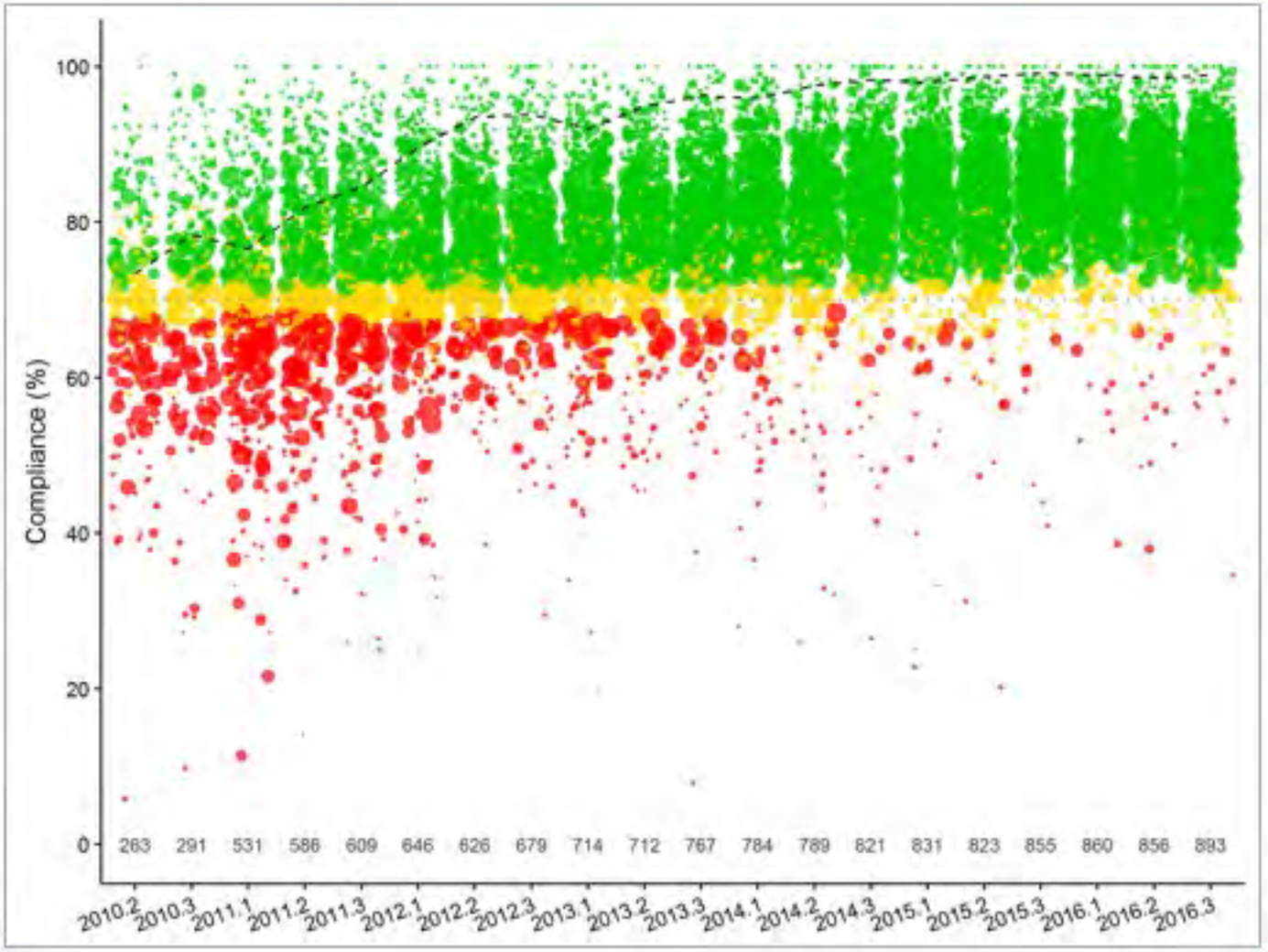
Acute hospitals: Principal referral hospitals, Group A hospitals, Group B hospitals, Group C hospitals, Group D hospitals, Very small hospitals,

Women's and children's hospitals: Children's hospitals, Women's hospitals, Other women's and children's hospitals

Psychiatric hospitals: Child, adolescent and young adult psychiatric hospitals, acute psychiatric hospitals, non-acute psychiatric hospitals, forensic psychiatric hospitals

Hand Hygiene Performance: Hospitals

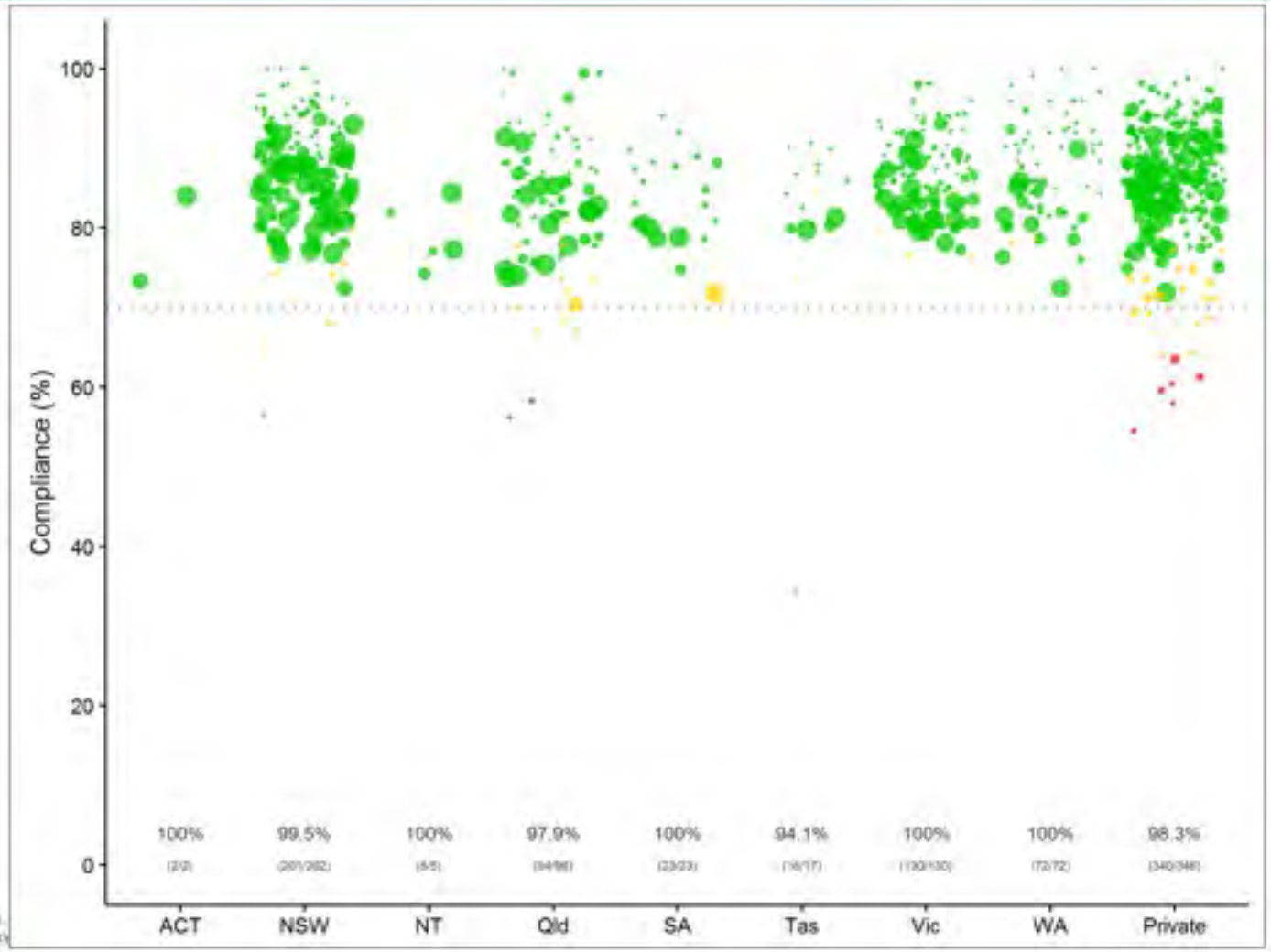
Period 2, 2010 – Period 3, 2016



Dashed line indicates proportion of organisations "similar" or "above" benchmark

Hand Hygiene Performance: Jurisdiction

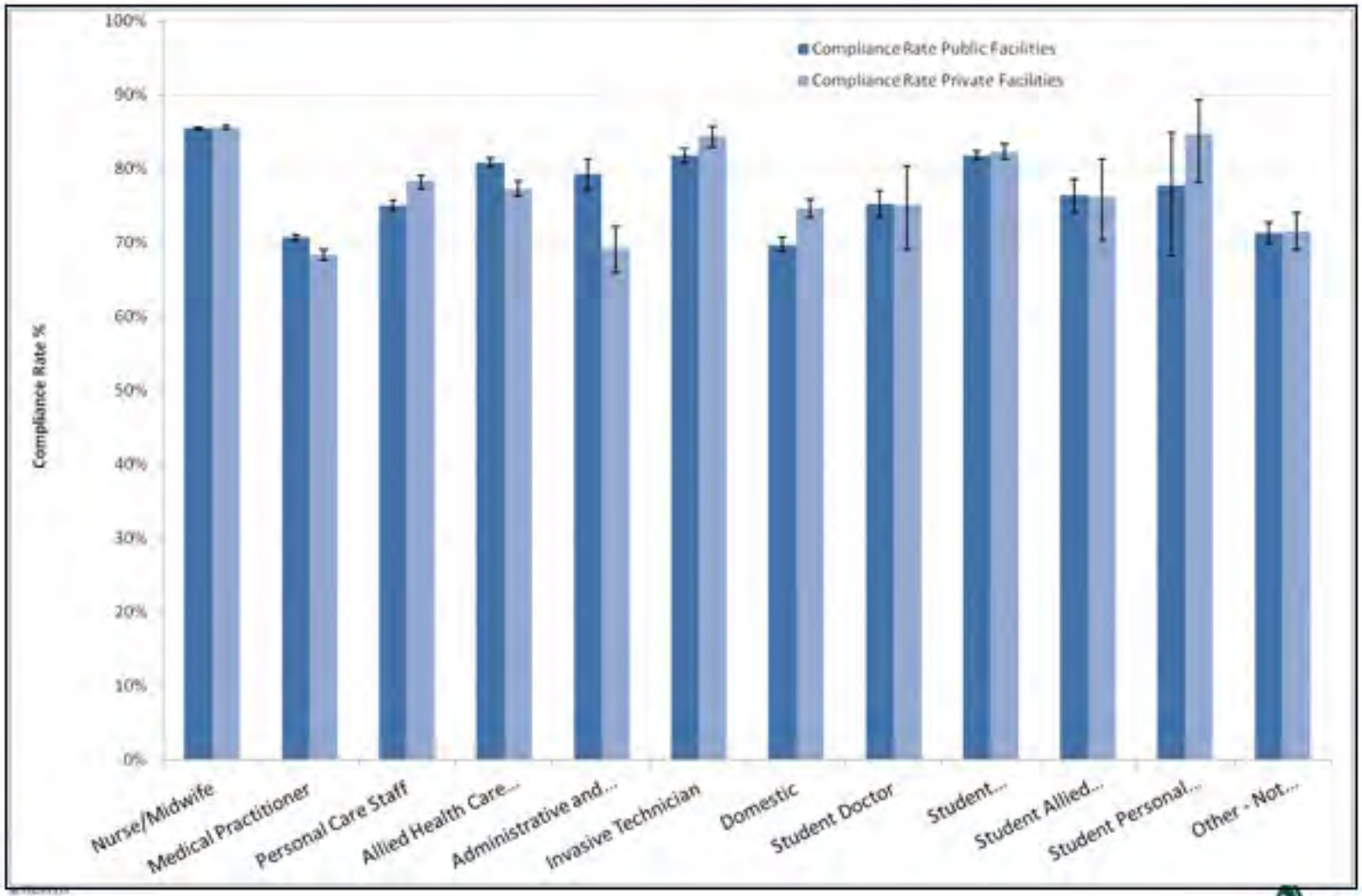
Hospitals - Period 3, 2016



Scale capped at 3000 moments

National Hand Hygiene Compliance Rates by HCW

535 Public facilities & 293 Private facilities
Period 3 (July-October) – 2014



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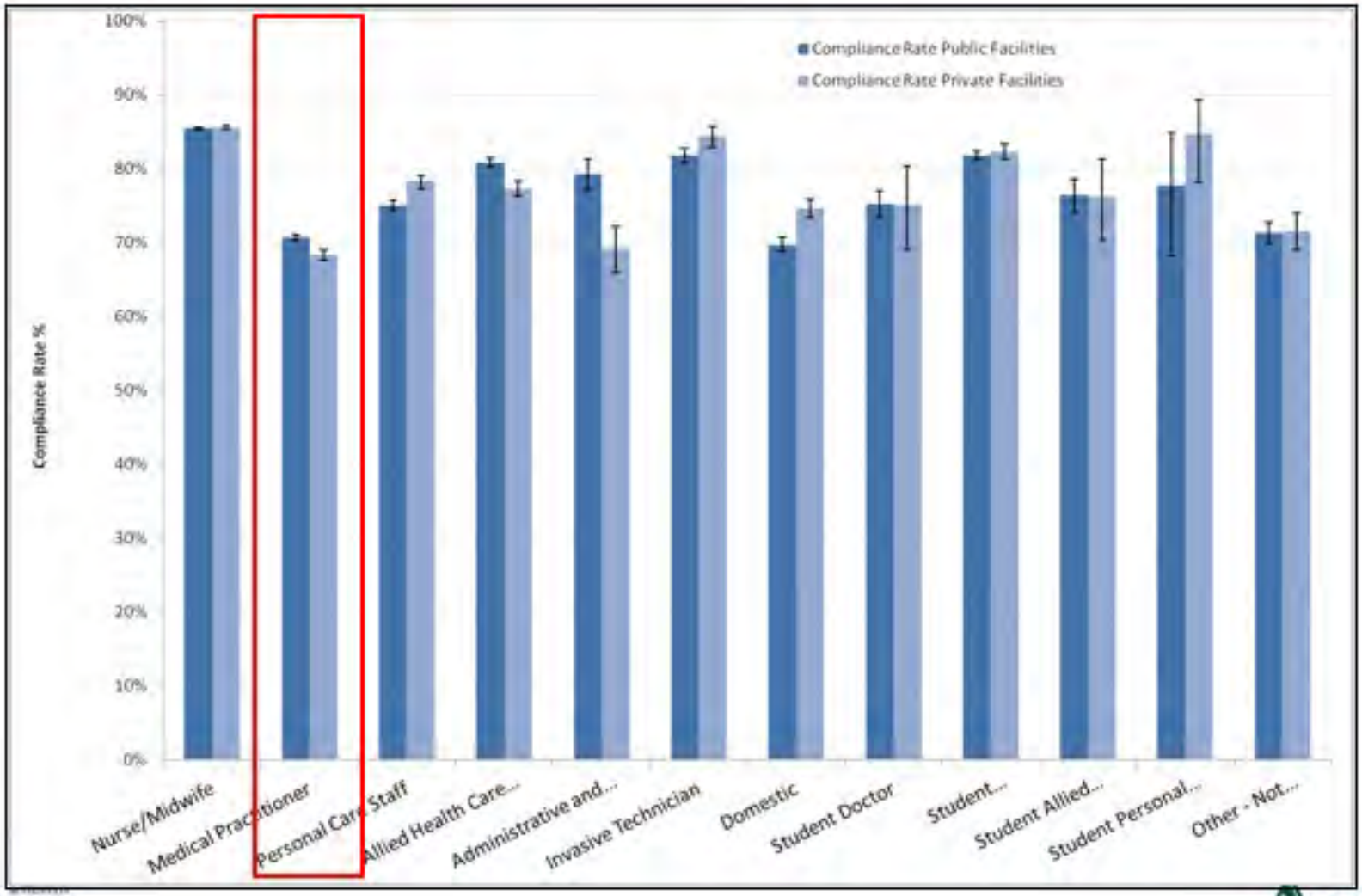

Other HHA initiatives

- Central HH database
- New direct-entry HH compliance App
  - i-Phones, other Smart-devices

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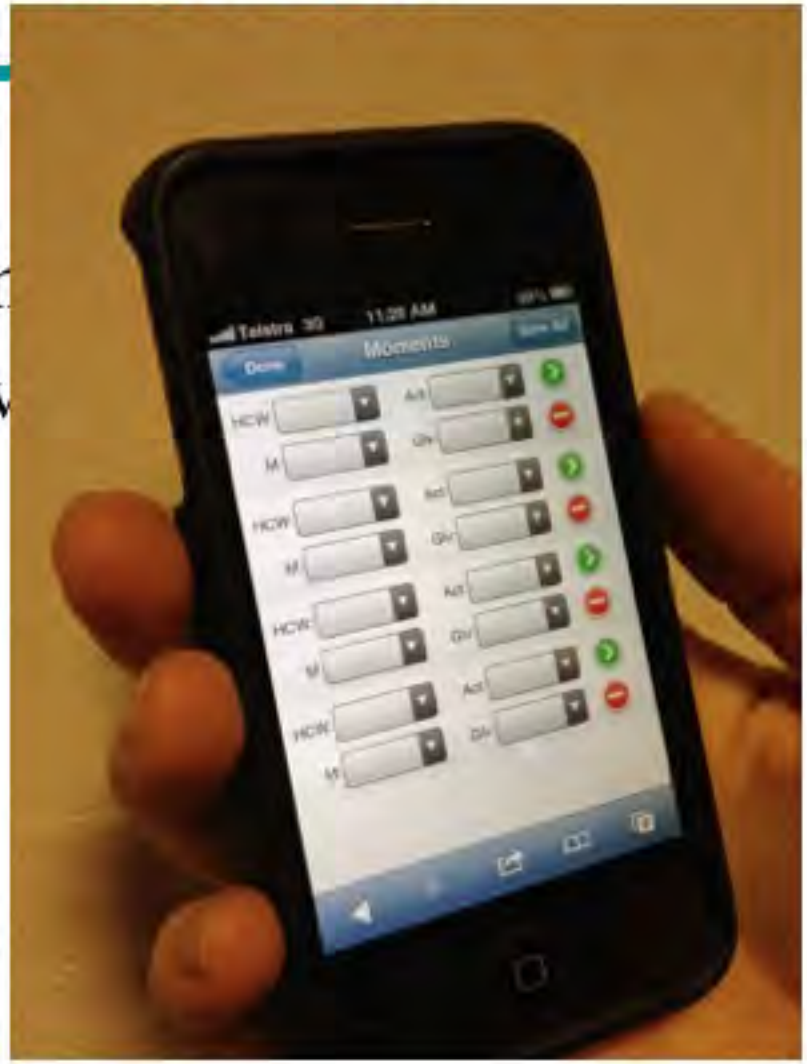

Other HHA initiatives

- Central HH database
- New direct-entry HH compliance App
  - i-Phones, other Smart-devices
  - Benefits:
    - Reduces data management time by 50%
    - No duplicate data entry and errors
    - Mobile devices common and cheap
    - Flexible reporting options
    - Potential – NZ, Hong Kong, WHO

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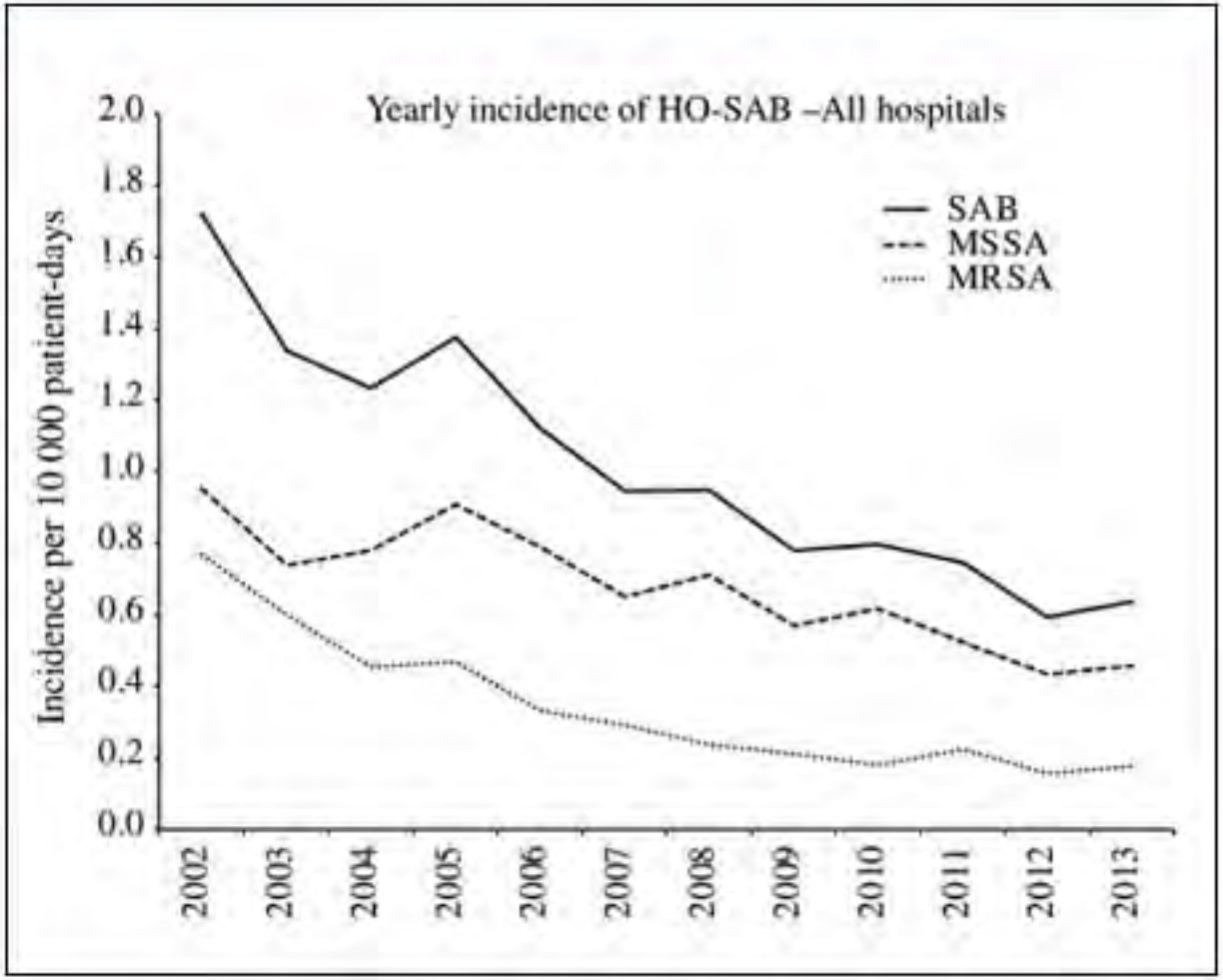
Health Quality & Safety Commission New Zealand

Austin Health

Declining SAB rates in Australia



Mitchell, Collignon, McCann *et al. Clin Infect Dis.* August 2014

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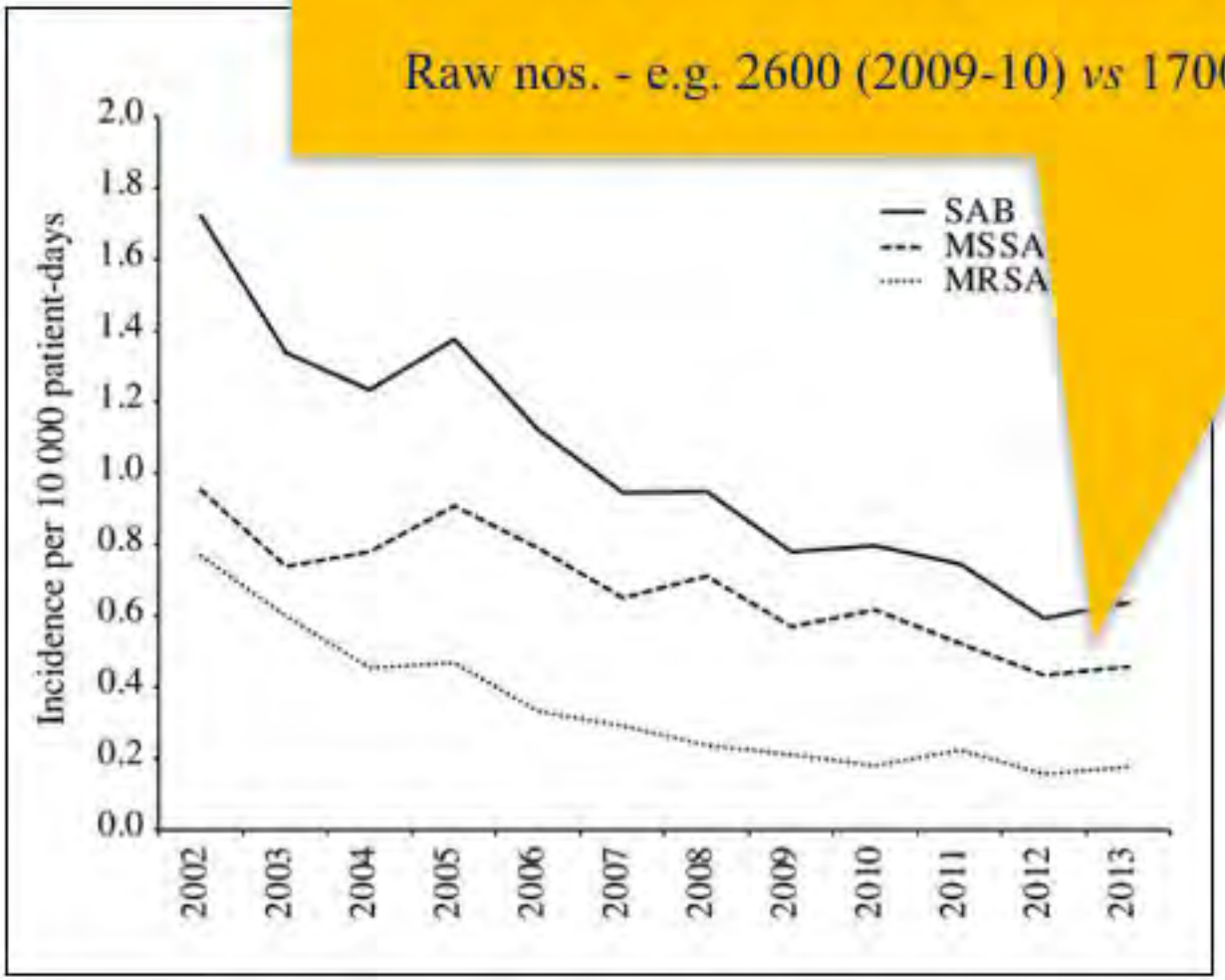
Declinin

Major reduction in national rates of healthcare-associated *S. aureus* bacteraemia

Raw nos. - e.g. 2600 (2009-10) *vs* 1700 (2012)



Mitchell, Collignon, McCann *et al. Clin Infect Dis.* August 2014

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National Safety and Quality Health Service Standards
September 2012
AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE
NSQHS STANDARDS

AUSTRALIAN COMM
ON SAFETY AND QUALI

NSQHS STANDARDS

Standard 1	–	Governance for Safety and Quality in Health Service Organisations
Standard 2	–	Partnering with Consumers
Standard 3	–	Preventing and Controlling Healthcare Associated Infections
Standard 4	–	Medication Safety
Standard 5	–	Patient Identification and Procedure Matching
Standard 6	–	Clinical Handover
Standard 7	–	Blood and Blood Products
Standard 8	–	Preventing and Managing Pressure Injuries
Standard 9	–	Recognising and Responding to Clinical Deterioration in Acute Health Care
Standard 10	–	Preventing Falls and Harm from Falls

MELBOURNE | DENTISTRY & HEALTH SCIENCES

AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

NSQHS STANDARDS

Preventing and Controlling Healthcare Associated Infections

Standard 3

The Preventing and Controlling Healthcare Associated Infections Standard:

Clinical leaders and senior managers of a health service organisation implement systems to prevent and manage healthcare associated infections and communicate these to the workforce to achieve appropriate outcomes. Clinicians and other members of the workforce use the healthcare associated infection prevention and control systems.


VOTE 1 LIBERAL
TANDBERG
WILL YOU STILL FUND THE ALCOHOL HAND HYGIENE PROGRAM?
WE'LL SEE WHAT'S LEFT OVER AFTER THE CELEBRATIONS

Nursing Standard **helping you to protect patients and staff**

Infection control

1 Palm to palm

2 Right palm over left back and left palm over right back

3 Palm to palm with fingers interlaced

4 Backs of fingers to opposing palms with fingers interlocked

5 Rotational rubbing of right thumb clasped in left palm and vice versa

6 Rotational rubbing backwards and forwards with clasped fingers of right hand in left palm and vice versa

Patients and staff in healthcare environments are vulnerable to infections, including methicillin-resistant *Staphylococcus aureus* (MRSA). Frequent and appropriate handwashing is a key principle to avoiding contamination. Here is a guide to effective handwashing and some useful tips for avoiding the spread of infection:

- Hands should be washed with soap and water or alcohol hand-rub using the correct technique before and after procedures and contact with patients.
- Disposable gloves and aprons should be worn for contact with body fluids, lesions and contaminated materials (wash hands after use).
- If taking a uniform home to clean, a hot wash should be used and the washing machine should not be overloaded.
- Linen should be handled carefully (not shaken) and transported in correct colour-coded laundry bags. Soft furnishings, such as curtains, should be cleaned regularly.
- Patient areas should be uncluttered and cleaned regularly.
- Compliance with infection control policies should be monitored through audits.

Other HHA initiatives

- Central HH database and data entry system
  - New direct-entry HH compliance App
- Adaptation of HHA system to become an AMR surveillance program
  - Linking HHA to AGAR

Establishing a National AMR Surveillance Program

- AMR surveillance using existing HHA database and mobile App technology
  - Aim: *"Define the clinical impact of AMR"*
  - Trial commenced last week – Melbourne and Perth

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HHA database and

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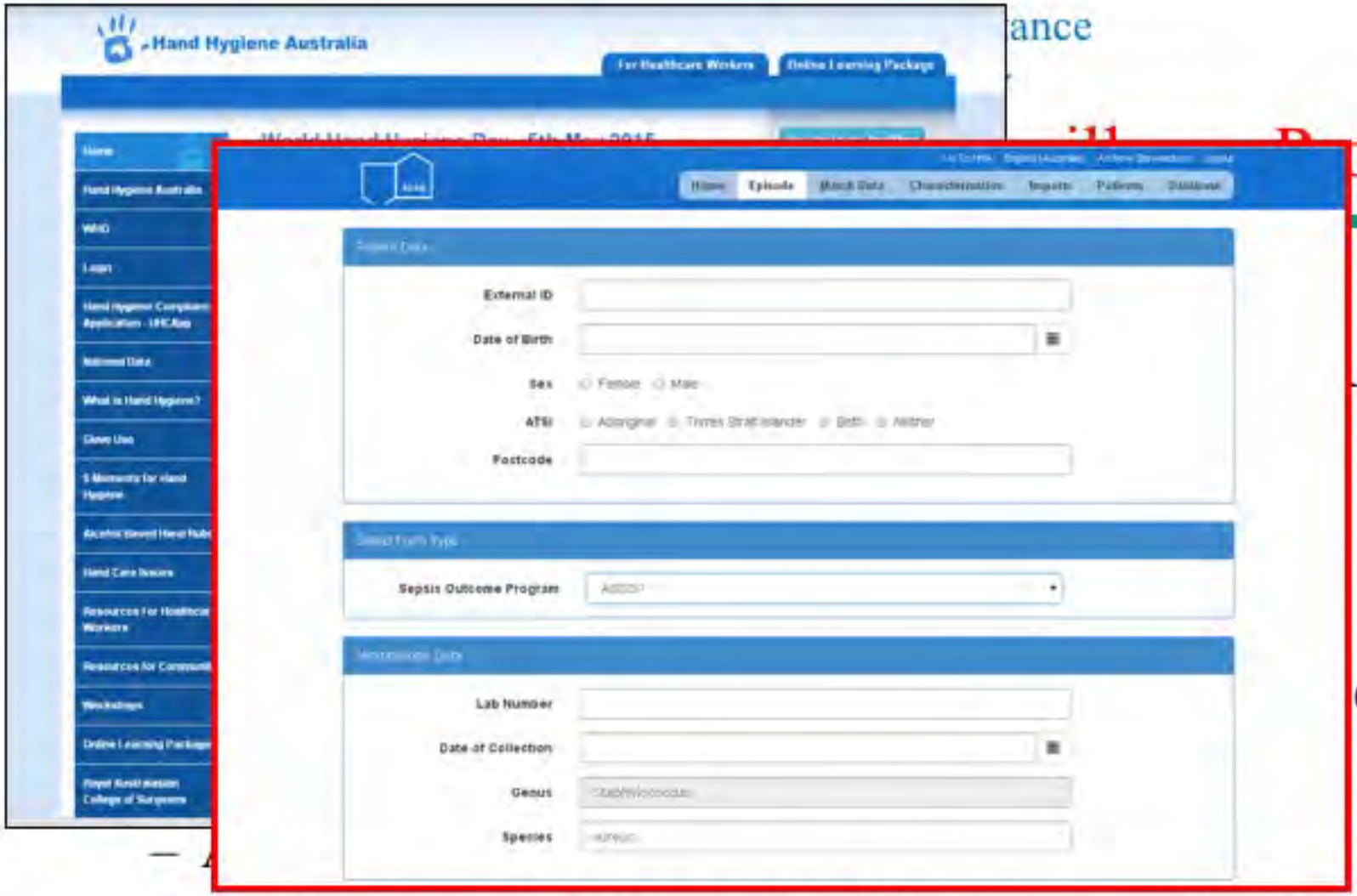

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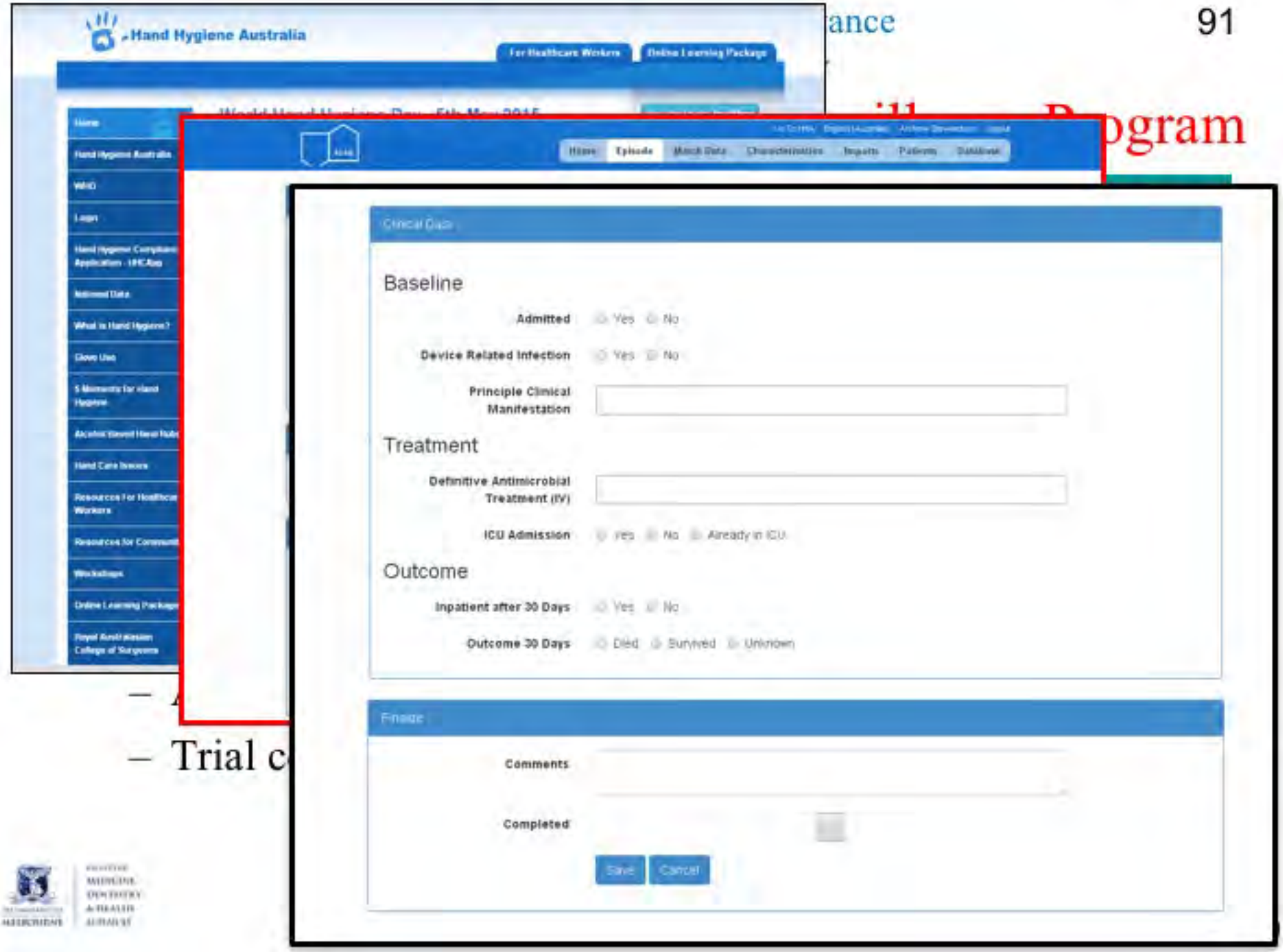

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Antibiotic Allergy and Antimicrobial Stewardship (AMS)

Antibiotic Allergy and Antimicrobial Stewardship (AMS)

Antibiotic Allergy and AMS

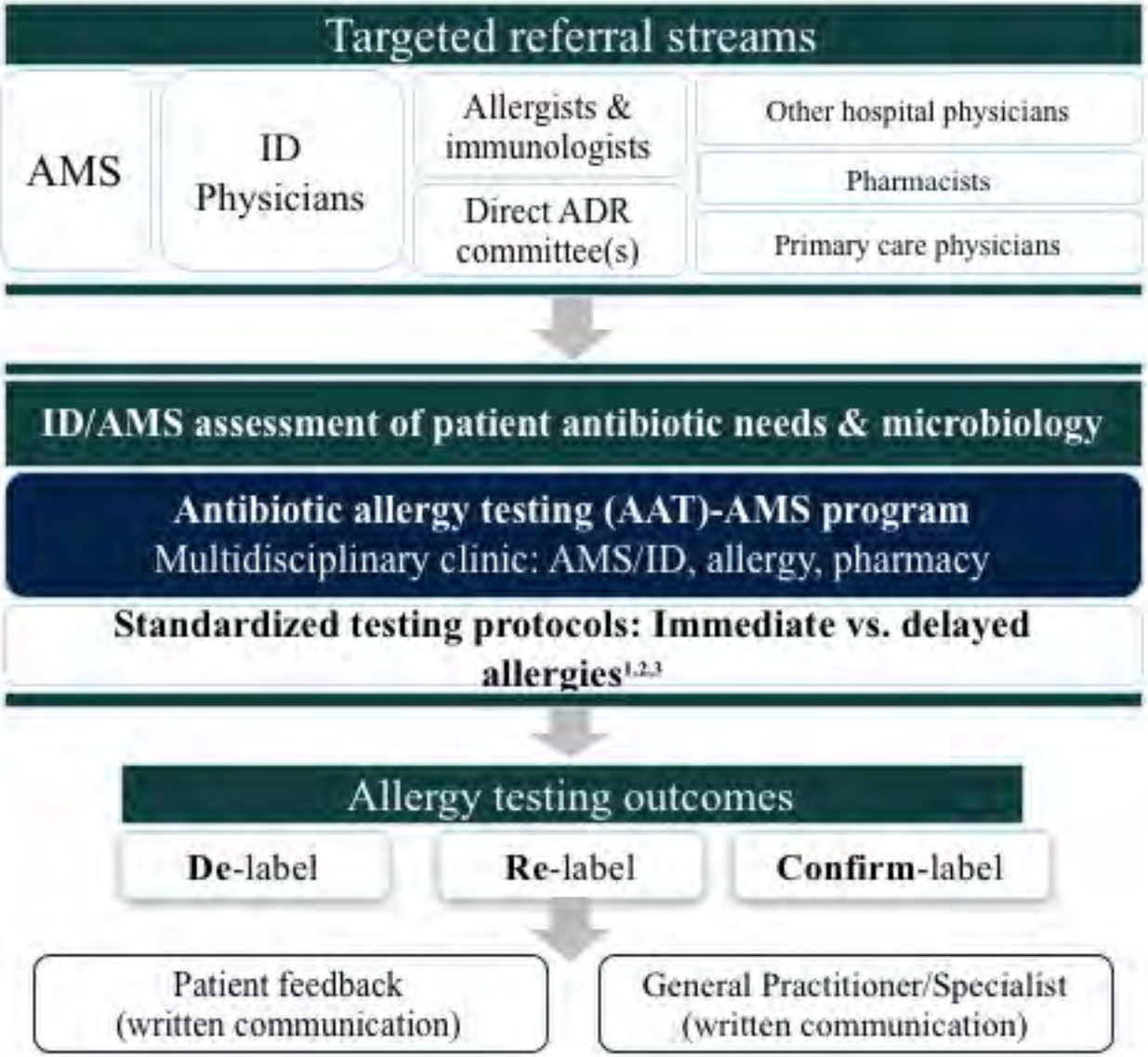
- Patient reported penicillin allergy prevalence 9%[1]
- Patient reported antibiotic allergy prevalence 18-24%[1]
- Penicillin allergy "labels" associated with excess length-of-stay, readmission, inappropriate antibiotic prescribing and antimicrobial resistance (inc. *Clostridium difficile* infection, MRSA, VRE)[2,3]

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

Comment: Allergy assessments and PCN skin testing can enhance use of first-line agents, but it is largely unstudied as a primary ASP intervention; however, ASPs should pro-

1. Trubiano *et al*. J Antimicrob Chemother 2016; 71(6):1715
2. Charneski *et al*. Pharmacotherapy 2011; 31 (8): 742
3. Macy *et al*. Curr Allergy Asthma Rep 2014; 14 (11): 476
4. https://www.cdc.gov/getsmart/week/downloads/getsmart-penicillin-factsheet.pdf
5. Barlam *et al*. Clin Infect Dis 2016; 62:e51

Austin Health Antibiotic Allergy Service



Fernandez *et al.* J Investig Allergol Clin Immunol 2013; Brockow *et al.* Allergy 2013; Bourke *et al.* J Allergy Clin Immunol Pract 2015

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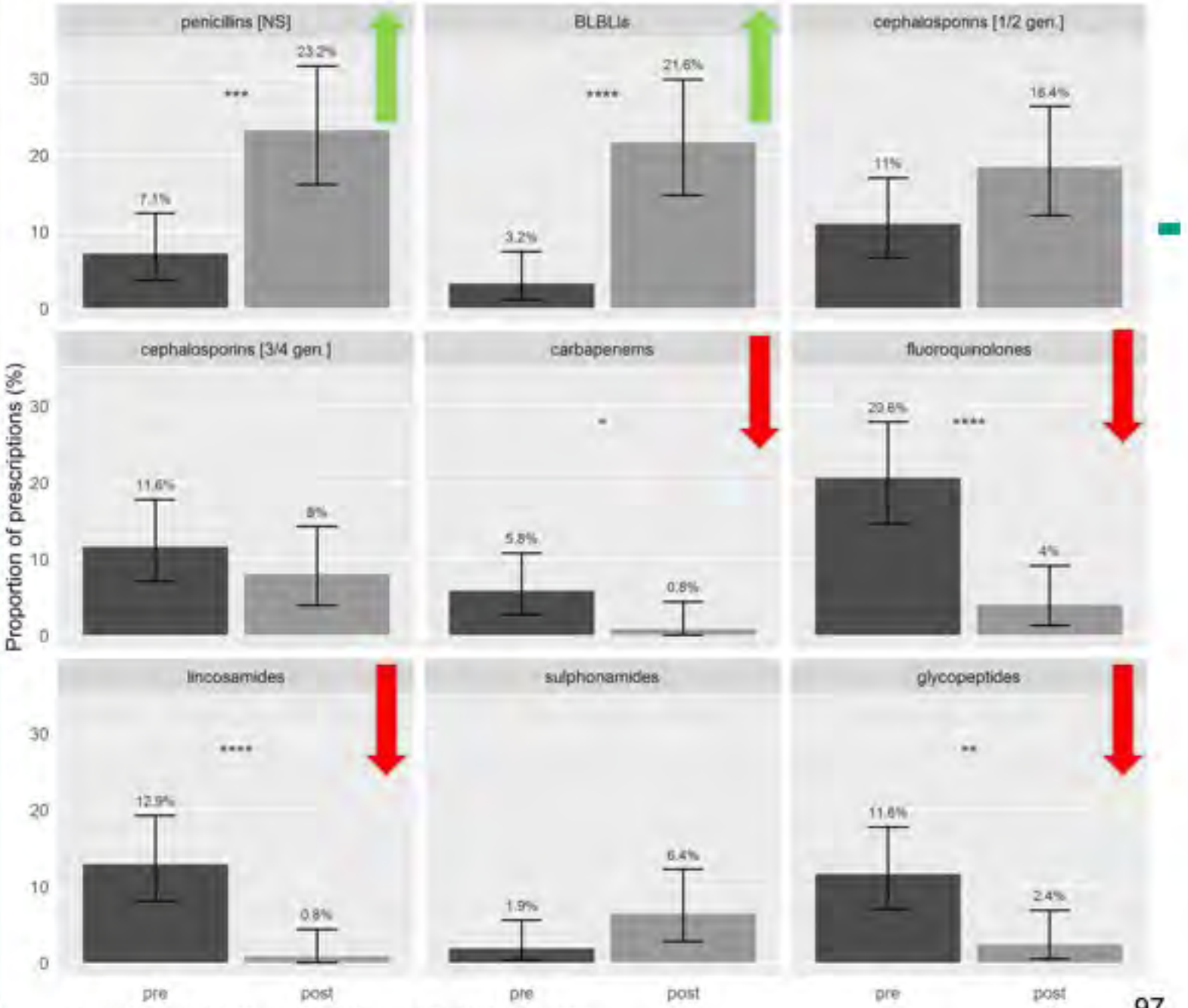
3 months pre-AAT

vs.

3 months post-AAT



Legend: * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$

Trubiano *et al.* CID 2016 (in press)

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Re-assessing Older Antibiotics

Re-assessing Older Antibiotics

REVIEWS OF ANTI-INFECTIVE AGENTS MAJOR ARTICLE

Louis D. Saravolatz, Section Editor

Forgotten Antibiotics: An Inventory in Europe, the United States, Canada, and Australia

Céline Pulcini,[1] Karen Bush,[2] William A. Craig,[3] Niels Frimodt-Møller,[4] M. Lindsay Grayson,[5] Johan W. Mouton,[6] John Turnidge,[7] Stephan Harbarth,[8] Inge C. Gyssens,[9,10] and the ESCMID Study Group for Antibiotic Policies

[1]Centre Hospitalier Universitaire de Nice, Service d'Infectiologie and Université de Nice Sophia-Antipolis, Faculté de Médecine, France; [2]Biology Department, Indiana University, Bloomington; [3]University of Wisconsin, School of Medicine and Public Health, Madison; [4]Department of Clinical Microbiology, Hvidovre Hospital, Copenhagen, Denmark; [5]Infectious Diseases Department, Austin Health and Department of Medicine, University of Melbourne, Victoria, Australia; [6]Department of Medical Microbiology, Radboud University Nijmegen Medical Centre and Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, the Netherlands; [7]SA Pathology, The University of Adelaide, SA, Australia; [8]Geneva University Hospitals and Medical School, Switzerland; [9]Department of Medicine, Radboud University Nijmegen Medical Centre and Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, the Netherlands; and [10]Hasselt University, Diepenbeek, Belgium

Clinical Infectious Diseases 2012;54(2):268–74

Re-assessing older agents

Fosfomycin

Re-assessing older agents

Fosfomycin

Review

Fosfomycin for the treatment of multidrug-resistant, including extended-spectrum β-lactamase producing, Enterobacteriaceae infections: a systematic review

Falagas *et al.* The Lancet ID 2010

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Matthew

AMERICAN SOCIETY FOR MICROBIOLOGY | Clinical Microbiology Reviews

Fosfomycin

Matthew E. Falagas,[a,b,c] Evridiki K. Vouloumanou,[a] George Samonis,[d] Konstantinos Z. Vardakas[a,b]

Alfa Institute of Biomedical Sciences, Athens, Greece[a]; Department of Internal Medicine-Infectious Diseases, Iaso General Hospital, Iaso Group, Athens, Greece[b]; Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA[c]; Department of Internal Medicine, University of Crete School of Medicine, Heraklion, Greece[d]

Clin Microbiol Rev. 2016; 29(2):321-47.

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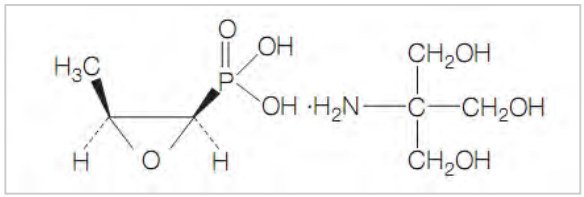
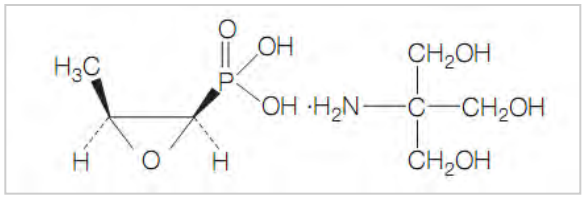


Fosfomycin

- Small molecule
- Broad spectrum of activity – esp. urinary pathogens (except *PsA*)
- Is the only representative of its class
- Target site unaffected by other ABx – no cross-class resistance

Mechanism of action:

- Bacterial cell wall inhibition – inactivation of enolpyruvate transferase =
  - Irreversible blockage of uridine diphosphate-N-acetylglucosamine condensation =
  - Blocks cell wall synthesis



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  - Blocks cell wall synthesis

Resistance – two mechanisms:

- Chromosomal mutation = reduced transport into cell
- Plasmid-mediated – fosfomycin inactivation
- Overall rates of resistance – low (<5-10%)

Karageorgopoulos *et al*. JAC 2012;
Michalopoulos *et al.*, Int J ID 2011

Fosfomycin

- Minimal serum protein binding
- Good tissue penetration
  - Soft tissue, bone, lung, heart valves, CNS
- PK/PD parameter – ? time-dependent (time above MIC)
- Oral preparations:
  - Fosfomycin-trometamol – Europe/USA/Australia
    - ~40% bioavailability (c.f. Fosfomycin-calcium - 10% bioavailability)
- IV Fosfomycin (fosfomycin disodium):
  - Availability
  - Dosage: 12-24 g/day in 2-4 divided doses (normal renal fn.)
  - Caution with doses >16 g/day – sodium overload and hypokalemia

Fosfomycin

- Minimal serum protein binding
- Good tissue penetration
  - Soft tissue, bone, lung, heart valves, CNS
- PK/PD parameter – ? time-dependent (time above MIC)
- Oral preparations:
  - Fosfomycin-trometamol – Europe/USA/Australia
    - ~40%
- IV Fosfom
  - Availabil
  - Dosage:
  - Caution v

- Oral – 3g (fosfomycin-trometamol)
- Safe
- Effective against many MDR Gram-negatives

MAJOR ARTICLE

Is Fosfomycin a Potential Treatment Alternative for Multidrug-Resistant Gram-Negative Prostatitis?

B. J. Gardiner,[1] A. A. Mahony,[1] A. G. Ellis,[2] N. Lawrentschuk,[3,4] D. M. Bolton,[3] P. T. Zeglinski,[2] A. G. Frauman,[2,5] and M. L. Grayson[1,5]

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Clinical Infectious Diseases 2014;58(4):e101–5

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- Prospective, 26 healthy males, BPH = TURP
- Single 3g Fosfo, mean 9.5 hs pre-TURP
- Assessed plasma, urine and prostate levels (P/T zones, non-inflamed)
- Mean overall prostate levels: 6.5 ± 4.9 µg/ml (R: 0.7-22.1)
  - 70% had concs ≥ 4 µg/ml
- Therapeutic concentrations detectable up to 17 hs post-dose
- Mean prostate:plasma ratio 0.67 ± 0.57

Clinical Infectious Diseases 2014;58(4):e101–5

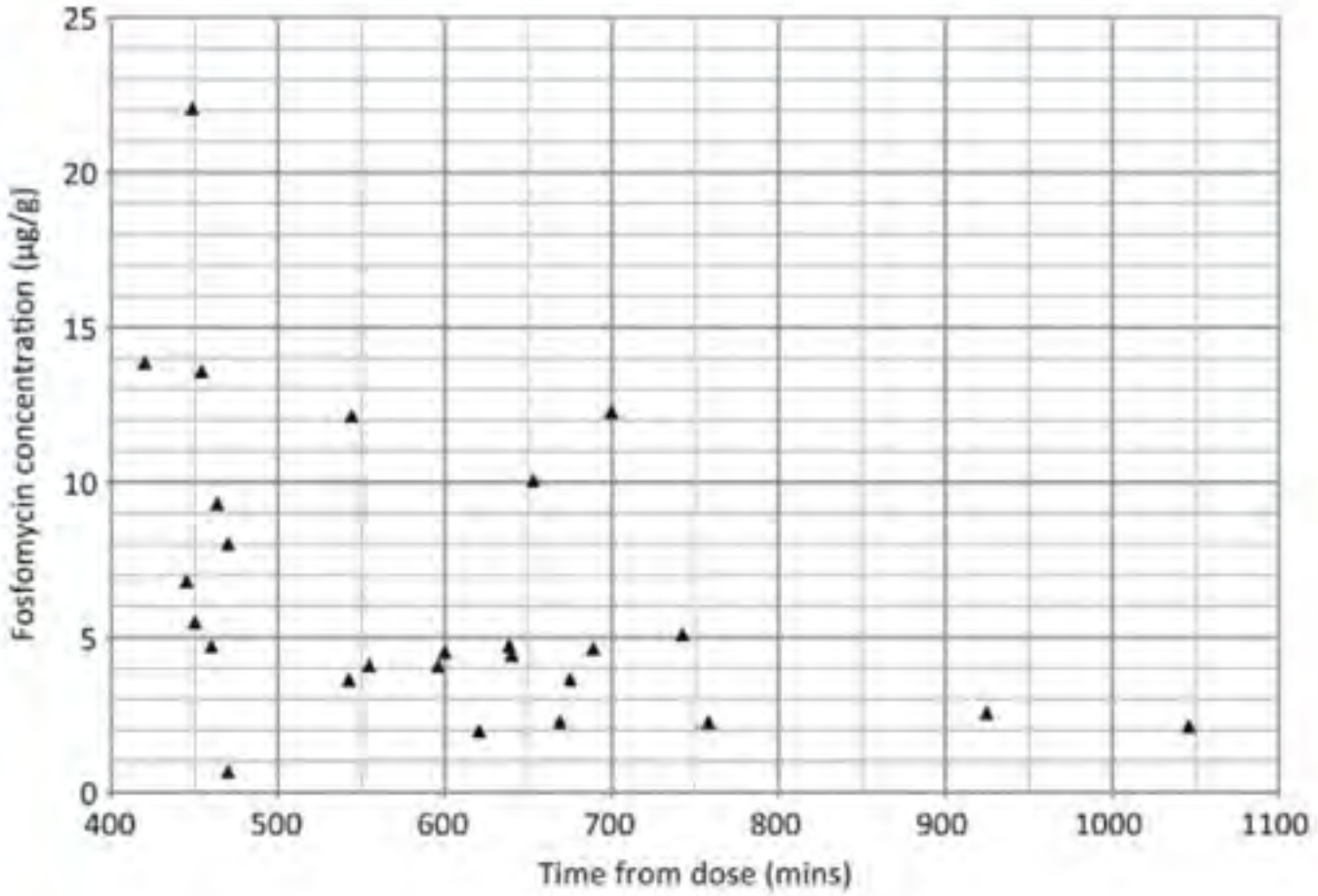


Figure 1. Mean fosfomycin prostate concentrations by time after single oral 3-g dose.

rob Chemother
093/jac/dkv067

Journal of Antimicrobial Chemotherapy

Optimal timing of oral fosfomycin administration for pre-prostate biopsy prophylaxis

Nathaniel J. Rhodes[1,2], Bradley J. Gardiner[3], Michael N. Neely[4,5], M. Lindsay Grayson[3,6], Andrew G. Ellis[6,7], Nathan Lawrentschuk[8,9], Albert G. Frauman[6,7], Kelly M. Maxwell[10], Teresa R. Zembower[11] and Marc H. Scheetz[1,2]*

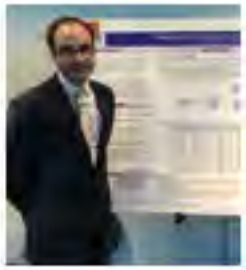
[1]Department of Pharmacy Practice, Midwestern University, Chicago College of Pharmacy, Downers Grove, IL, USA; [2]Department of Pharmacy, Northwestern Memorial Hospital, Chicago, IL, USA; [3]Department of Infectious Diseases, Austin Health, Heidelberg, Victoria, Australia; [4]Laboratory of Applied Pharmacokinetics and Bioinformatics, Saban Research Institute, Children's Hospital Los Angeles, Los Angeles, CA, USA; [5]Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; [6]Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia; [7]Department of Clinical Pharmacology, Austin Health, Heidelberg, Victoria, Australia; [8]Department of Surgery, Urology Unit, University of Melbourne, Melbourne, Victoria, Australia; [9]Olivia Newton-John Cancer Research Institute, Austin Health, Heidelberg, Victoria, Australia; [10]Department of Urology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; [11]Division of Infectious Diseases, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

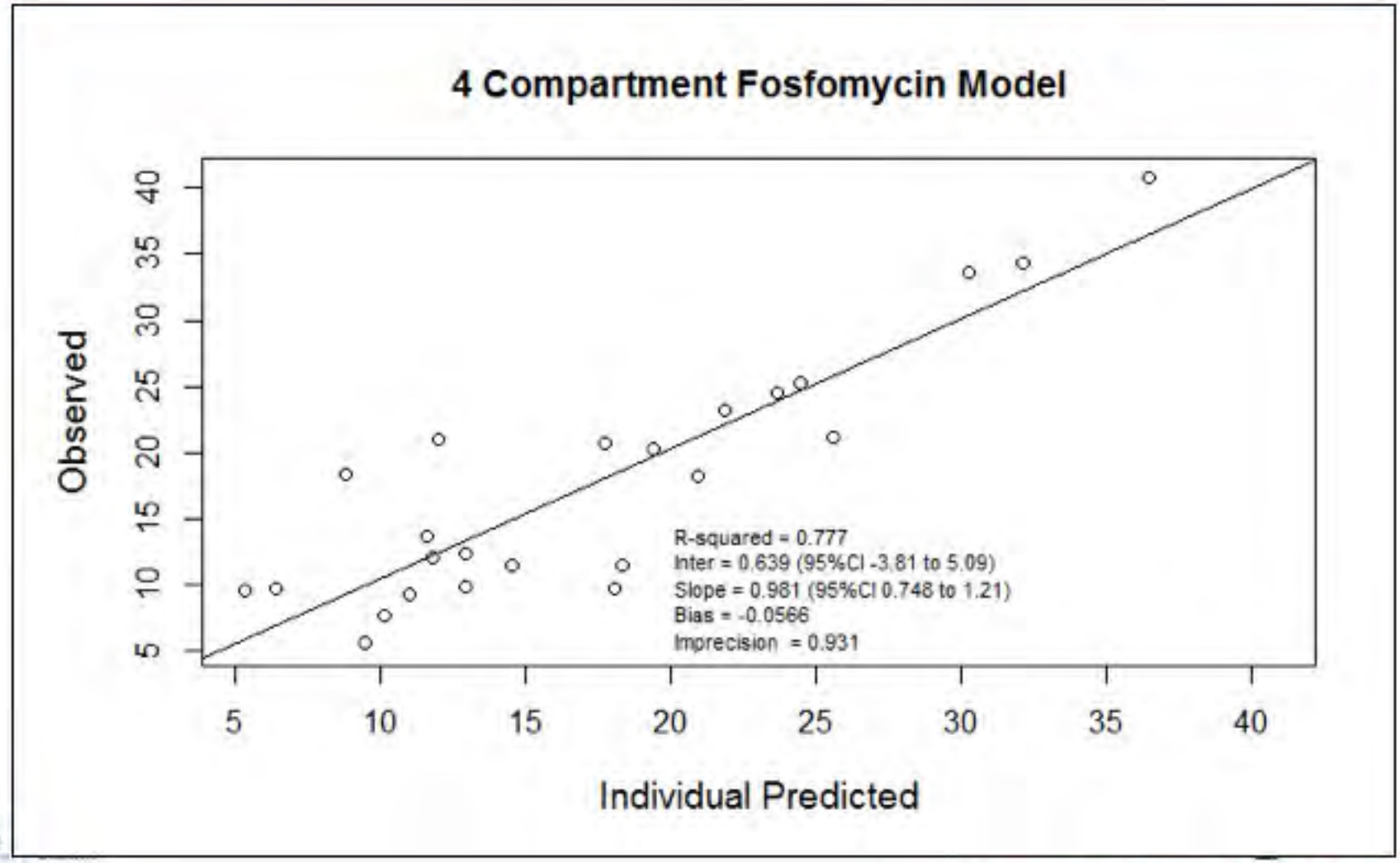
- Modelling – give oral fosfomycin 1-4 hs pre-prostate biopsy
- Avoid use if MIC >4 μg/ml

J Antimicrob Chemother 2015; 70: 2068–2073

Two plasma levels – 3g Fosfomycin

Two plasma levels – 3g Fosfomycin





Courtesy of Marc Scheetz & John Day

Fosfomycin

Treatment of Prostatitis

Fosfomycin
Treatment of Prostatitis

Fosfomycin for Treatment of Prostatitis: New Tricks for Old Dogs

M. Lindsay Grayson,[1,2] Nenad Macesic,[1] Janine Trevillyan,[1,3] Andrew G. Ellis,[2,4] Phillip T. Zeglinski,[2] Nicholas H. Hewitt,[1] Bradley J. Gardiner,[1] and Albert G. Frauman[2,4]

[1]Department of Infectious Diseases, Austin Health, [2]Department of Medicine, University of Melbourne, [3]Department of Infectious Diseases, Alfred Health, and [4]Department of Clinical Pharmacology, Austin Health, Melbourne, Australia

(See the Editorial Commentary by Falagas and Rafailidis on pages 1144–6.)

Fosfomycin
Treatment of Prostatitis

- Two patients with MDR *E. coli* prostatitis
- Failed multiple previous Rx , including prolonged meropenem
- Fosfomycin MIC 1 μg/ml (E-test)
- Treated with 3g oral fosfomycin daily (and 2x daily)
  - Patient 1 – 16 weeks
  - Patient 2 – 12 weeks

- Both cured 6 mths after completion of therapy

Grayson *et al.* Clin Infect Dis 2015; 61:1141-3.

Fosfomycin

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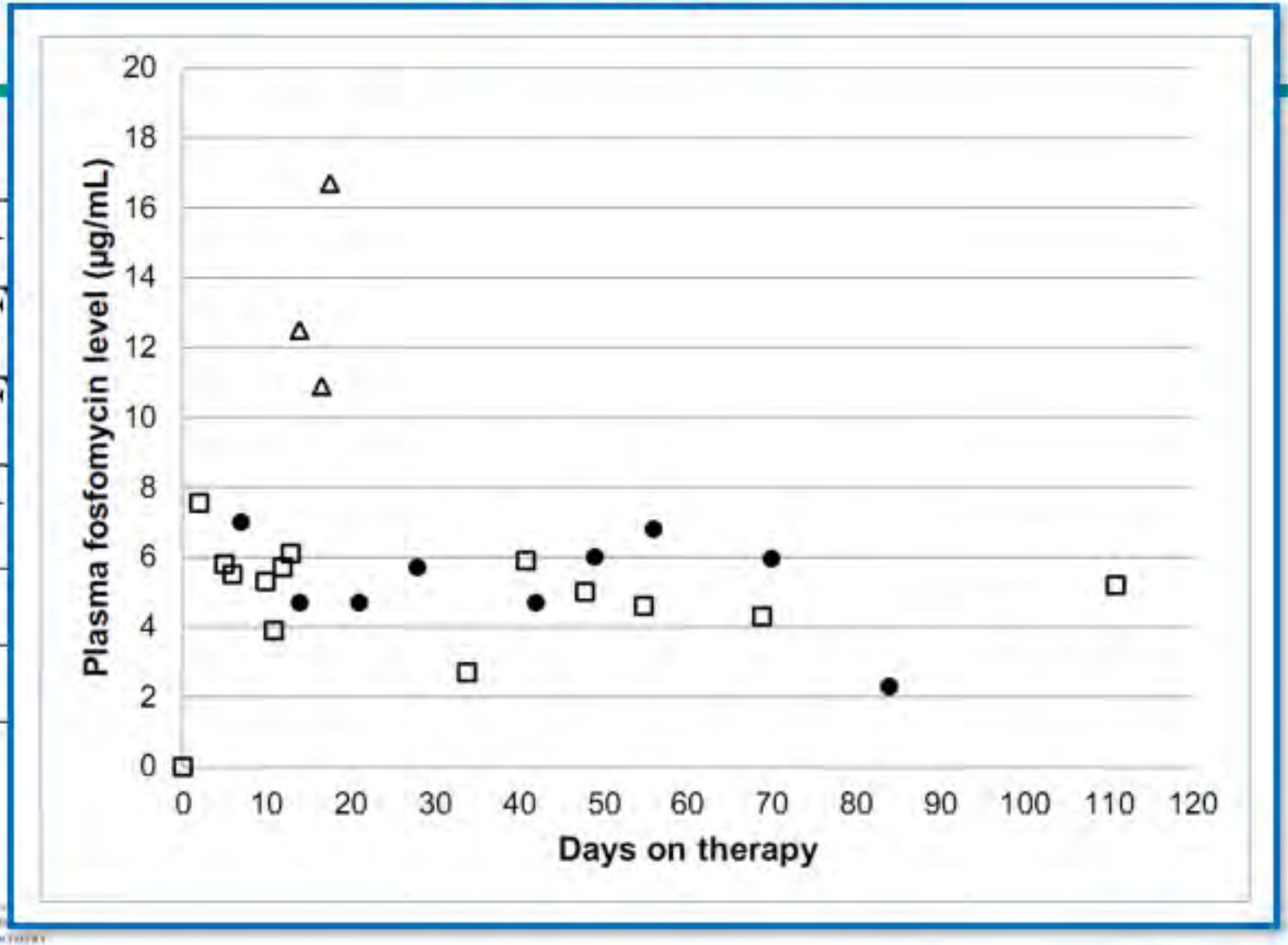

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Fosfomycin

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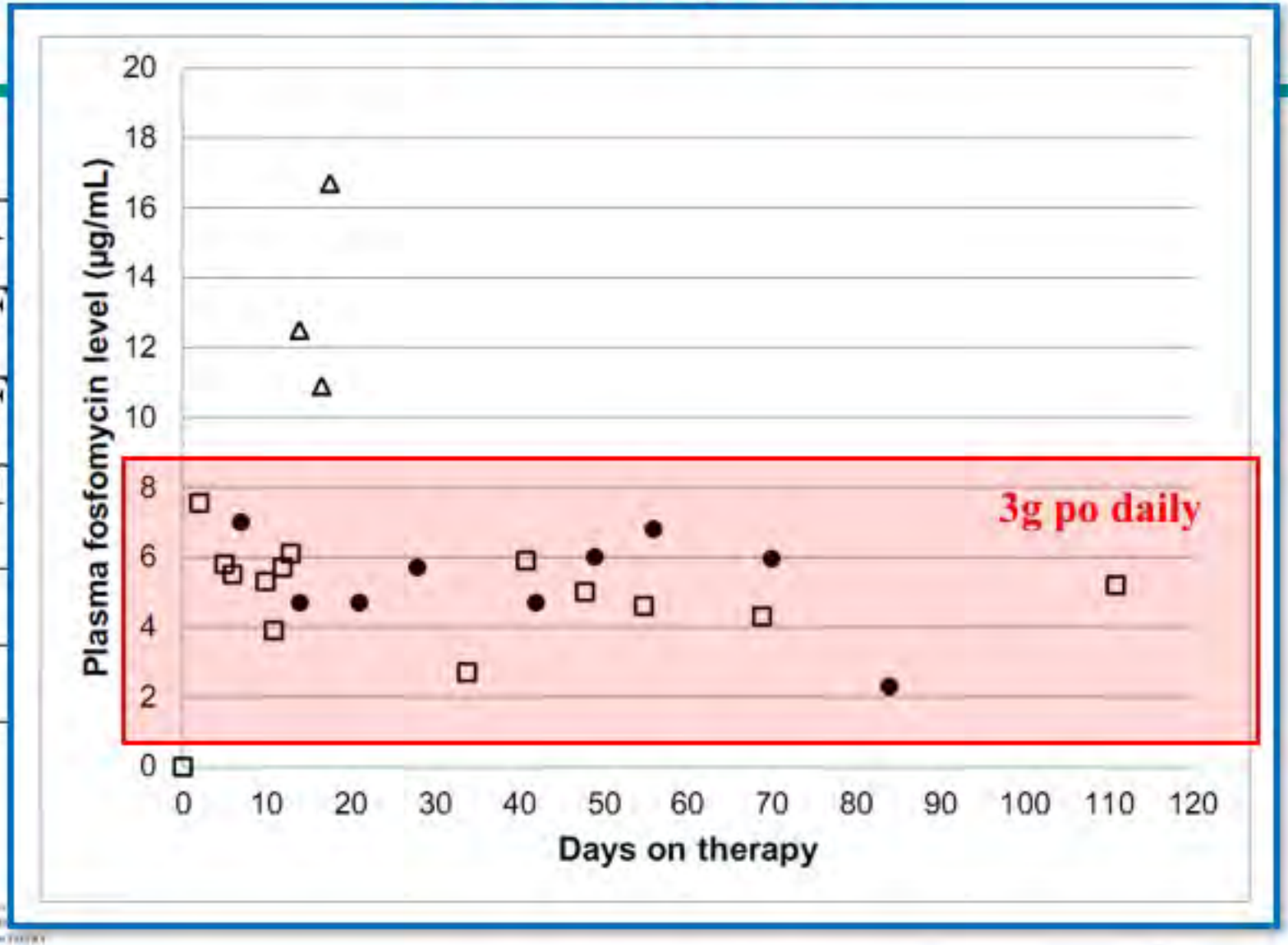

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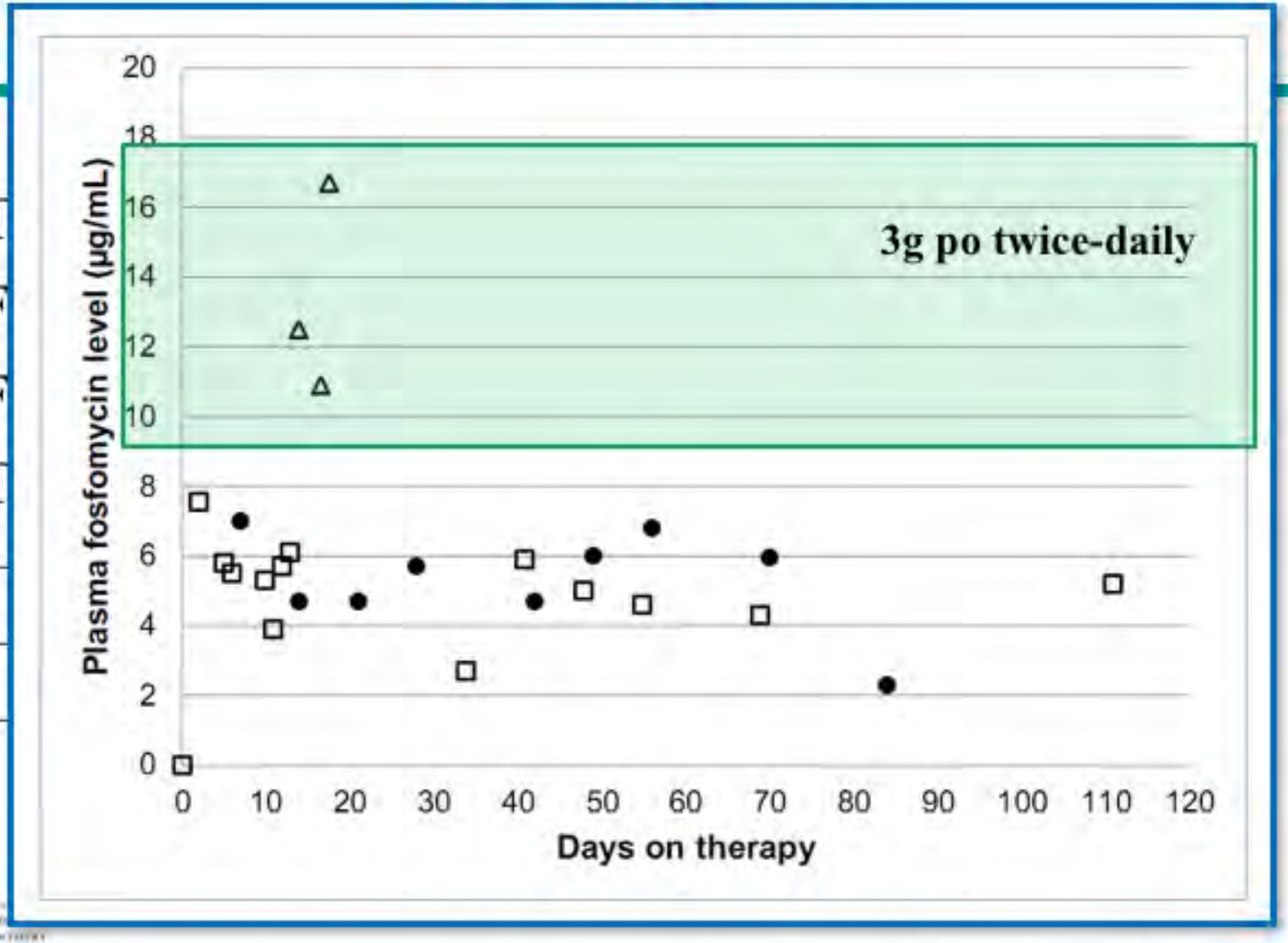


Grayson *et al*. Clin Infect Dis 2015 (*in press*).

Fosfomycin

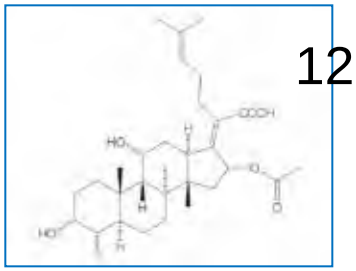
Treatment of Prostatitis

Key considerations:

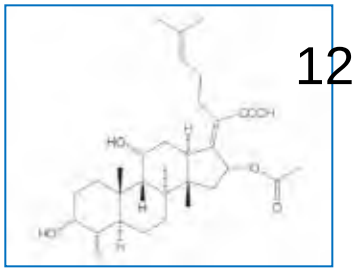
- What is the MIC? - probably needs to be ≤4 μg/ml
- Need to use 3g daily - can the patient tolerate this?
  - ? Try 3g twice-daily – but diarrhoea likely
- Treatment duration uncertain - ?12 weeks

Grayson *et al.* Clin Infect Dis 2015; 61:1141-3.

Fusidic acid

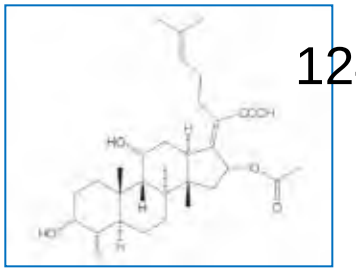


Fusidic acid



- Used in Europe and Australia – many years
- Activity – *S. aureus*, *S. epidermidis*
- Inhibits protein synthesis by preventing translocation of elongation factor G (EF-G) from the ribosome
  - Steroid structure chemically related to cephalosporin P
    - Formed from *Cephalosporium acremonium*
  - Mode action explains its efficacy and lack of cross-resistance between fusidic acid and beta-lactams (e.g. MRSA)
  - "Steroid antibiotics" – due to resemblance to prednisolone ; own class
  - *fus*A gene encodes for EF-G

Fusidic acid



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  - *fus*A gene encodes for EF-G
- Resistance – two mechanisms:
  - FusA – reduced affinity with target ribosomal EF-G
  - FusB – plasmid-mediated protection of EF-G from fusidic acid
    - now most prevalent

Fusidic acid

ANTIMICROBIAL RESISTANCE INVITED ARTICLE

George M. Eliopoulos, Section Editor

Dumb and Dumber—The Potential Waste of a Useful Antistaphylococcal Agent: Emerging Fusidic Acid Resistance in *Staphylococcus aureus*

Benjamin P. Howden[1,2] and M. Lindsay Grayson[1,3,4]

[1]Infectious Diseases Department, Austin Health, Heidelberg, and Departments of [2]Microbiology and [3]Epidemiology and Preventive Medicine, Monash University, and [4]Department of Medicine, University of Melbourne, Melbourne, Australia

Clinical Infectious Diseases 2006; 42:394–400

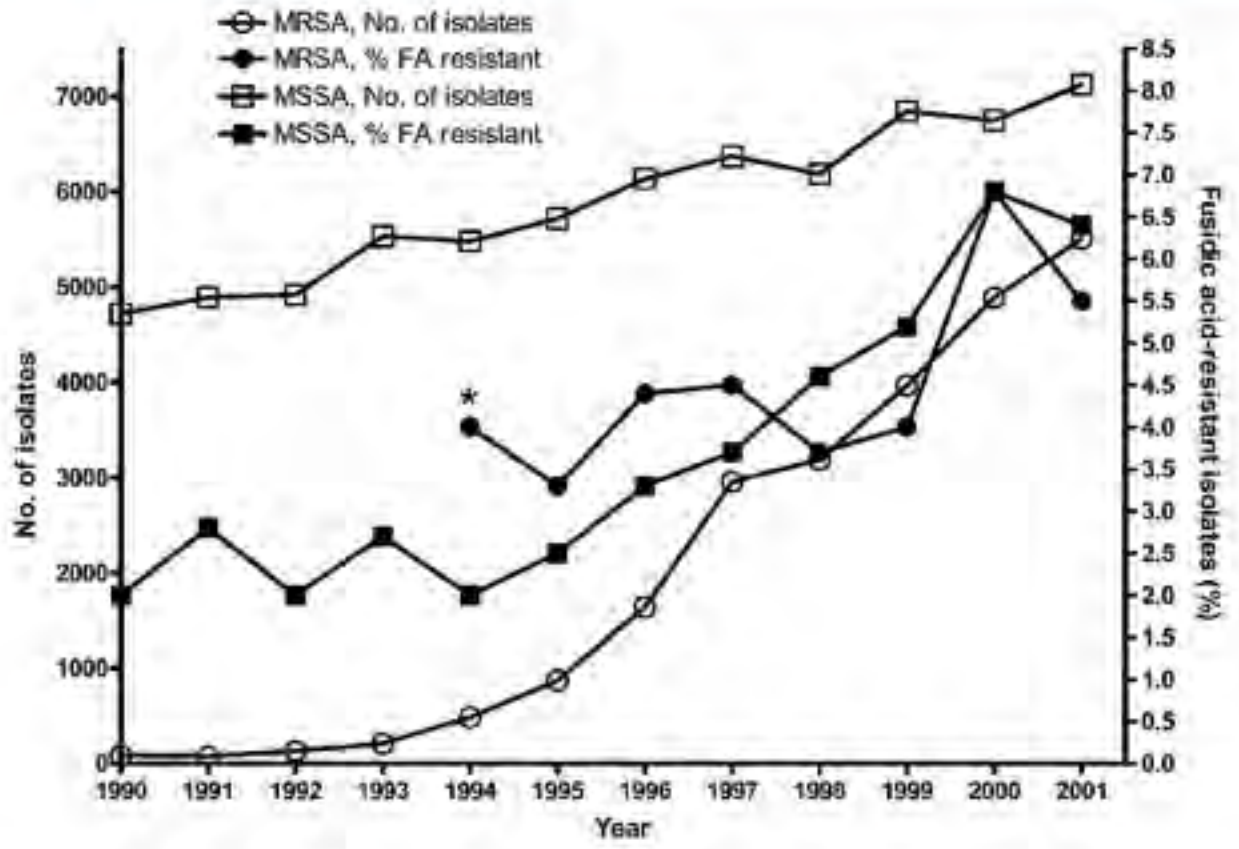

Figure 1. Number of methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) bloodstream isolates and percentage of those isolates that were fusidic acid (FA) resistant in the United Kingdom, 1990–2001. Prior to 1994, the numbers of MRSA isolates were very low, and percentage rates of FA resistance were variable. For those years, MRSA isolate numbers (and the percentage that were FA resistant) were as follows: 1990, 92 (1.8%); 1991, 74 (12.5%); 1992, 131 (7.9%); and 1993, 207 (10.6%). Based on data from [52].

Issues with Fusidic acid

- Need to use in combination to avoid resistance
  - Usually rifampicin
- Nausea - at some doses (esp. the elderly)
- Interactions – esp. statins

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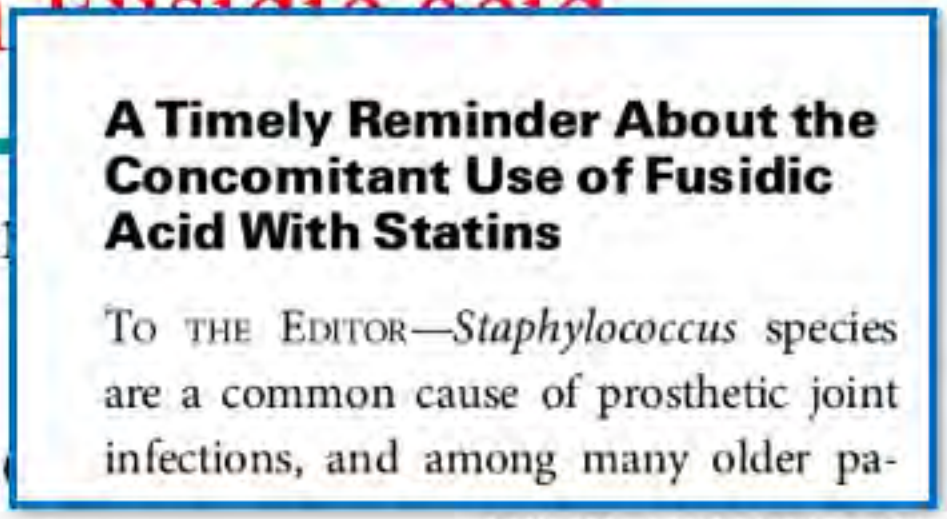

A Timely Reminder About the Concomitant Use of Fusidic Acid With Statins

TO THE EDITOR—*Staphylococcus* species are a common cause of prosthetic joint infections, and among many older pa-

CID 2013:57 (15 July) • 329

Issues with Fusidic acid

- Need to use in combination to avoid resistance
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- Nausea - at some doses (esp. the elderly)
- Interactions – esp. statins
- Useful for long-term oral suppression of MRSA
  - e.g. prosthetic joint sepsis

Issues with Fusidic acid

ORIGINAL ARTICLE

10.1111/j.1469-0691.2007.01691.x

Treatment of staphylococcal prosthetic joint infections with debridement, prosthesis retention and oral rifampicin and fusidic acid

C. A. Aboltins[1], M. A. Page[1], K. L. Buising[1], A. W. J. Jenney[1], J. R. Daffy[1], P. F. M. Choong[2] and P. A. Stanley[1]

[1]Department of Infectious Diseases and [2]Department of Orthopaedic Surgery, St Vincent's Hospital, Melbourne, Victoria, Australia

bid resistance

e elderly)

Outcome of Debridement and Retention in Prosthetic Joint Infections by Methicillin-Resistant Staphylococci, with Special Reference to Rifampin and Fusidic Acid Combination Therapy

T. N. Peel,[a,b] K. L. Buising,[a] M. M. Dowsey,[b,c] C. A. Aboltins,[a] J. R. Daffy,[a] P. A. Stanley,[a] P. F. M. Choong[b,c]

Department of Infectious Diseases, St. Vincent's Hospital, Melbourne, Victoria, Australia[a]; Department of Surgery, University of Melbourne, Melbourne, Victoria, Australia[b]; Department of Orthopaedic Surgery, St. Vincent's Hospital, Melbourne, Victoria, Australia[c]

AAC 2013; 57:350-355; CMI 2007; 13:586-591.

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  - e.g. prosthetic joint sepsis
- In USA – Cempra Pharmaceuticals (CEM-102)
  - ?low serum levels in combination with rifampicin

Issues with Fusidic acid

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

A Randomized Study Evaluating Oral Fusidic Acid (CEM-102) in Combination With Oral Rifampin Compared With Standard-of-Care Antibiotics for Treatment of Prosthetic Joint Infections: A Newly Identified Drug–Drug Interaction

Richard Pushkin,[1] Maria D. Iglesias-Ussel,[1,2] Kara Keedy,[1] Chris MacLauchlin,[1] Diane R. Mould,[3] Richard Berkowitz,[4] Stephan Kreuzer,[5] Rabih Darouiche,[6] David Oldach,[1] and Prabha Fernandes[1]

[1]Cempra Inc, and [2]University of North Carolina, Chapel Hill; [3]Projections Research Inc, Phoenixville, Pennsylvania; [4]Phoenix Clinical Research, Tamarac, Florida; [5]Memorial Bone and Joint Clinic and University of Texas Health Science Center at Houston, and [6]Departments of Medicine, Surgery, and Physical Medicine and Rehabilitation, Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, Texas

Clin Infect Dis. 2016; 15;63(12):1599-1604.

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- In USA – C
  - – ?low seru

- Inconsistent with Australian experience
- ? possible HLA impact
- Large assessment underway with new FA assay

Overview

- The view from Mars
- Antimicrobial Resistance
  - Setting the scene for Australia
  - Current status – politics, resistance and prescribing
  - What is missing?
- New approaches
  - Building an IPC "fire-break"
  - New approaches to AMS
  - Re-assessing older agents
- The daunting future for Australia
  - What we can do about it

The impending tsunami

The impending tsunami

The impending tsunami

Contamination of the food chain

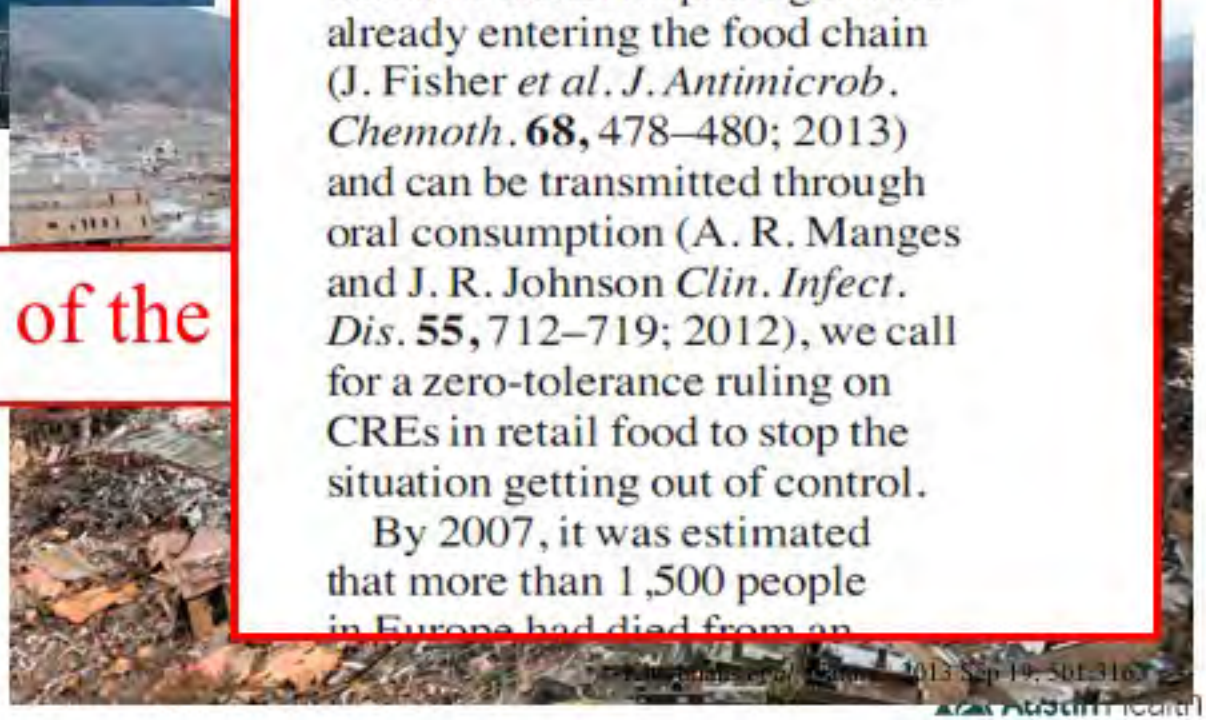
The impen

Contamination of the

Ban resistant strains from food chain

No reliable treatment is available for humans infected with carbapenem-resistant Enterobacteriaceae (CREs; see *Nature* **499,** 394–396; 2013). Because these antibiotic-resistant bacterial pathogens are already entering the food chain (J. Fisher *et al*. *J. Antimicrob. Chemoth*. **68,** 478–480; 2013) and can be transmitted through oral consumption (A. R. Manges and J. R. Johnson *Clin. Infect. Dis*. **55,** 712–719; 2012), we call for a zero-tolerance ruling on CREs in retail food to stop the situation getting out of control.

By 2007, it was estimated that more than 1,500 people in Europe had died from an



Issues

- International trade rules allow testing for drug residues, not AMR pathogens
- Australia (2012) – Senate enquiry:
  - 341 tests on 194 seafood consignments – 96.4% passed
  - Positives – fluoroquinolones in prawns (VN)
  - ++ small testing program

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or

Antibiotic Use in Australian Agriculture

- Chicken – yes (high)
- Pork – yes (moderate) - but ?decreasing
- Beef – yes – grain-fed beef (not pasture-fed)
- Lamb – no
- Dairy – yes (small) – impact uncertain
- Seafood – Australia none – but massive in Asia
- Crops – uncertain – the “new frontier”

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- Seafood – Australia none – but massive in Asia
- Crops – uncertain – the "new frontier"
- ? new initiatives – e.g. insect farming

A new approach is needed in Australia

- Legislate to require foods to be tested for AMR pathogens as well as ABx residues
  - Test local produce and imports
- Reassess importation of some vaccines
- Greater focus on infection control in farms
- Include AMR and antibiotic use on all farming and food production agendas – a "One Health" approach
- Re-position Australian food as:
  - High quality and safe
  - Greater focus on quality *vs* price and quantity

Australian AMR Summit

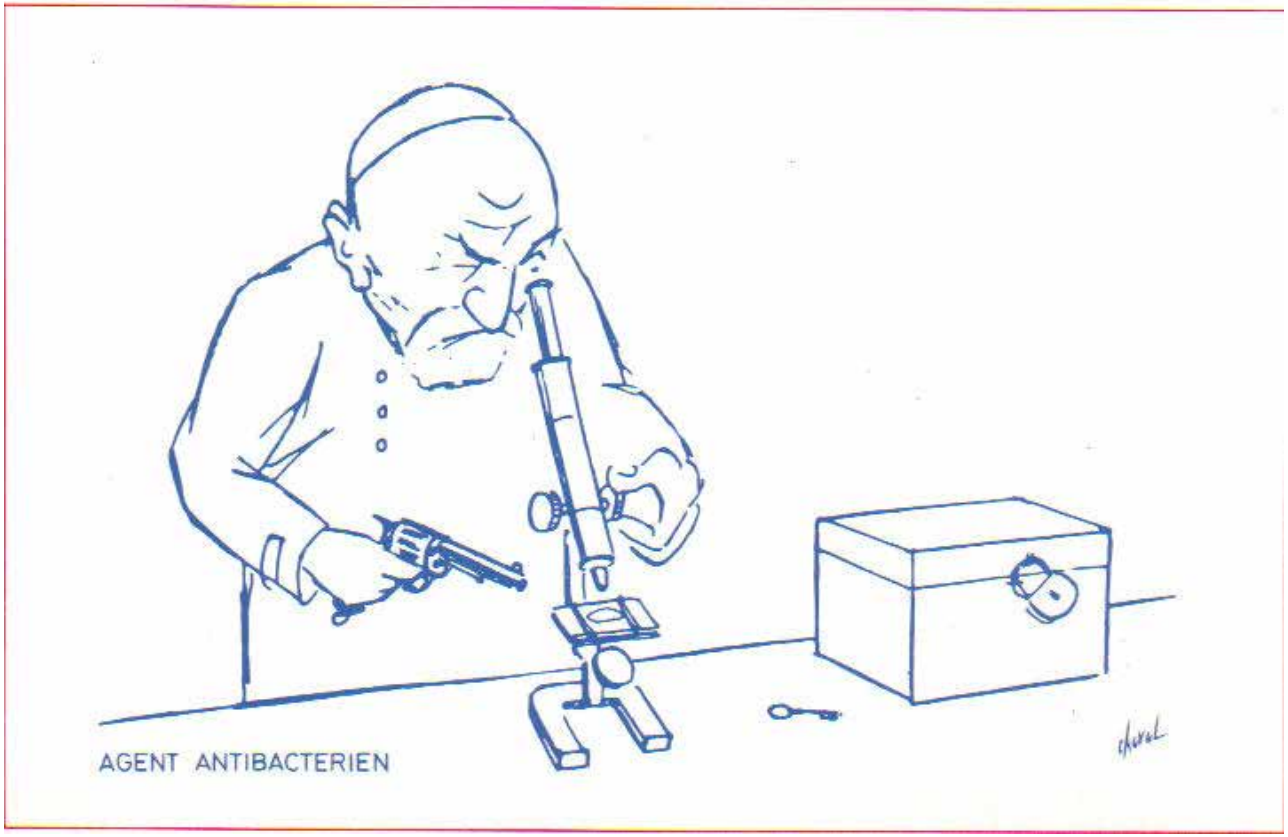
29th June 2017

- What is Australia's current progress re. AMR?
- Defining AMR progress according to WHO "4 pillars" of *One Health*:
  - Surveillance
  - IPC
  - Antimicrobial stewardship
  - Research & Development - vaccines, rapid diagnostics (POCTs), practical IPC initiatives, new drugs
- Need a "*National AMR Co-ordinating Centre*"

Conclusions

- AMR is no longer simply a health issue
  - It is also a social, economic and environmental issue
- Current situation re. new antimicrobial development is a major problem – will take a decade to fix
  - Need to reassess some older drugs
- We need to establish an infection control "fire-break"
  - Practical steps can be implemented - ?mandatory
- Reassess-restrict the use of antibiotics in agriculture
- Urgent need for improved national coordination

What is in the Future without Antibiotics?



Courtesy of the Institut Pasteur, 2001

Thanks to Teleclass Education

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