Therapeutic Guidelines

Therapeutic Guidelines
40 years of Antibiotic Guidelines Anniversary Seminar

New approaches to fighting antimicrobial resistance

Prof. M. Lindsay Grayson

Infectious Diseases & Microbiology Department, Austin Health, Melbourne
Director, Hand Hygiene Australia
Department of Medicine, University of Melbourne

The University of Melbourne | Faculty of Medicine, Dentistry & Health Sciences

Hand Hygiene Australia

Austin Health

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

- A “view from Mars” of the current situation
- The 4 “pillars” of AMR control
- Need for a new approach (“rules”) in:
  - Antimicrobial stewardship
  - AMR surveillance
  - New drug development
- Predicting the future of the Antibiotic Guidelines

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 in common infections:
  - Skin infections – “Golden staph” (MRSA)
  - Pneumonia, urinary tract, STDs
  - Diarrhoea - Salmonella, Campylobacter, VRE
  - Tuberculosis – XDR-TB

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ns) – antibiotics

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  - R-TB

This can't be right!

No-one could be so completely stupid!

WHO and CDC

Four "pillars" of AMR control

1. Improve Infection Prevention and Control
2. Practical Antimicrobial Stewardship
3. Improve AMR surveillance and outbreak response
4. Research and Development
   - Rapid diagnostics
   - New antimicrobial development
   - Innovations in infection control

WHO and CDC

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Basics of controlling Superbugs

1. Limit emergence of new MDR pathogens

2. Limit transmission of existing MDR pathogens

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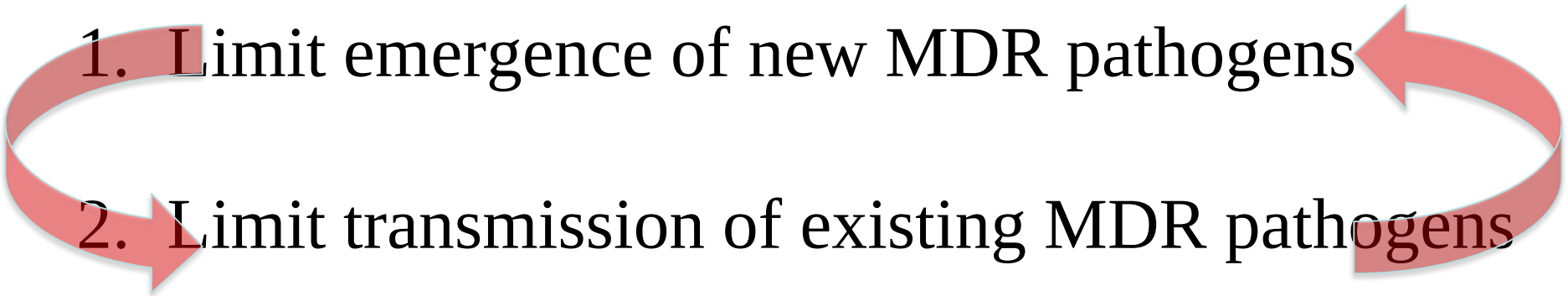

Creating an Infection Control "Fire-break"

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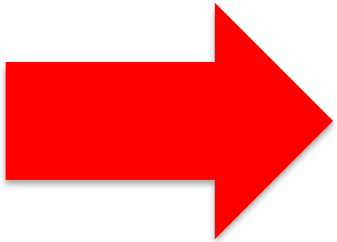
Creating an Infection Control "Fire-break"



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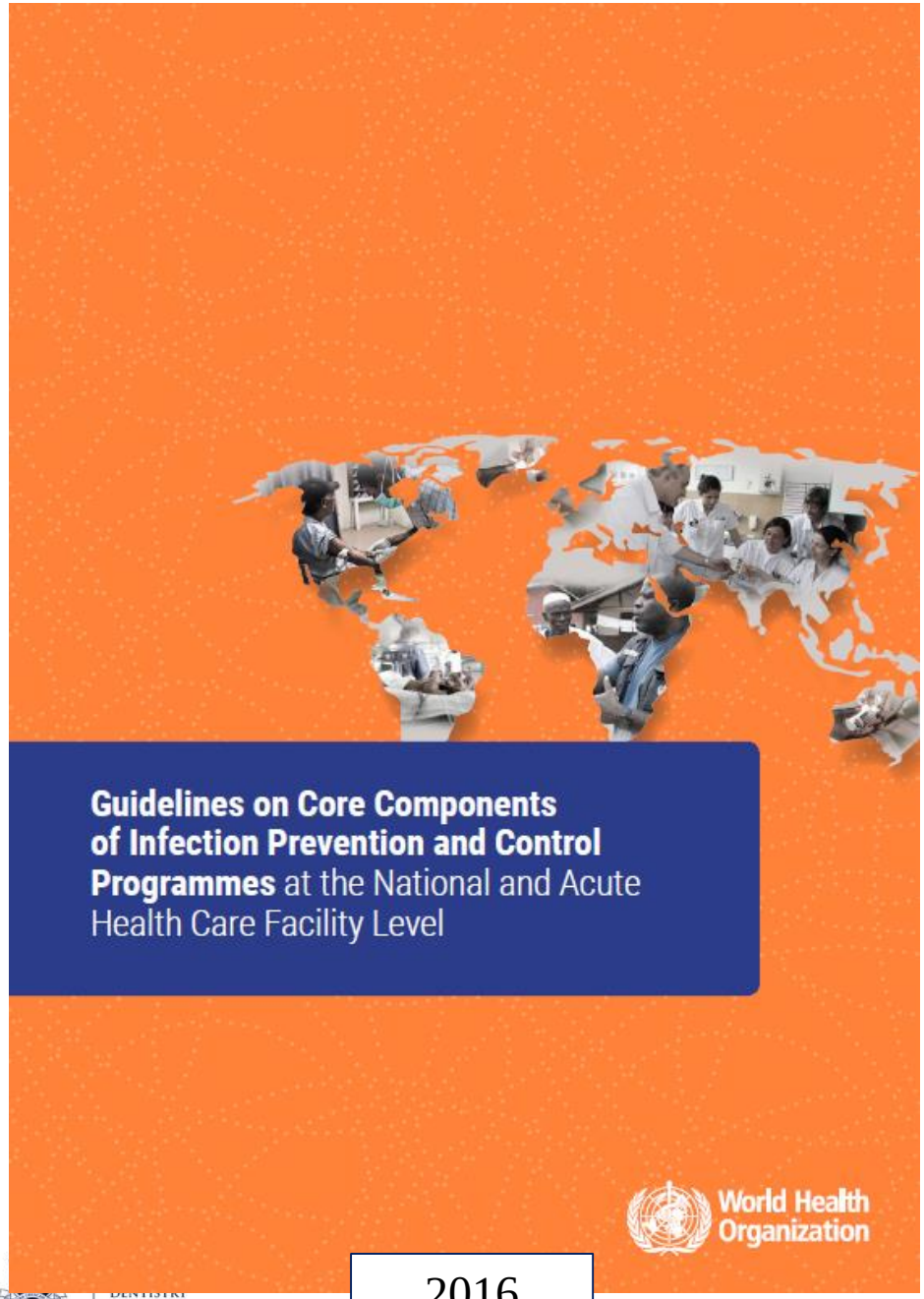
Guidelines on Core Components of Infection Prevention and Control Programmes at the National and Acute Health Care Facility Level
World Health Organization


Dr Benedetta Allegranzi

2016

Guidelines on Core Components of Infection Prevention and Control Programmes at the National and Acute Health Care Facility Level

2016

Guideline Recommendations (R) & Good Practice Statements (GPS)

1	IPC programmes	R1a *Strong* 1b *GPS*	An IPC programme with a dedicated, trained team should be in place in each **acute health care facility** for the purpose of preventing HAI and combating AMR through IPC good practices. Stand-alone, active **national** IPC programmes with clearly defined objectives, functions and activities for the purpose of preventing HAI and combating AMR through IPC good practices should be established. National IPC programmes should be linked to other relevant national programmes and professional organizations.
2	Evidence-based guidelines	R2 *Strong*	Evidence-based guidelines should be developed and implemented for the purpose of reducing HAI and AMR. Education and training of the relevant health care workers on guideline recommendations and monitoring of adherence with guideline recommendations should be undertaken to achieve successful implementation.
3	Education & training	R3a *Strong* 3b *GPS*	At the **facility** level, IPC education should be in place for all health care workers by utilizing team- and task-based strategies that are participatory and include bedside and simulation training to reduce the risk of HAI and AMR. The **national** IPC programme should support education and training of the health workforce as one of its core functions.
4	Surveillance	R4a *Strong* R4b *Strong*	**Facility**-based HAI surveillance should be performed to guide IPC interventions and detect outbreaks, including AMR surveillance with timely feedback of results to health care workers and stakeholders and through national networks. **National** HAI surveillance programmes and networks that include mechanisms for timely data feedback and with the potential to be used for benchmarking purposes should be established to reduce HAI and AMR.
5 NEW	Multimodal Strategies	R5a *Strong* R5b *Strong*	At the **facility** level, IPC activities should be implemented using multimodal strategies to improve practices and reduce HAI and AMR. **National** IPC programmes should coordinate and facilitate the implementation of IPC activities through multimodal strategies at the national or sub-national level.
6 NEW	Monitoring, audit & feedback	R6a *Strong* R6b *Strong*	Regular monitoring/audit and timely feedback of health care practices should be undertaken according to IPC standards to prevent and control HAIs and AMR at the health care **facility** level. Feedback should be provided to all audited persons and relevant staff. A **national** IPC monitoring and evaluation programme should be established to assess the extent to which standards are being met and activities are being performed according to the programme's goals and objectives. Hand hygiene monitoring with feedback should be considered as a key performance indicator at the national level.
7 NEW	Workload, staffing & bed occupancy	R7 *Strong*	In order to reduce the risk of HAI and the spread of AMR, the following should be addressed: (1) bed occupancy should not exceed the standard capacity of the facility; (2) health care worker staffing levels should be adequately assigned according to patient workload.
8 NEW	Built environment, materials & equipment	8a *GPS* R8b *Strong*	At the **facility** level, patient care activities should be undertaken in a clean and/or hygienic environment that facilitates practices related to the prevention and control of HAI, as well as AMR, including all elements around the WASH infrastructure and services and the availability of appropriate IPC materials and equipment. At the **facility** level, materials and equipment to perform appropriate hand hygiene should be readily available at the point of care.

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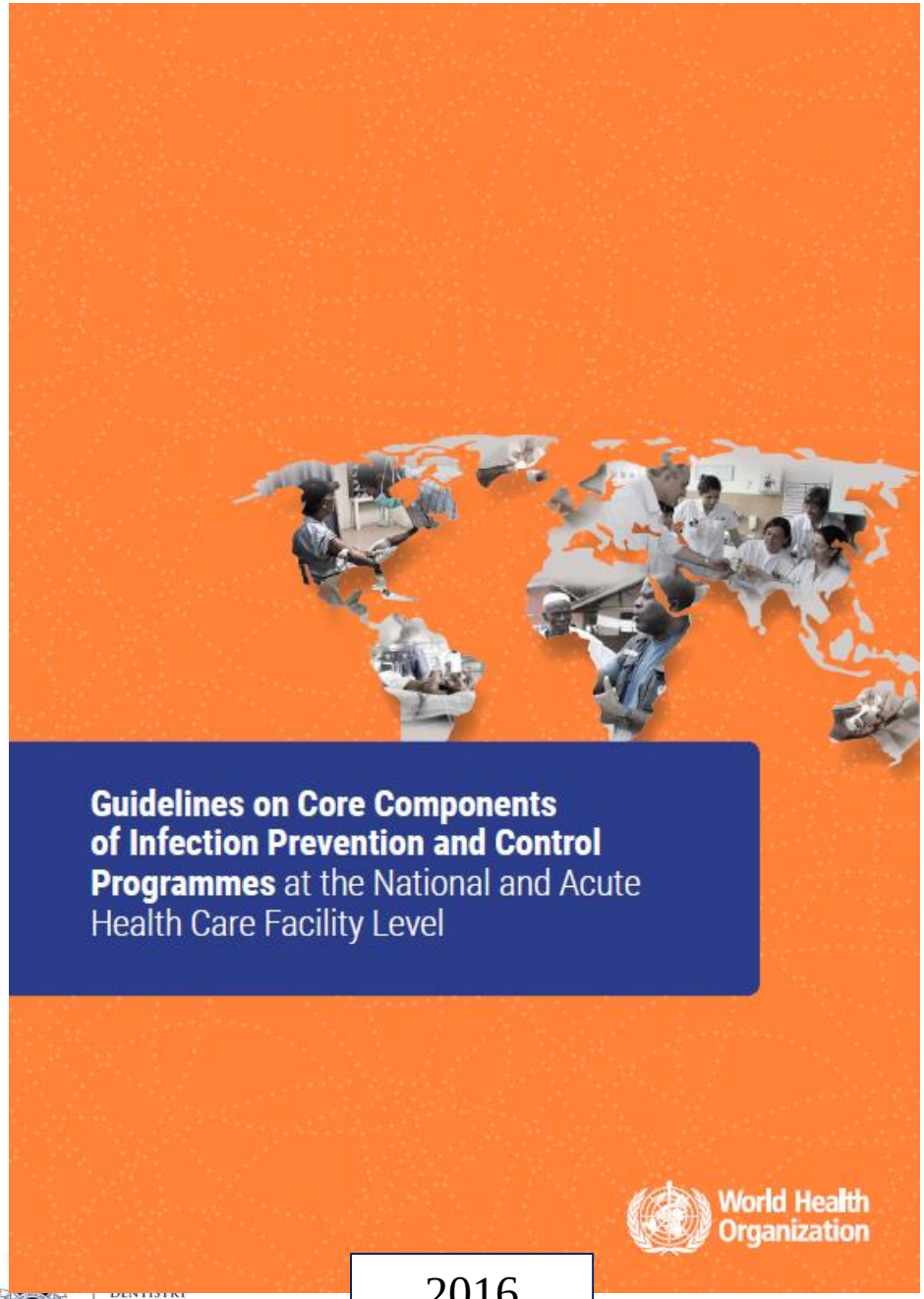
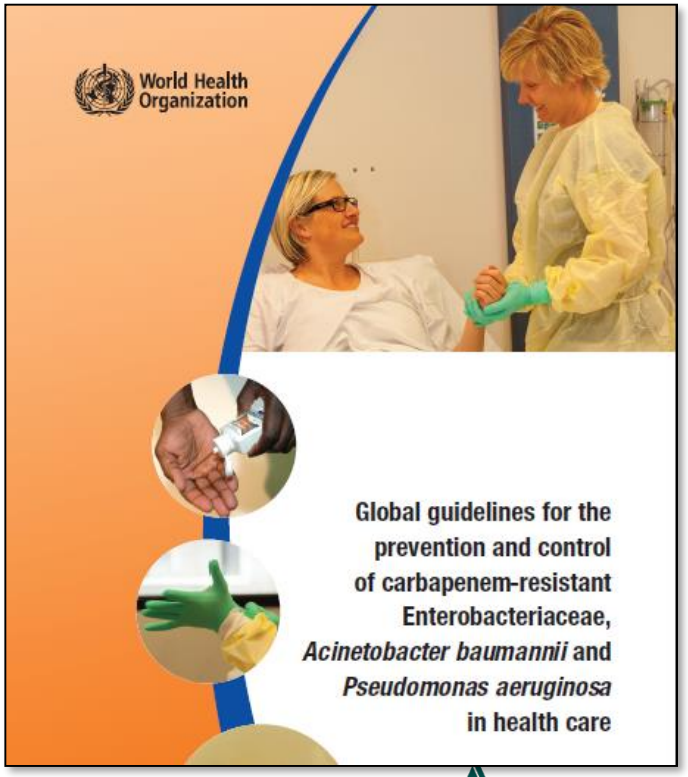


2016



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Austin Health

The solution:

Controlling AMR in Hospitals

4 Key Infection Control Interventions

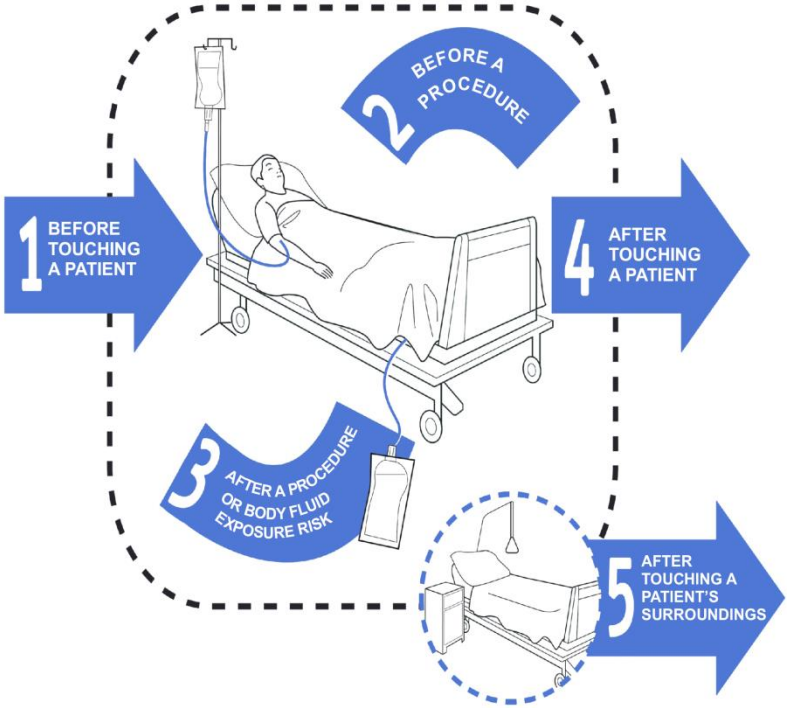
National standards for:

1. Hand Hygiene
2. Hospital cleaning
3. Invasive device insertion and maintenance
4. Improved hospital design


WORLD ALLIANCE
for PATIENT SAFETY
Clean Care is Safer Care
World Health Organization

Hand Hygiene Australia

5 Moments for HAND HYGIENE



AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTHCARE

World Health Organization

Effects of the Australian National Hand Hygiene Initiative after 8 years on infection control practices, health-care worker education, and clinical outcomes: a longitudinal study

M Lindsay Grayson, Andrew J Stewardson, Philip L Russo, Kate E Ryan, Karen L Olsen, Sally M Havers, Susan Greig, Marilyn Cruickshank, on behalf of Hand Hygiene Australia and the National Hand Hygiene Initiative

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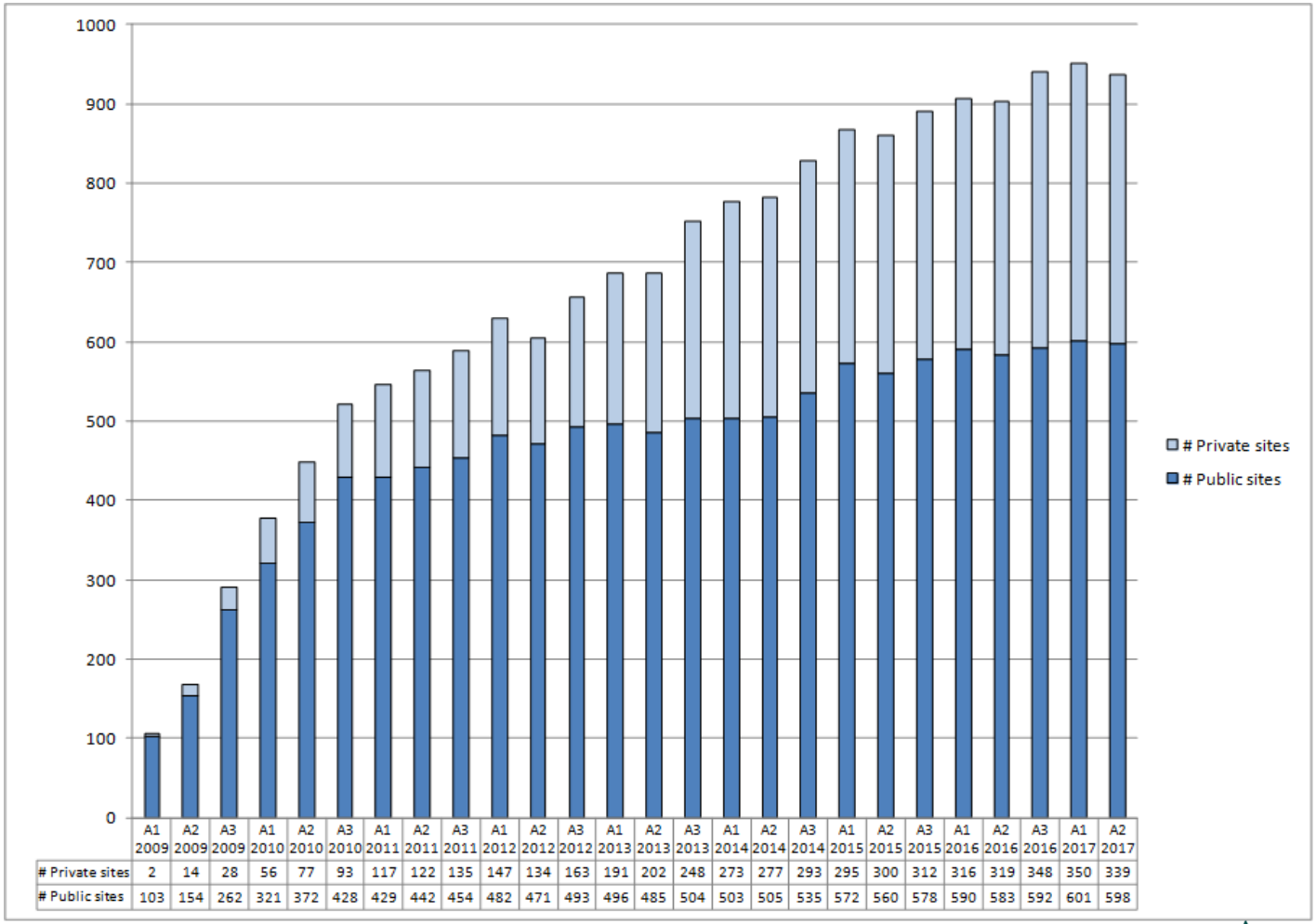
Australian NHHI participation – Private and Public

Period 1, 2009 – Period 2, 2017

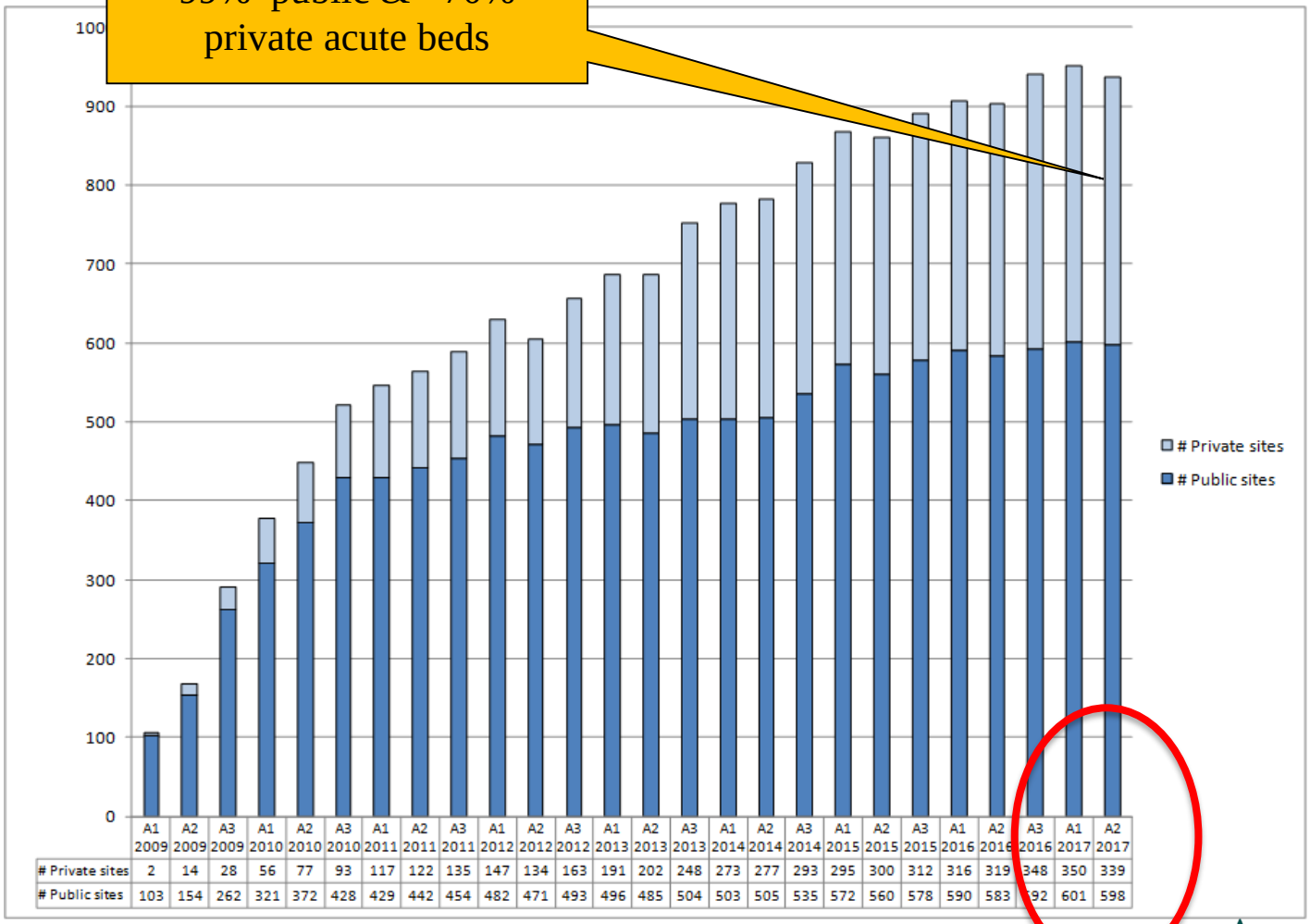


	A1 2009	A2 2009	A3 2009	A1 2010	A2 2010	A3 2010	A1 2011	A2 2011	A3 2011	A1 2012	A2 2012	A3 2012	A1 2013	A2 2013	A3 2013	A1 2014	A2 2014	A3 2014	A1 2015	A2 2015	A3 2015	A1 2016	A2 2016	A3 2016	A1 2017	A2 2017
# Private sites	2	14	28	56	77	93	117	122	135	147	134	163	191	202	248	273	277	293	295	300	312	316	319	348	350	339
# 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	601	598

Australian NHHI participation – Private and Public

Period 1, 2009 – Period 2, 2017

99% public & >70% private acute beds



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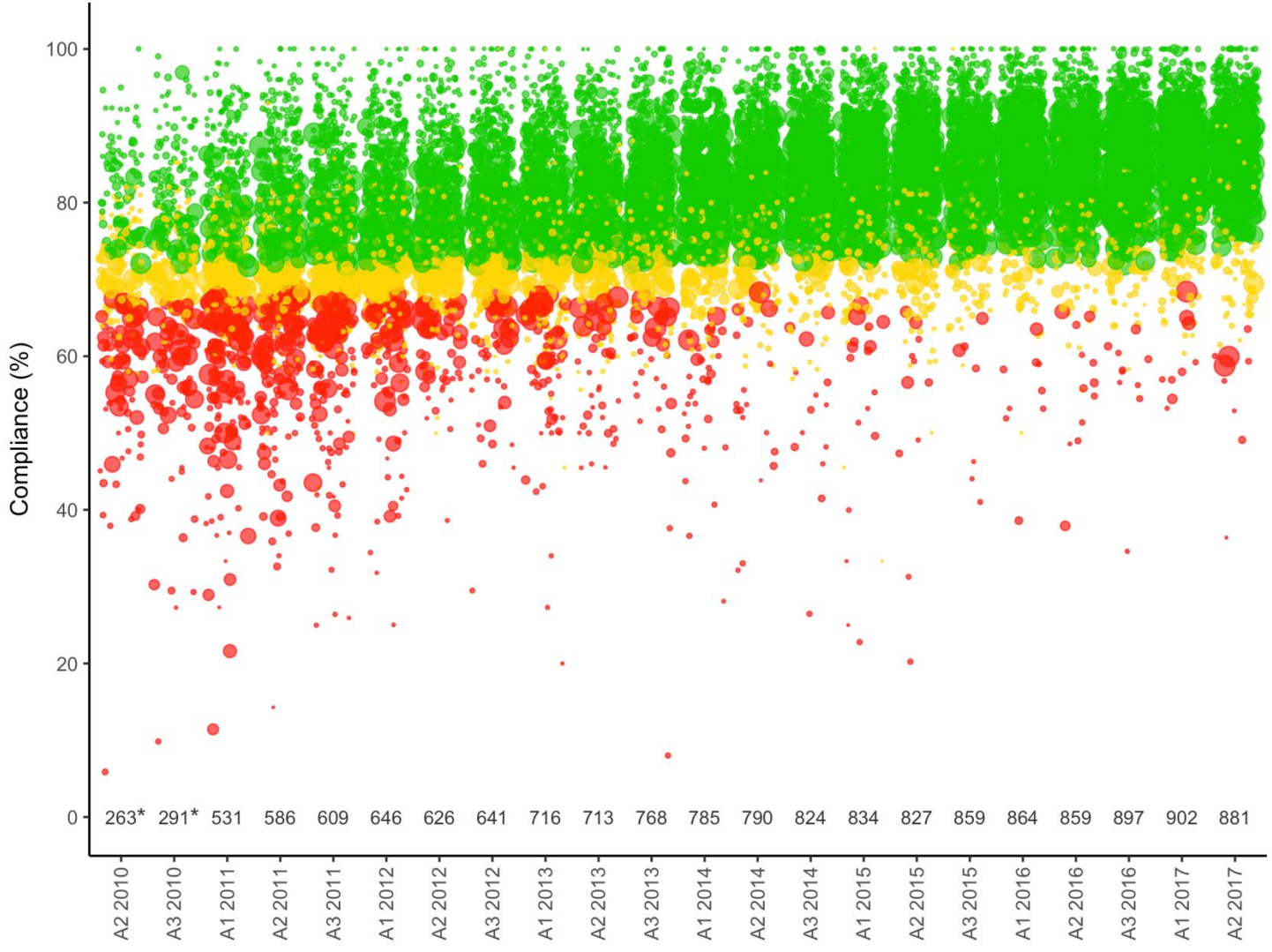
Hand Hygiene Performance: Hospitals

70% benchmark

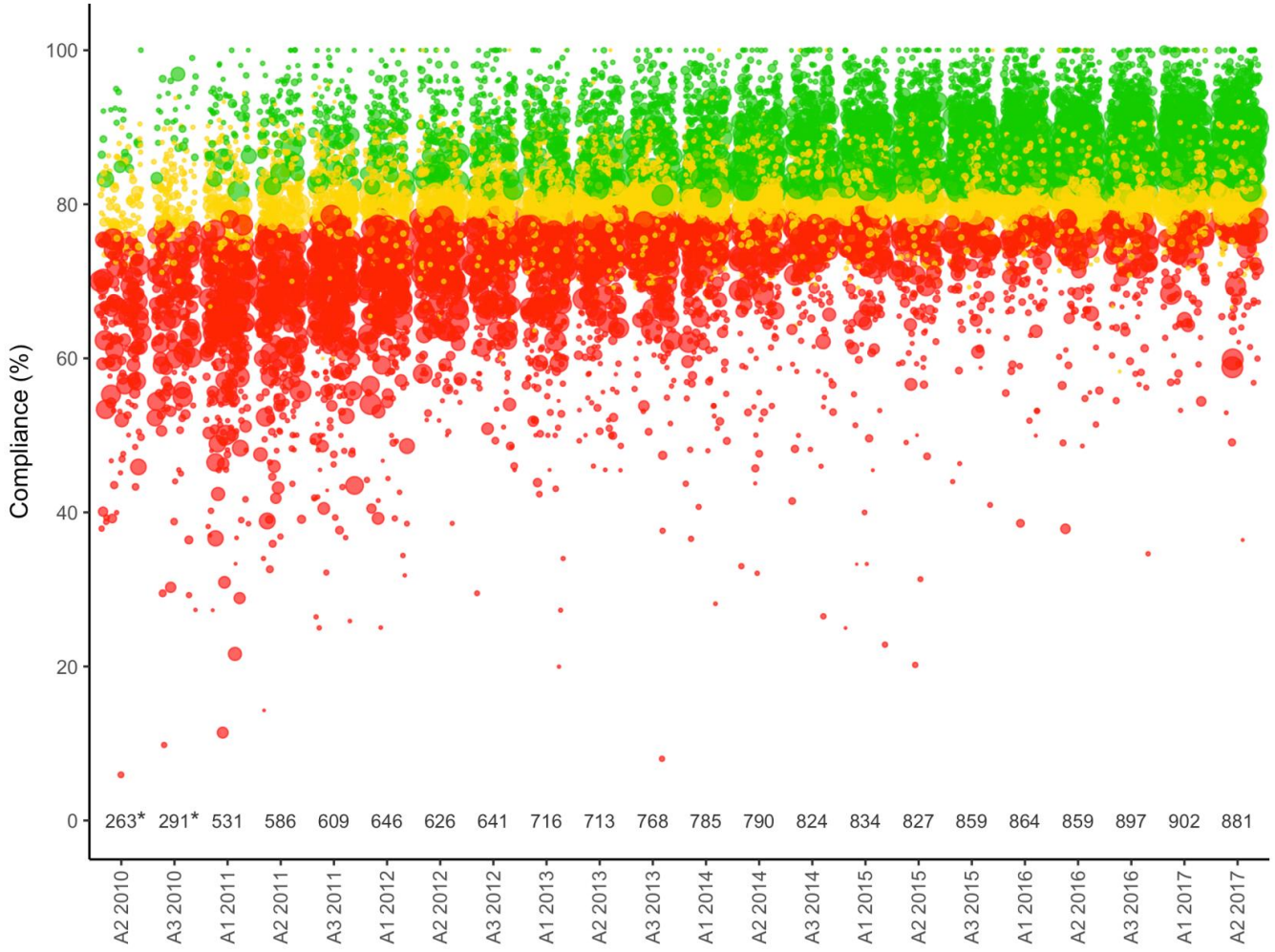
Period 2, 2010 – Period 2, 2017



Hand Hygiene Performance: Hospitals

80% benchmark

Period 2, 2010 – Period 2, 2017

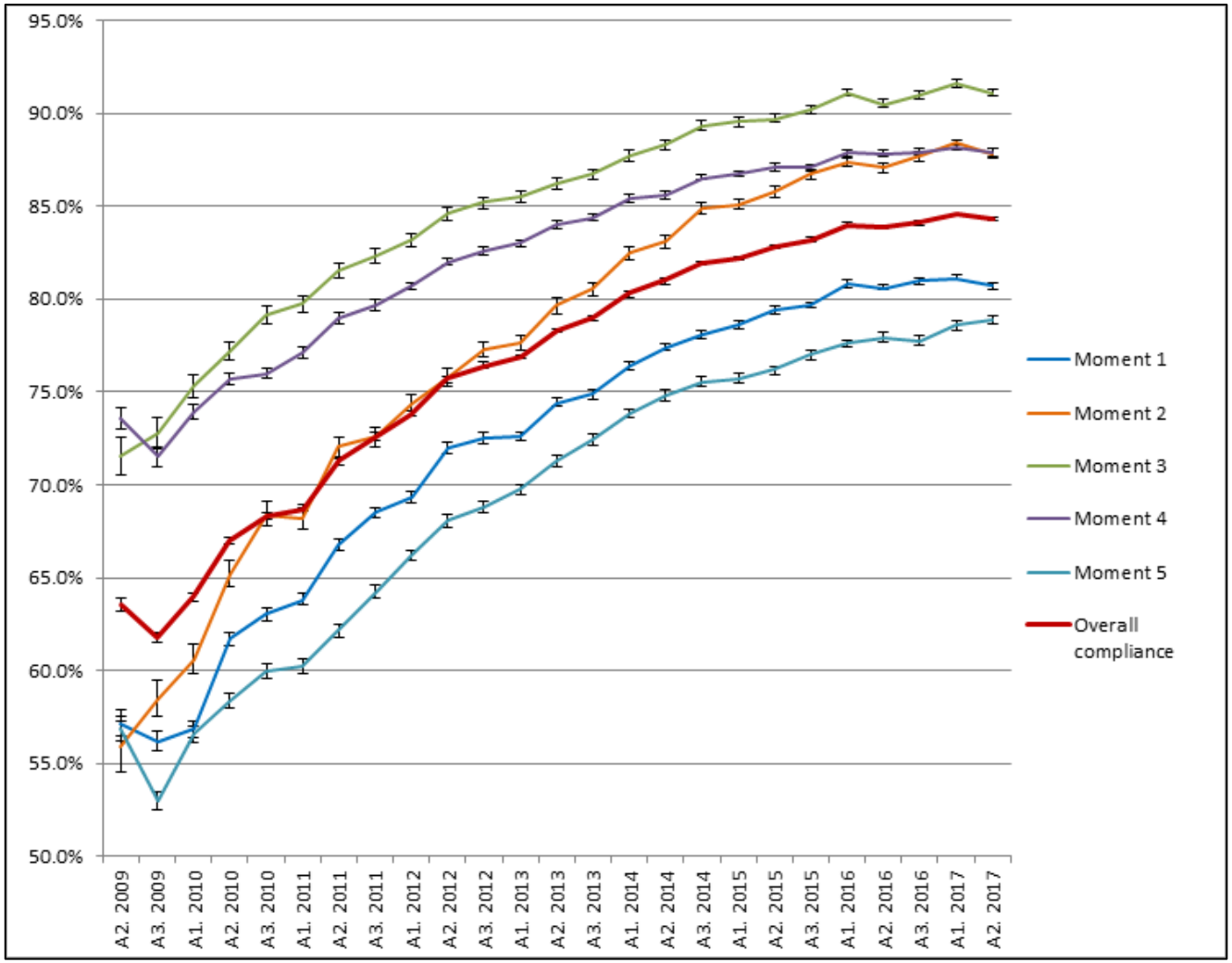


Dashed line indicates proportion of organisations "similar" or "above" benchmark

Changes in HHC per 5-Moments

All healthcare facilities

(Audit 2, 2009 - Audit 2, 2017)



Changes in HHC per HCW group

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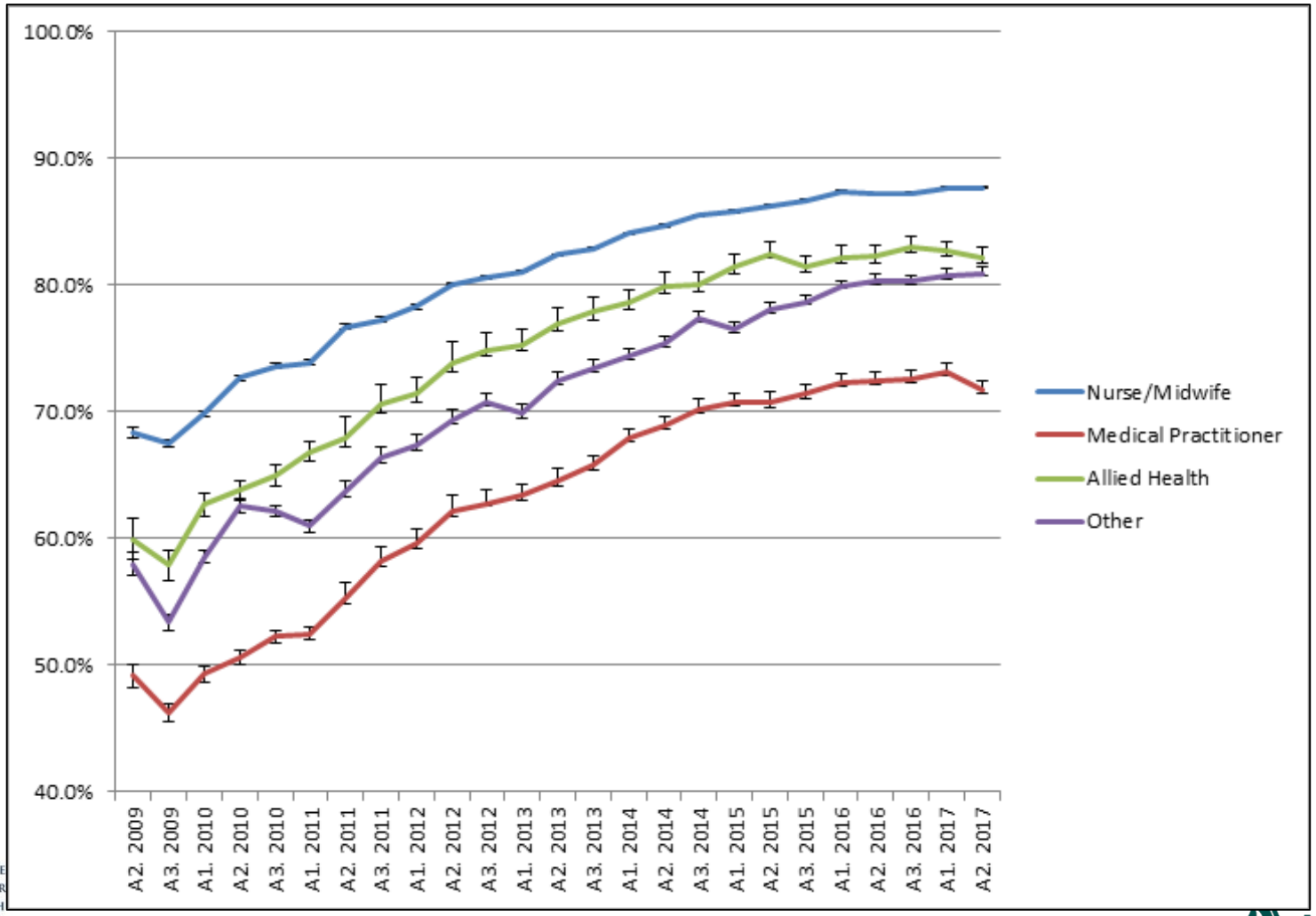

HHA initiatives

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

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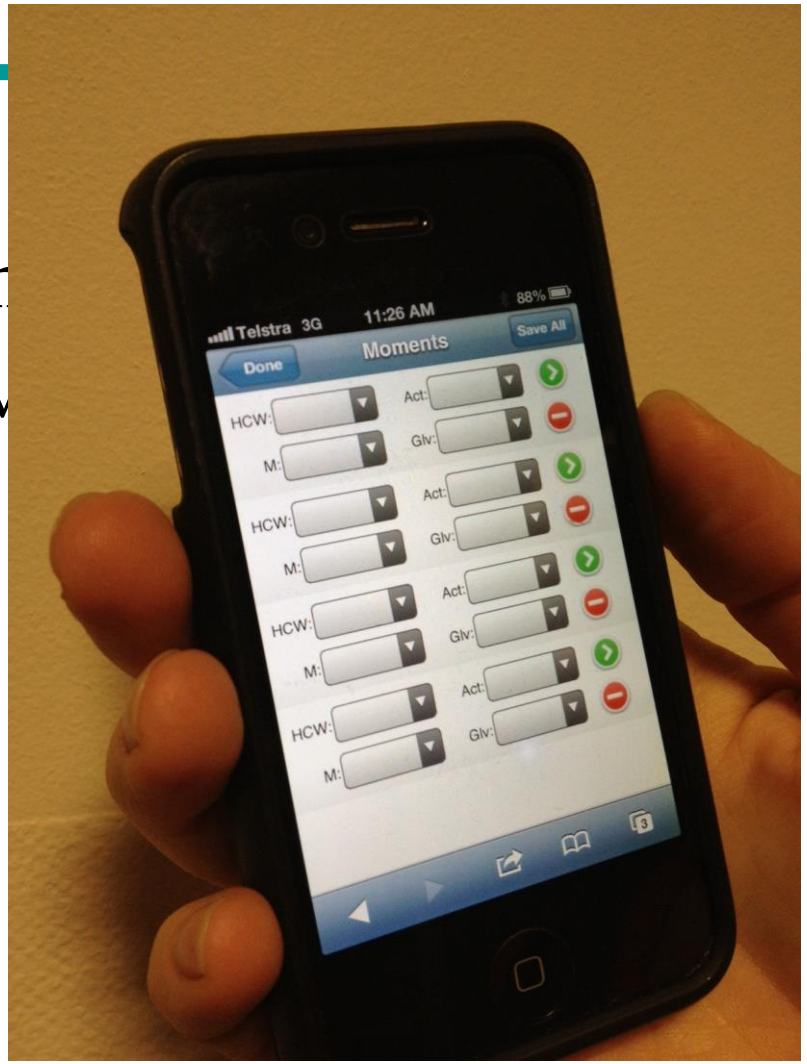

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- New direct-entry HH compliance App
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  - Benefits:
    - Reduces data management time by 50%
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    - Mobile devices common and cheap
    - Flexible reporting options
    - Potential – NZ, Israel, Hong Kong, WHO

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hand hygiene NZ
ringa horoia,aotearoa

Health Quality & Safety Commission New Zealand
Kupu Taurangi Hauora o Aotearoa

The University of Melbourne | Faculty of Medicine, Dentistry & Health Sciences

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Cost of HHA – 2015/2016

2015 - 2016 financial year

- NHHI - in maintenance/embedment phase
- Australian public and private hospitals:
  - 10.6 million patient hospitalisations (“separations”)
  - 29,846,000 hospital patient-days
- HHA annual budget = AUD $643,246
- Equivalent to an annual cost nationally of:
  - 2.2 cents per inpatient-day OR
  - 6.1 cents per patient hospital admission

AIHW. Health services series no. 77. July 2017.
http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129560038

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Results

Impact on healthcare-associated *S. aureus* bacteraemia rates

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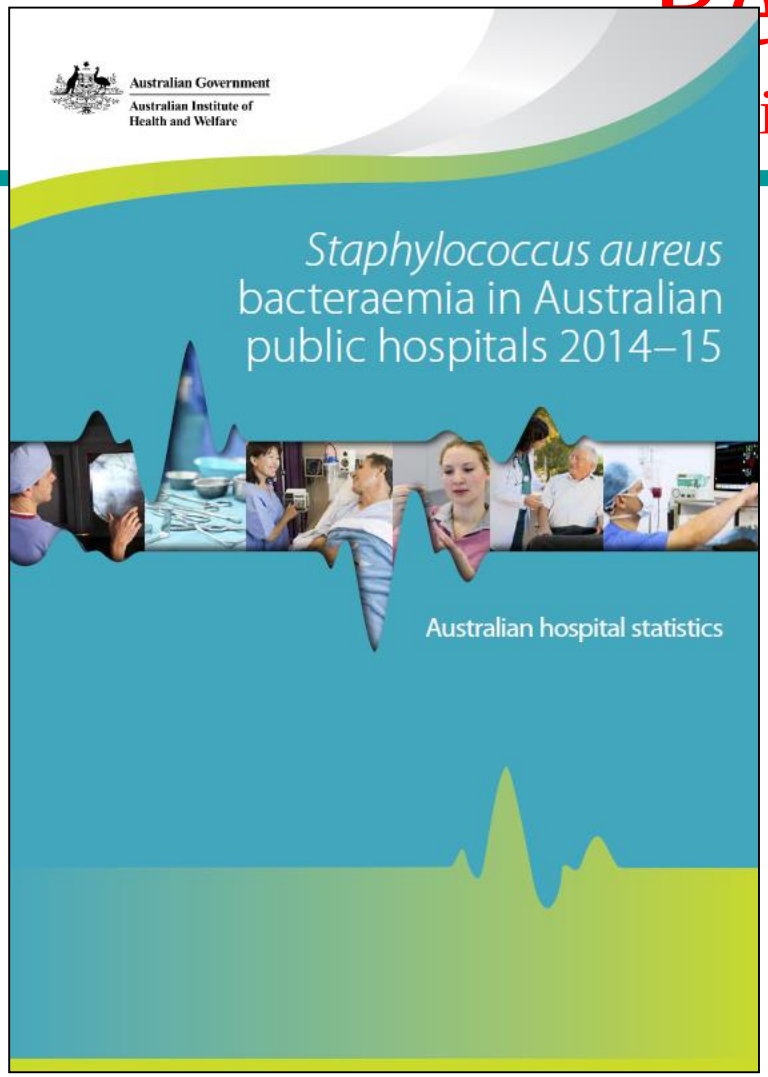

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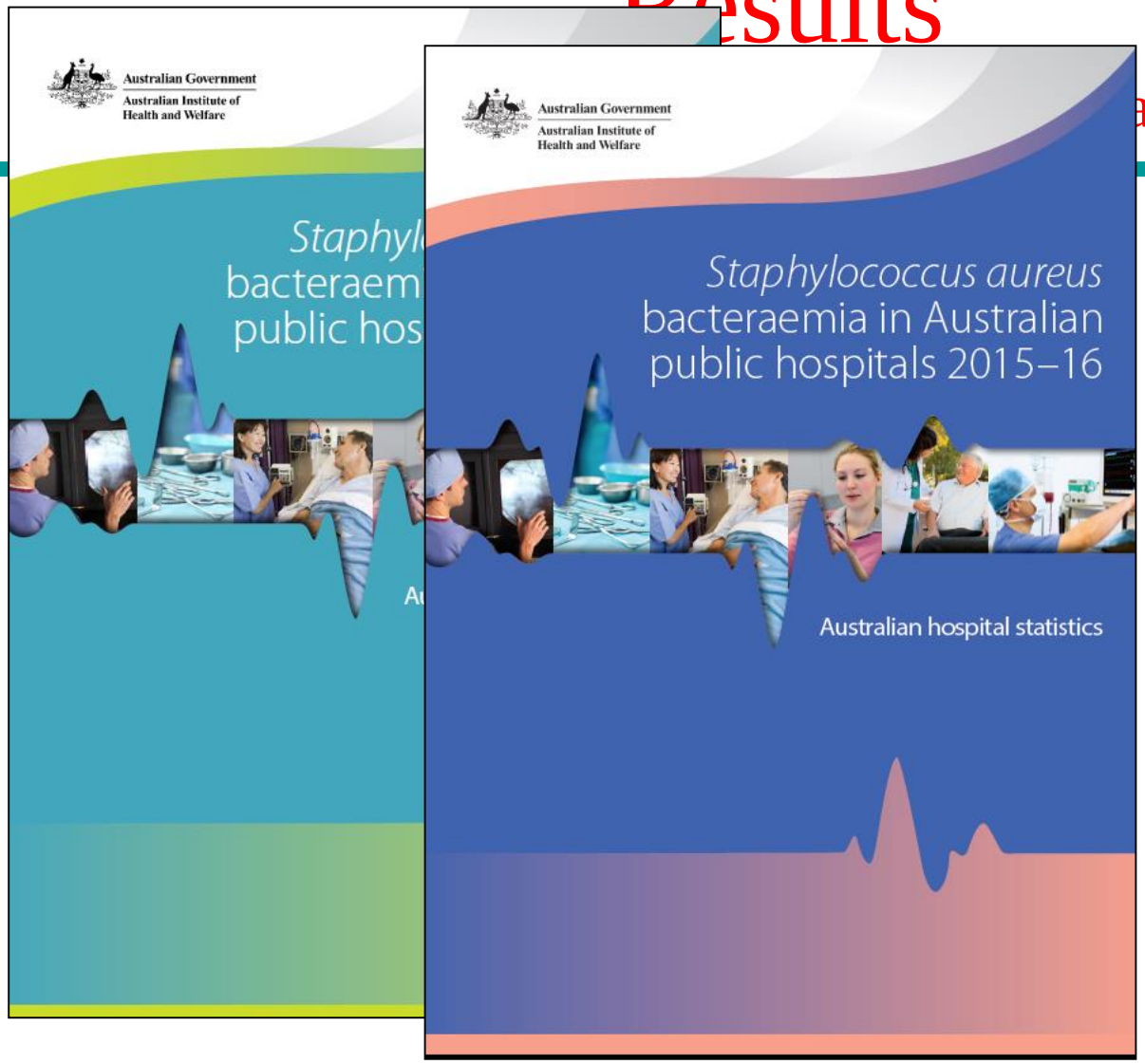
acteraemia rates



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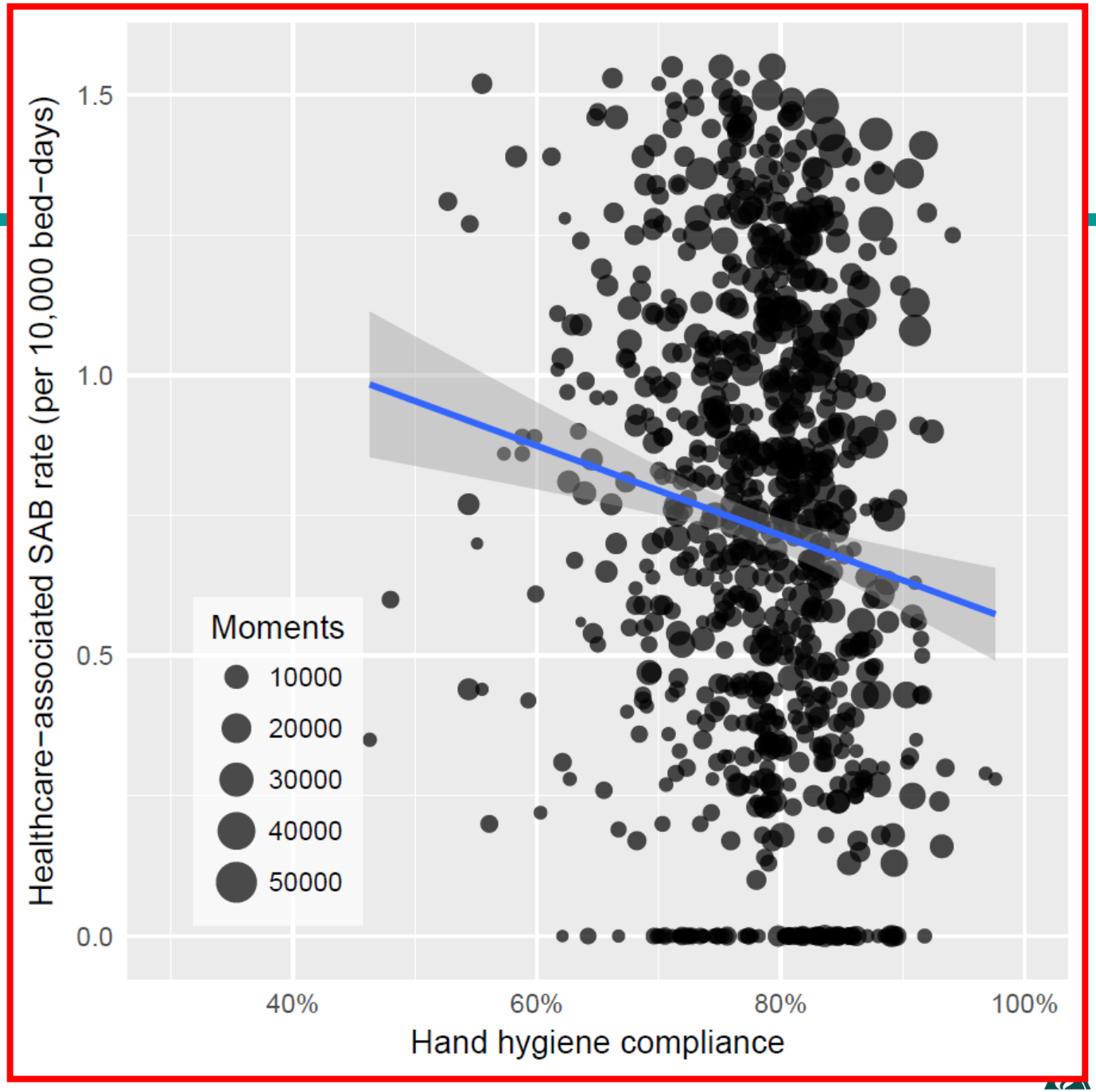
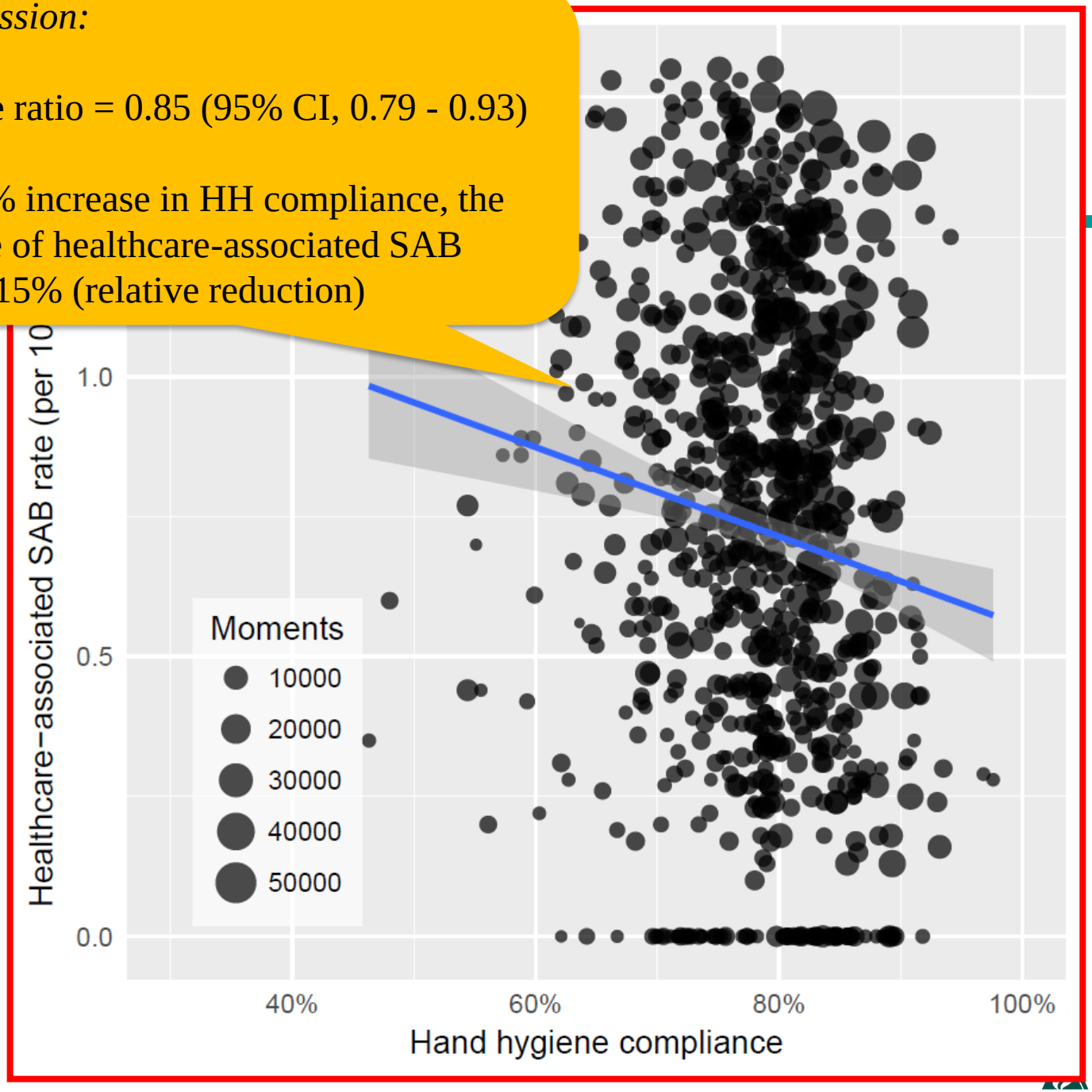

Healthcare−associated SAB rate (per 10,000 bed−days)
1.5
1.0
0.5
0.0
Moments
10000
20000
30000
40000
50000
40%
60%
80%
100%
Hand hygiene compliance

Poisson regression:

Incidence rate ratio = 0.85 (95% CI, 0.79 - 0.93)

For every 10% increase in HH compliance, the incidence rate of healthcare-associated SAB decreases by 15% (relative reduction)



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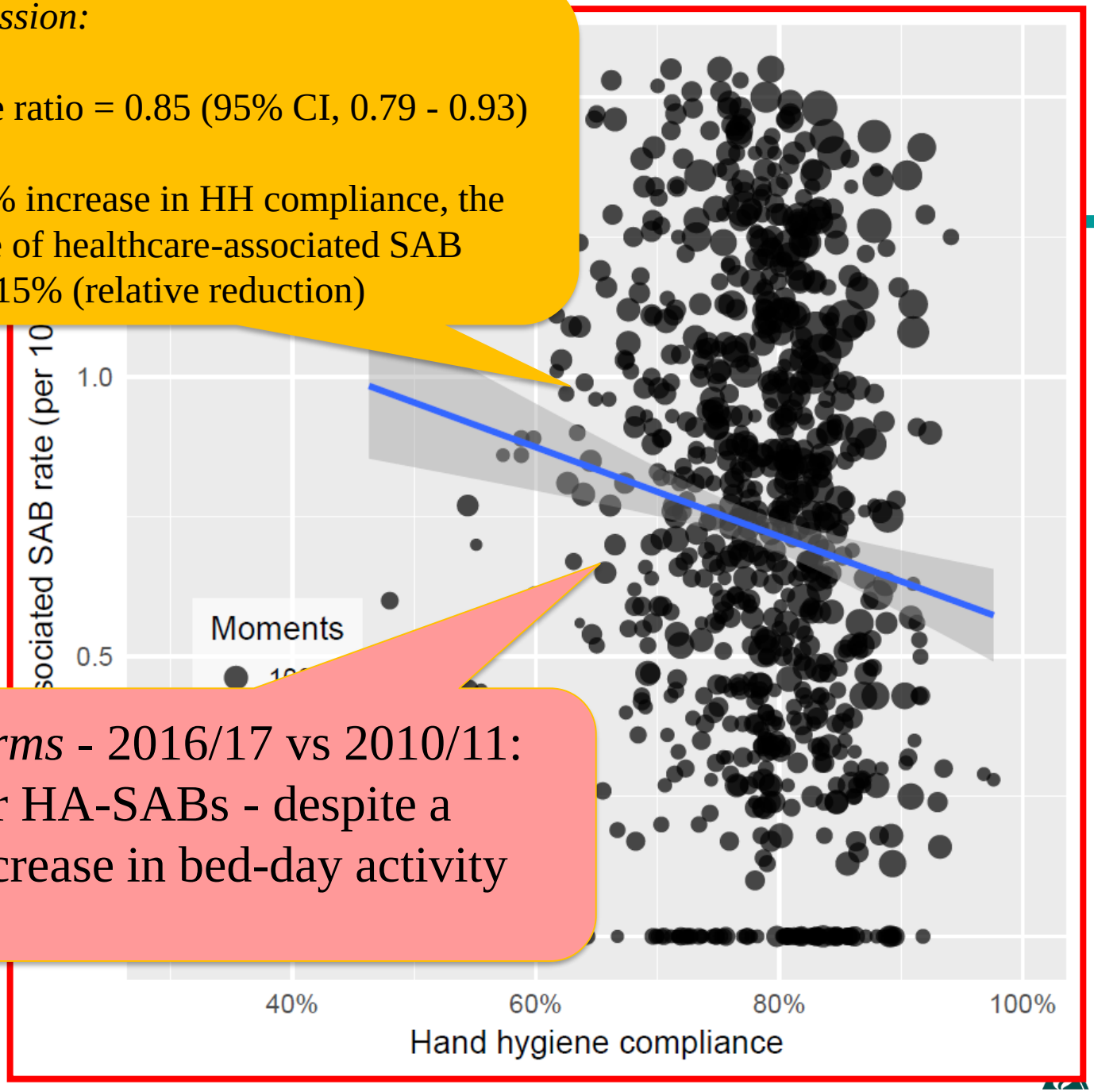
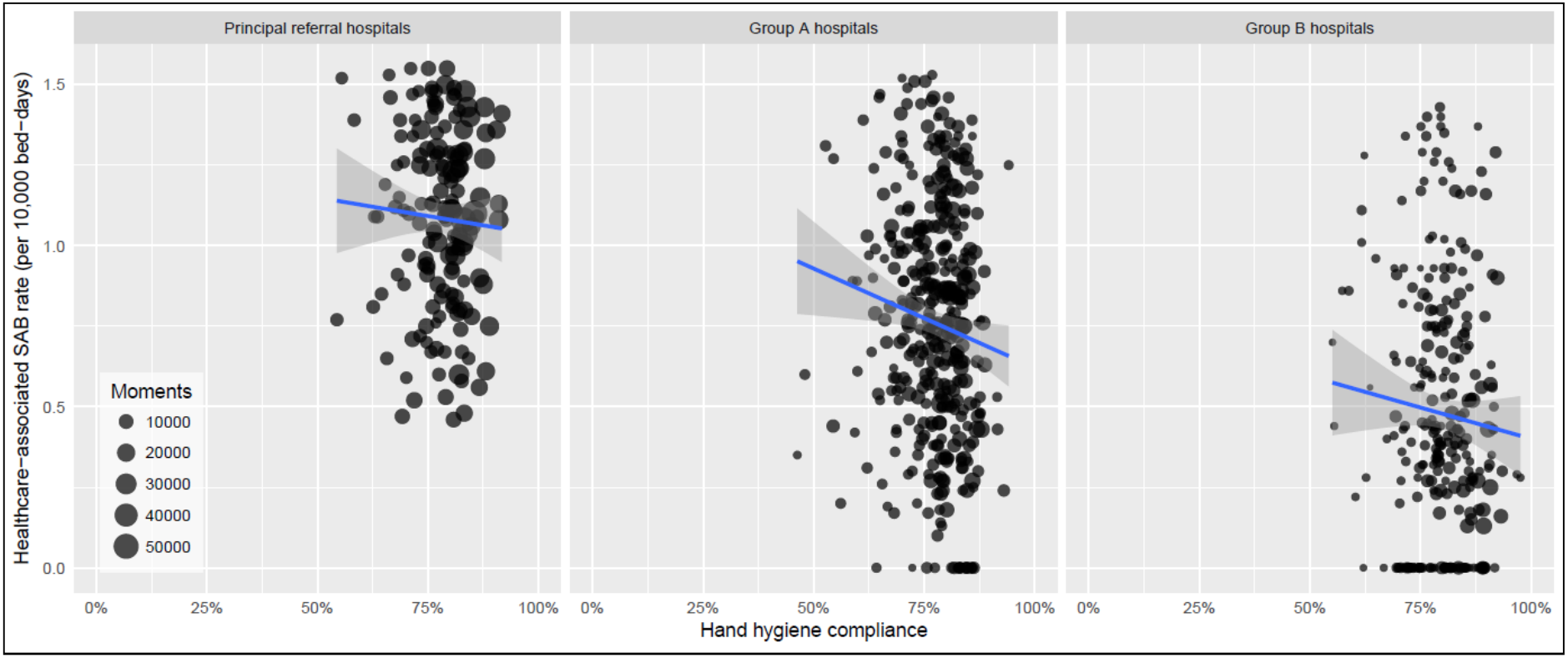


In real terms - 2016/17 vs 2010/11: 372 fewer HA-SABs - despite a 14.6% increase in bed-day activity

Results

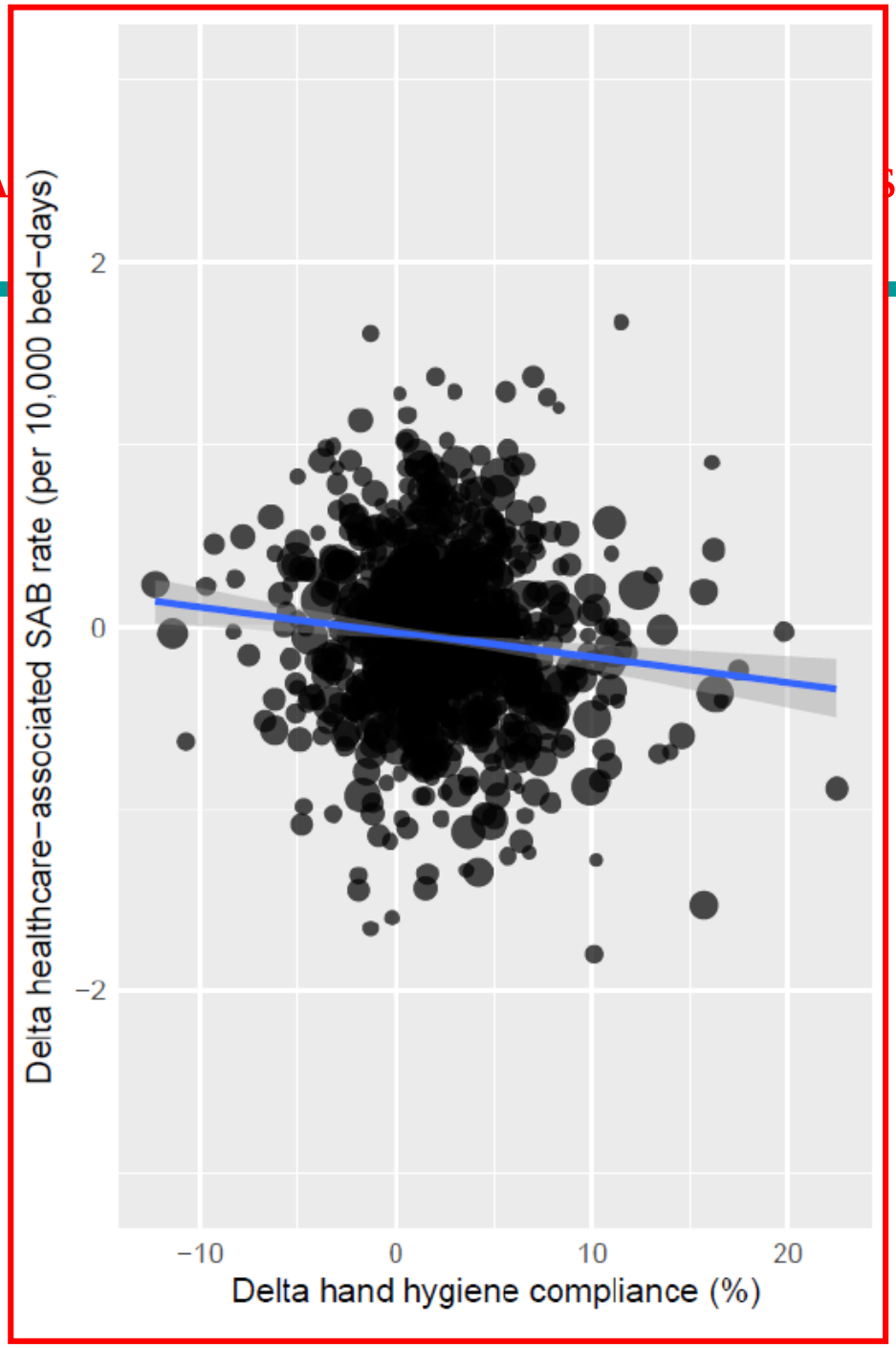
HA-SAB rates *vs* HH compliance per site



Results

HA-SAB rates *vs* HH compliance per site
Delta analysis

HA site


Delta healthcare−associated SAB rate (per 10,000 bed−days)
2
0
−2
−10
0
10
20
Delta hand hygiene compliance (%)

Community Engagement & Politics

THE UNIVERSITY OF MELBOURNE
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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.

Hand Hygiene Australia

Summary

- HHA program – largest & most successful worldwide
  - Currently 1017 sites - 99% all acute public beds
  - >12.0M HH Moments recorded so far
- Marked improvement in national HH compliance rates
  - June 2018 – 85.1%
  - Medical staff – 74.5%
  - ~95% hospitals are “similar to” or >80%
- NHHI = marked reduction in HA-SAB rates

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Comment

The Australian National Hand Hygiene Initiative: framework for future research

Lancet Infect Dis 2018
Published Online
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http://dx.doi.org/10.1016/S1473-3099(18)30598-X
See Online/Articles
http://dx.doi.org/10.1016/S1473-3099(18)30491-2

In *The Lancet Infectious Diseases*, M Lindsay Grayson and colleagues[1] report a national campaign to promote hand hygiene compliance that has been in operation throughout Australia since 2009.

Hand hygiene plays a major part in any infection prevention programme, but securing compliance with hand hygiene protocols is notoriously difficult.[2] Maintaining long-term improvement is an even greater challenge.[3] WHO published comprehensive

Over the past 20 years, a great deal of energy has been invested in establishing why hand hygiene compliance is poor. Early publications were based on supposition.[5] Theories from health psychology and health education were later suggested as barriers to compliance[6] or taken as the conceptual frameworks to underpin empirical studies.[7,8] More recently, there has been a drive to develop theories that explain poor compliance at the level of the individual health worker.[9] But, as early writers pointed out[10]

The solution:

Controlling AMR in Hospitals

4 Key Infection Control Interventions

National standards for:

1. Hand Hygiene
2. Hospital cleaning
3. Invasive device insertion and maintenance
4. Improved hospital design

Journal of Hospital Infection 82 (2012) 234–242

Available online at www.sciencedirect.com

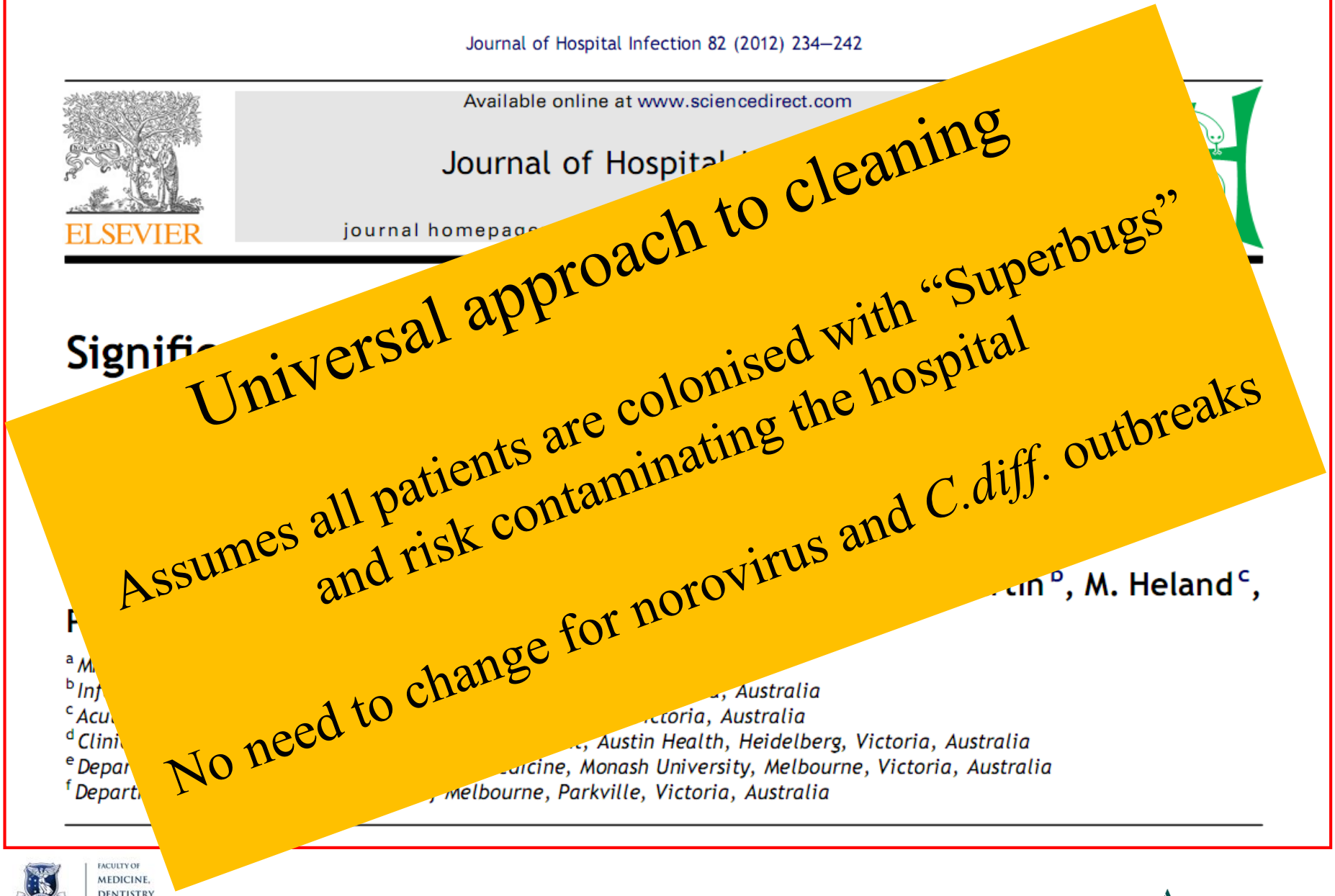
Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Significant reduction in vancomycin-resistant enterococcus colonization and bacteraemia after introduction of a bleach-based cleaning–disinfection programme

E.A. Grabsch [a,1], A.A. Mahony [b,*,1], D.R.M. Cameron [b], R.D. Martin [b], M. Heland [c], P. Davey [d], M. Petty [c], S. Xie [a], M.L. Grayson [a,b,e,f]

[a] *Microbiology Department, Austin Health, Heidelberg, Victoria, Australia*
[b] *Infectious Diseases Department, Austin Health, Heidelberg, Victoria, Australia*
[c] *Acute Operations Department, Austin Health, Heidelberg, Victoria, Australia*
[d] *Clinical Information–Analysis–Reporting Department, Austin Health, Heidelberg, Victoria, Australia*
[e] *Department of Epidemiology & Preventive Medicine, Monash University, Melbourne, Victoria, Australia*
[f] *Department of Medicine, University of Melbourne, Parkville, Victoria, Australia*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ELSEVIER
Universal approach to cleaning
Assumes all patients are colonised with "Superbugs" and risk contaminating the hospital
No need to change for norovirus and C.diff. outbreaks

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Practical Antimicrobial Stewardship

- Fundamental change in approach is needed

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Would you treat a cancer without knowing whether:

A. Is it actually a cancer?
B. What type of cancer it is?

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New "rules":

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   - How do we build this into our health system?
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   - Rapid diagnostics = important research item

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Problem areas – “sanctuary sites”:

- Brain
- Bone
- Prostate
- Eye
- Abscesses

Practical Antimicrobial Stewardship

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How often do we even think to check?
What options do we currently have to measure levels?

Practical Antimicrobial Stewardship

Is the dose correct?

"Dumb" clinical behaviour

AAC
Journals.ASM.org

Electronic Estimations of Renal Function Are Inaccurate in Solid-Organ Transplant Recipients and Can Result in Significant Underdosing of Prophylactic Valganciclovir

J. Trevillyan,[a] P. Angus,[b,e] E. Shelton,[b] J. Whitlam,[c] F. Ierino,[c,e] J. Pavlovic,[b] D. Gregory,[c] K. Urbancic,[a] J. Torresi,[a,e] A. Testro,[b,e] M. L. Grayson[a,d,e]

Infectious Diseases,[a] Gastroenterology,[b] and Nephrology[c] Departments, Austin Health, Heidelberg, Victoria, Australia; Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia[d]; Department of Medicine, University of Melbourne, Victoria, Australia[e]

In a prospective study of solid-organ transplant recipients (n = 22; 15 hepatic and 7 renal) receiving valganciclovir for cytomegalovirus (CMV) prophylaxis, electronic estimation of glomerular filtration rate (eGFR) underestimated the true GFR (24-h urine creatinine clearance) by >20% in 14/22 (63.6%). Its use was associated with inappropriate underdosing of valganciclovir, while the Cockroft-Gault equation was accurate in 21/22 patients (95.4%). Subtherapeutic ganciclovir levels (≤0.6 mg/liter) were common, occurring in 10/22 patients (45.4%); 7 had severely deficient levels (<0.3 mg/liter).

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Practical Antimicrobial Stewardship

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3. Reassess the impact of mass treatment programs

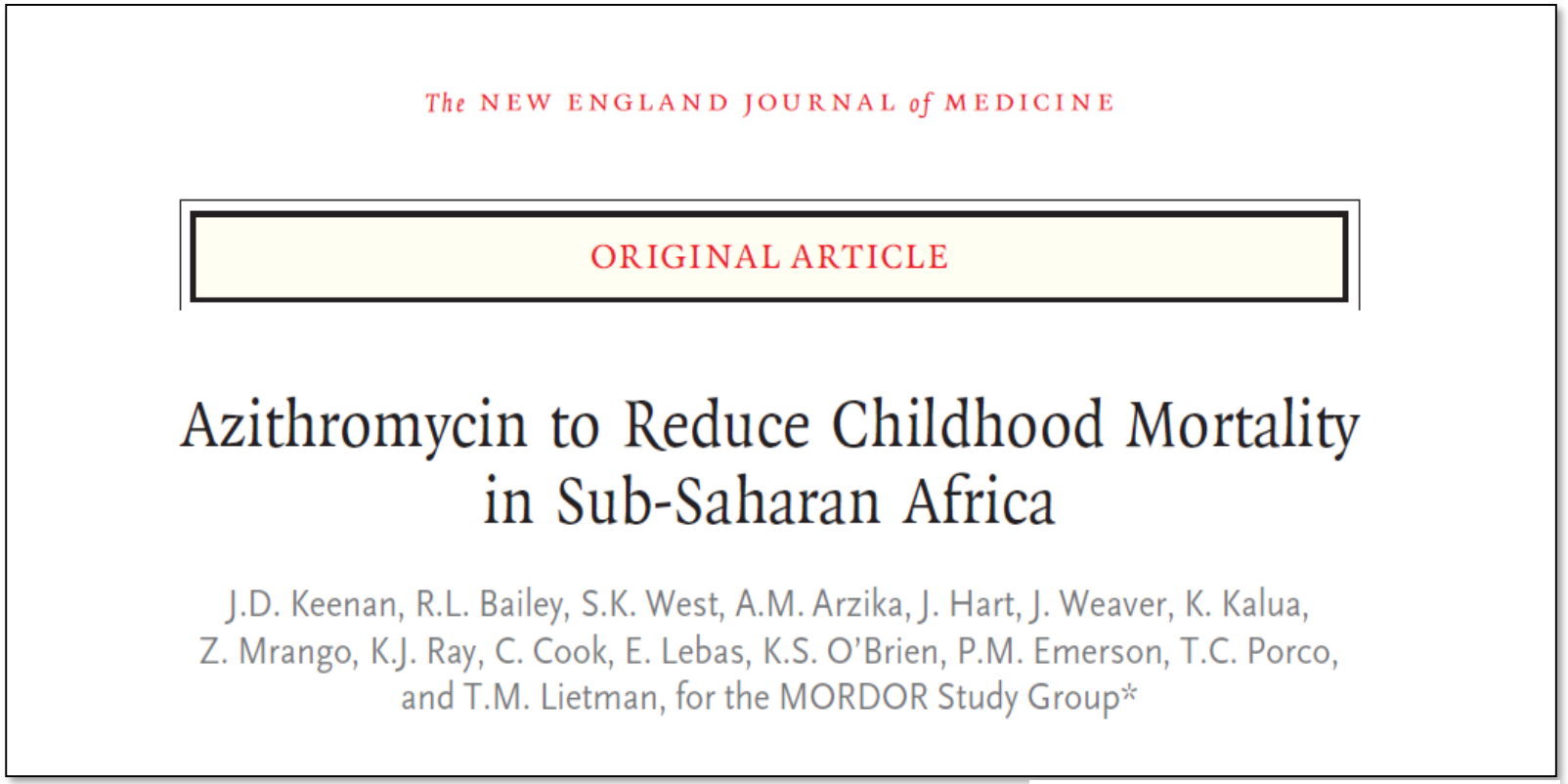
Practical Antimicrobial Stewardship

? Impact of mass treatment programs on AMR

- Azithromycin
  - Children

Practical Antimicrobial Stewardship

? Impact of mass treatment programs on AMR

- 

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Azithromycin to Reduce Childhood Mortality in Sub-Saharan Africa

J.D. Keenan, R.L. Bailey, S.K. West, A.M. Arzika, J. Hart, J. Weaver, K. Kalua, Z. Mrango, K.J. Ray, C. Cook, E. Lebas, K.S. O'Brien, P.M. Emerson, T.C. Porco, and T.M. Lietman, for the MORDOR Study Group*

N Engl J Med 2018;378:1583-92.

? Impact of mass treatment programs on AMR

- Azithromycin
  - Children
  - Chronic pulmonary disease
- Rifaximin – end-stage liver disease; other
- Oral vancomycin – primary sclerosing cholangitis
- Fluoroquinolones – SBP

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WHO and CDC

Four "pillars" of AMR control

1. Improve Infection Prevention and Control
2. Practical Antimicrobial Stewardship
3. Improve AMR surveillance and outbreak response
4. Research and Development
   - Rapid diagnostics
   - New antimicrobial development
   - Innovations in infection control

Improving AMR surveillance

Humans – hospitals:

- Standardise screening:
  - High-risk patients
  - Returned travellers
  - Build this into hospital budgets
- MDR pathogens need to become “Notifiable”

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Animals & Agriculture:

- Many unanswered questions:
  - What is the optimal specimen - ?food

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McLellan et al. Antimicrobial Resistance and Infection Control (2018) 7:30
https://doi.org/10.1186/s13756-018-0322-4

Antimicrobial Resistance and Infection Control

RESEARCH Open Access

Superbugs in the supermarket? Assessing the rate of contamination with third-generation cephalosporin-resistant gram-negative bacteria in fresh Australian pork and chicken

Jade E. McLellan[1†], Joshua I. Pitcher[1†], Susan A. Ballard[2], Elizabeth A. Grabsch[2], Jan M. Bell[3], Mary Barton[4] and M. Lindsay Grayson[1,2,5*]

Abstract

Background: Antibiotic misuse in food-producing animals is potentially associated with human acquisition of multidrug-resistant (MDR; resistance to ≥ 3 drug classes) bacteria via the food chain. We aimed to determine if MDR Gram-negative (GNB) organisms are present in fresh Australian chicken and pork products.

Methods: We sampled raw, chicken drumsticks (CD) and pork ribs (PR) from 30 local supermarkets/butchers across Melbourne on two occasions. Specimens were sub-cultured onto selective media for third-generation cephalosporin-resistant (3GCR) GNBs, with species identification and antibiotic susceptibility determined for all unique colonies. Isolates were assessed by PCR for SHV, TEM, CTX-M, AmpC and carbapenemase genes (encoding IMP, VIM, KPC, OXA-48, NDM).

Results: From 120 specimens (60 CD, 60 PR), 112 (93%) grew a 3GCR-GNB ($n = 164$ isolates; 86 CD, 78 PR); common species were *Acinetobacter baumannii* (37%), *Pseudomonas aeruginosa* (13%) and *Serratia fonticola* (12%), but only one *E. coli* isolate. Fifty-nine (36%) had evidence of 3GCR alone, 93/163 (57%) displayed 3GCR plus resistance to one additional antibiotic class, and 9/163 (6%) were 3GCR plus resistance to two additional classes. Of 158 DNA specimens, all were negative for ESBL/carbapenemase genes, except 23 (15%) which were positive for AmpC, with 22/23 considered to be inherently chromosomal, but the sole *E. coli* isolate contained a plasmid-mediated CMY-2 AmpC.

Conclusions: We found low rates of MDR-GNBs in Australian chicken and pork meat, but potential 3GCR-GNBs are common (93% specimens). Testing programs that only assess for *E. coli* are likely to severely underestimate the diversity of 3GCR organisms in fresh meat.

Keywords: Infection, Antibiotic resistance, Foodborne

Improving AMR surveillance

Humans – hospitals:

- Standardise screening:
  - High-risk patients
  - Returned travellers
  - Build this into hospital budgets
- MDR pathogens need to become “Notifiable”

Animals & Agriculture:

- Many unanswered questions:
  - What is the optimal specimen - ?food
  - ? Safety of imported foods – especially seafood
  - Need for a standardised national surveillance program – local and imported foods

WHO and CDC

Four "pillars" of AMR control

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   - Rapid diagnostics
   - New antimicrobial development
   - Innovations in infection control

Large US and European Pharmaceutical Companies Conducting Antibacterial Research

1980 (N=36)

Abbott
Astra
Ayerst
Bayer
Beecham
Bristol-Myers
Burroughs
Ciba-Geigy
Dow
DuPont
Glaxo
Hoechst
ICI
Lederle
Lilly
Marion
Merck
Merrell
Miles
Parke Davis
Pfizer
Pharmacia
Proctor & Gamble
Rhone-Poulenc
Rorer
Roche
Roussel
Sandoz
Sanofi
Schering
SmithKline
Squibb
Upjohn
Warner-Lambert
Wellcome
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- Squibb
- Upjohn
- Warner-Lambert
- Wellcome
- Wyeth

1998 (N=20)

- Abbott
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- Glaxo Wellcome
- Hoechst Marion Roussel
- Johnson & Johnson
- Lilly
- Merck
- Novartis
- Parke Davis
- Pfizer
- Pharmacia & Upjohn
- Rhone-Poulenc Rorer
- Roche
- Sanofi
- Schering
- SmithKline Beecham
- Wyeth-Ayerst
- Zeneca

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Wyeth-Ayerst
Zeneca

2010 (N=4 to 7)

AstraZeneca
Glaxo SmithKline
(Johnson & Johnson)
(Merck-Schering Plough)
Novartis
(Pfizer - Wyeth)
Sanofi-Aventis

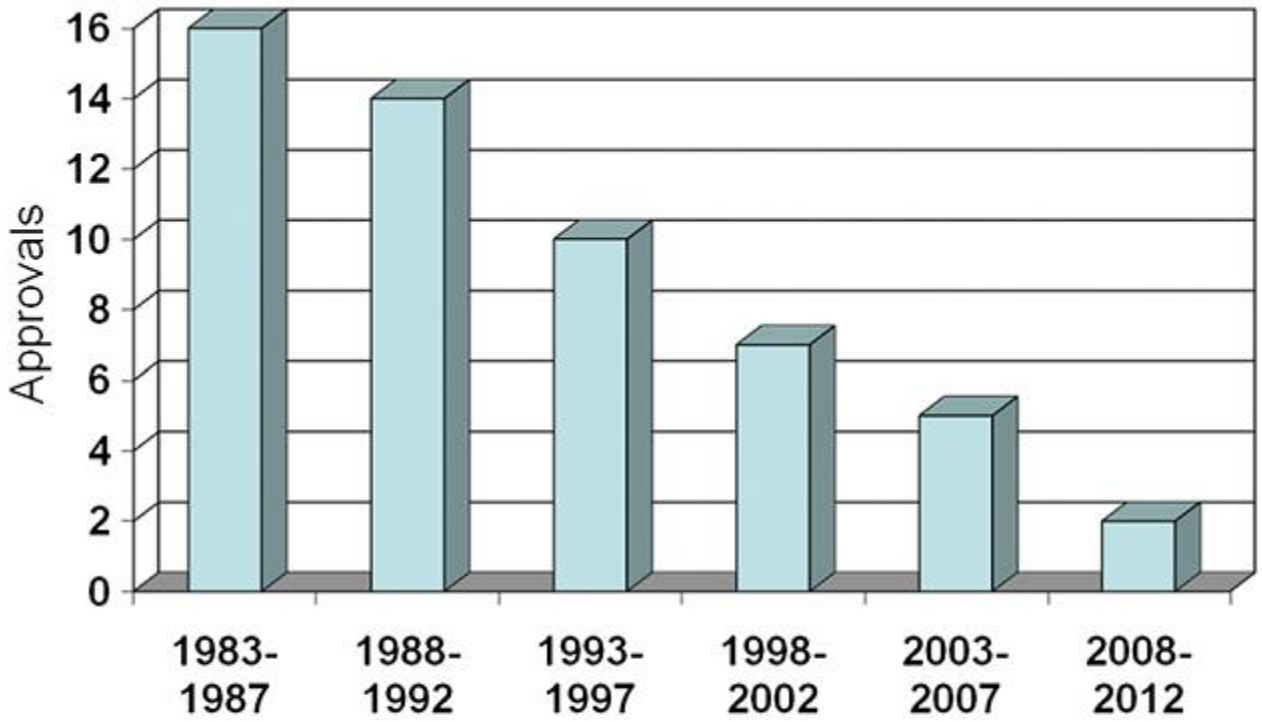
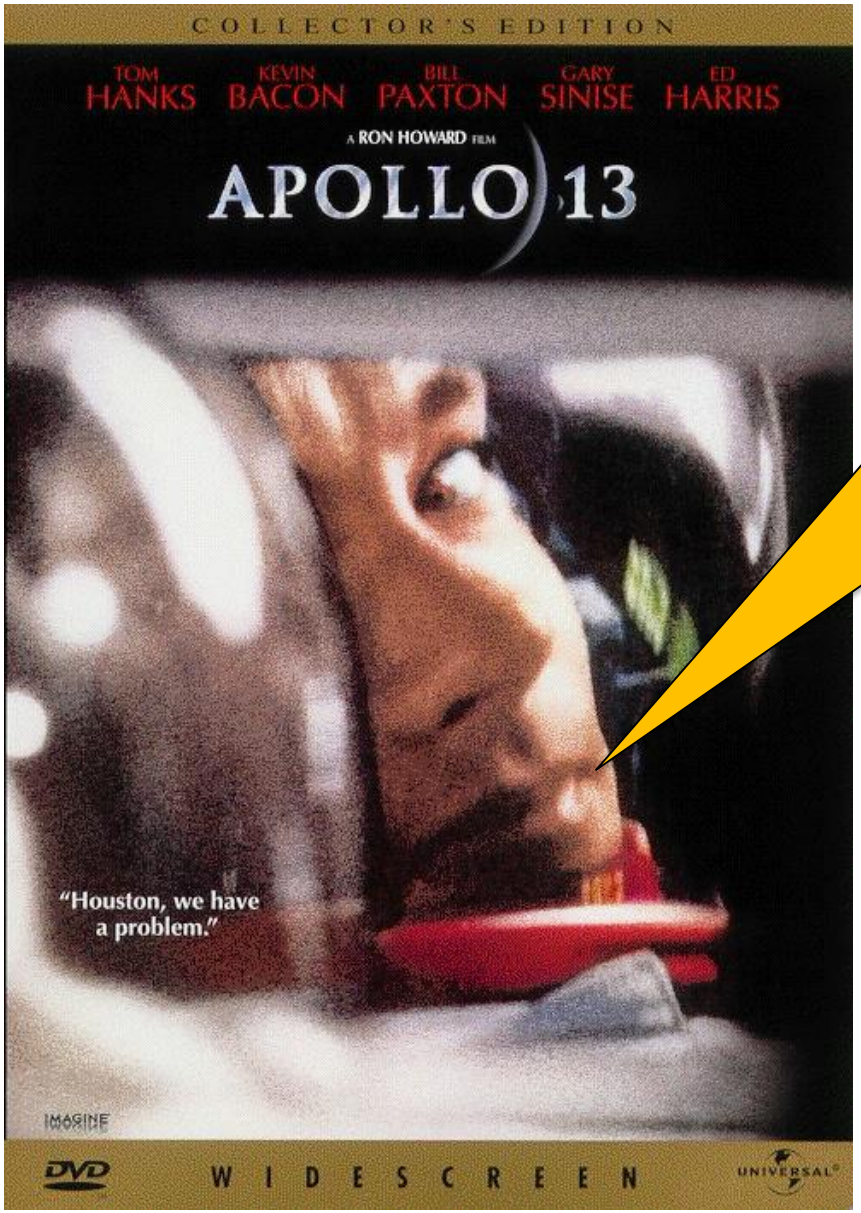


Figure 1. New systemic antibacterial agents approved by the US Food and Drug Administration per 5-year period, through 2012. Modified from Spellberg 2004 [23].


Bad Bugs
Need Drugs
10x'20
Ten new ANTIBIOTICS by 2020



Houston, we have a problem!

New antimicrobial development

- Patchy advances:

Class	Progress
Antivirals	Good (HIV, viral hepatitis, influenza)
Antifungals	Reasonable, but more needed due to an increasingly immune-compromised population
Antiparasitic	Limited - human and animals
Antibiotics	Poor

- Incentives
- Current drugs too cheap

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- ?Tax current agents to provide development funding

New Antibiotics

- BLA-BLA-inhibitor combinations
- New classes - Anti-siderophore agents
- None with good activity against NDM-type resistance

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- BLA-BLA-inhibitor combinations
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- Nc

Articles

Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis

Evelina Tacconelli, Elena Carrara, Alessia Savoldi*, Stephan Harbarth, Marc Mendelson, Dominique L Monnet, Céline Pulcini, Gunnar Kahlmeter, Jan Kluytmans, Yehuda Carmeli, Marc Ouellette, Kevin Outterson, Jean Patel, Marco Cavaleri, Edward M Cox, Chris R Houchens, M Lindsay Grayson, Paul Hansen, Nalini Singh, Ursula Theuretzbacher, Nicola Magrini, and the WHO Pathogens Priority List Working Group†*

Lancet Infect Dis 2018; 18; 318–27

Published Online December 21, 2017 http://dx.doi.org/10.1016/

Summary

Background The spread of antibiotic-resistant bacteria poses a substantial threat to morbidity and mortality worldwide. Due to its large public health and societal implications, multidrug-resistant tuberculosis has been long regarded by WHO as a global priority for investment in new drugs. In 2016, WHO was requested by member states to create a priority list of other antibiotic-resistant bacteria to support research and development of effective drugs.

New Antibiotics

- BLA-BLA-inhibitor combinations
- New classes - Anti-siderophore agents
- None with good activity against NDM-type resistance

- Reassessing older agents:
  - Colistin
  - Fosfomycin
  - Fusidic acid

Need to get the basics right or we will once again be effectively…..

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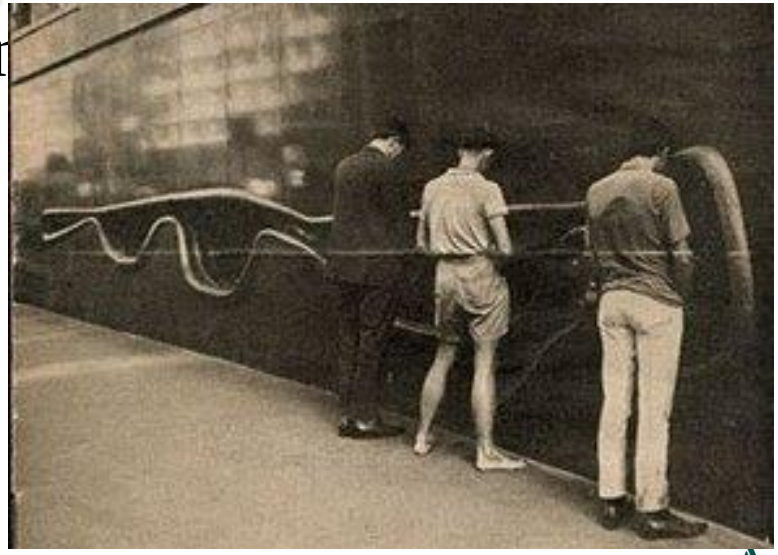

Need to get the basics right or we

We need the Antibiotic Guidelines more than ever!

Predicting the future of the Antibiotic Guidelines

Greater emphasis on:

- Having an accurate diagnosis
  - Less syndromic prescribing
- Appropriate dosage to ensure efficacy
  - Real-time measurement of drug levels – all agents

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- Enhanced role of vaccination to prevent AMR
  - But vaccination really only helps with 1 of the 4 infection groupings

Predicting the future of the

Four broad bacterial infection categories:

1. Skin & soft-tissue
2. Respiratory/meningitis*****
3. STDs
4. Gut-related – impact of contaminated food

G

-
-
  - Real-time measurement of drug levels –
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Predicting the future of the Antibiotic Guidelines

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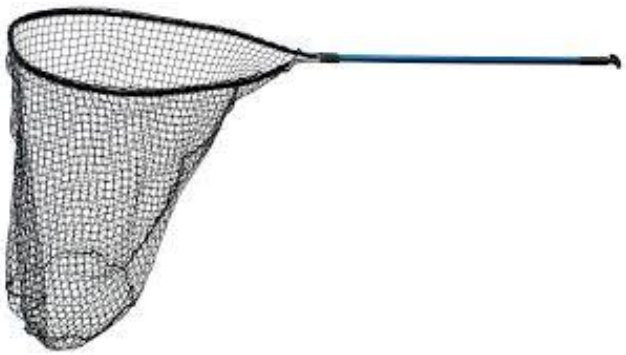
- Appropriate dosage to ensure efficacy
  - Real-time measurement of drug levels – all agents
- Enhanced role of vaccination to prevent AMR
  - But vaccination really only helps with 1 of the 4 infection groupings
- Dealing with the challenges:
  - Obesity (correct dose; tissue penetration; diabetes)
  - Increase in immune-compromised patients
    - Selective immunosuppression associated with "MABs"
    - Increase in specific infections linked to specific chemo agents
  - Loss of entire drug classes

Cover of future Antibiotic Guidelines



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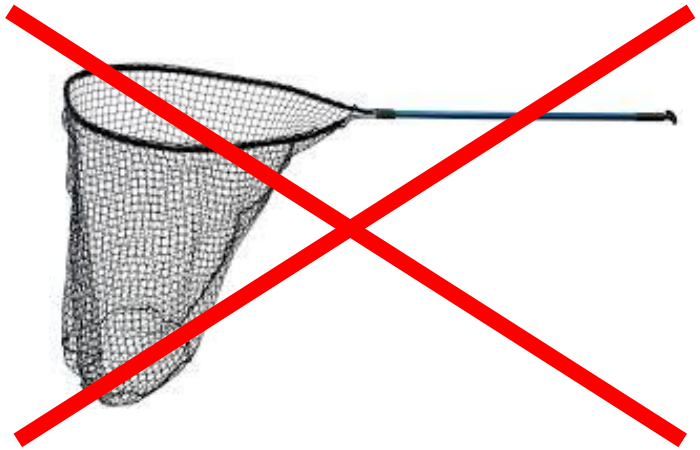
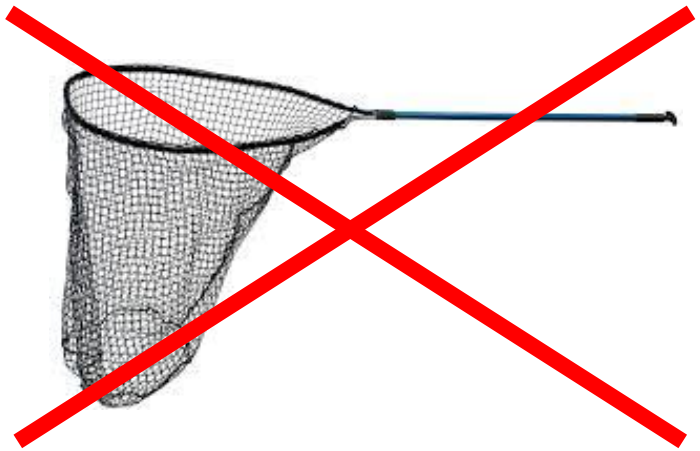
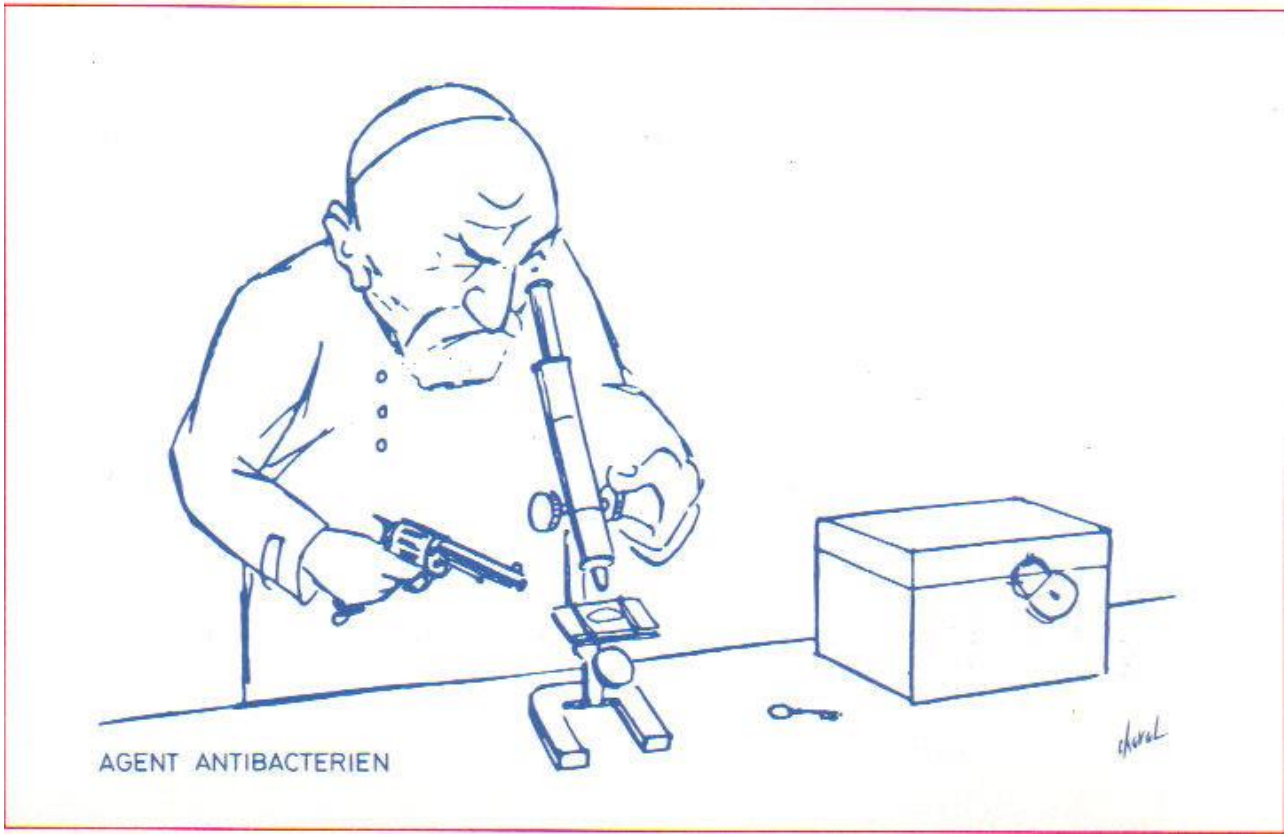


Therapeutic Guidelines

Cover of future Antibiotic Guidelines



What is in the future without Antibiotics?



Courtesy of the Institut Pasteur, 2001