Contents

Welcome Message

Welcome Message

Welcome to the “APEC Conference on Strategies against the Evolving Threats from Antimicrobial Resistance (AMR): From Awareness to Concrete Action”.

Antimicrobial resistance (AMR) has become a critical public health issue globally due to the overuse of antimicrobials and the spread of the resistant strains of bacteria in the environment. AMR threatens our ability to treat common infectious diseases, resulting in prolonged illness, disability, and death and poses a significant health, economic and social burden on the society. Considering the urgent need for APEC members to take appropriate actions against the growing antimicrobial resistance, Chinese Taipei proposed this project to provide APEC developing economies with a platform to share and discuss the preparedness efforts for effective management of AMR.

This conference will include the following activities: (1) interactive sessions that will focus on strengthening surveillance and laboratory capacity to combat AMR, policies to promote antimicrobial stewardship programs, and infection control strategies to contain AMR, (2) poster presentation that showcases the latest development in AMR diagnostics, treatment, and management and (3) site visit to Linkou Chang Gung Memorial Hospital

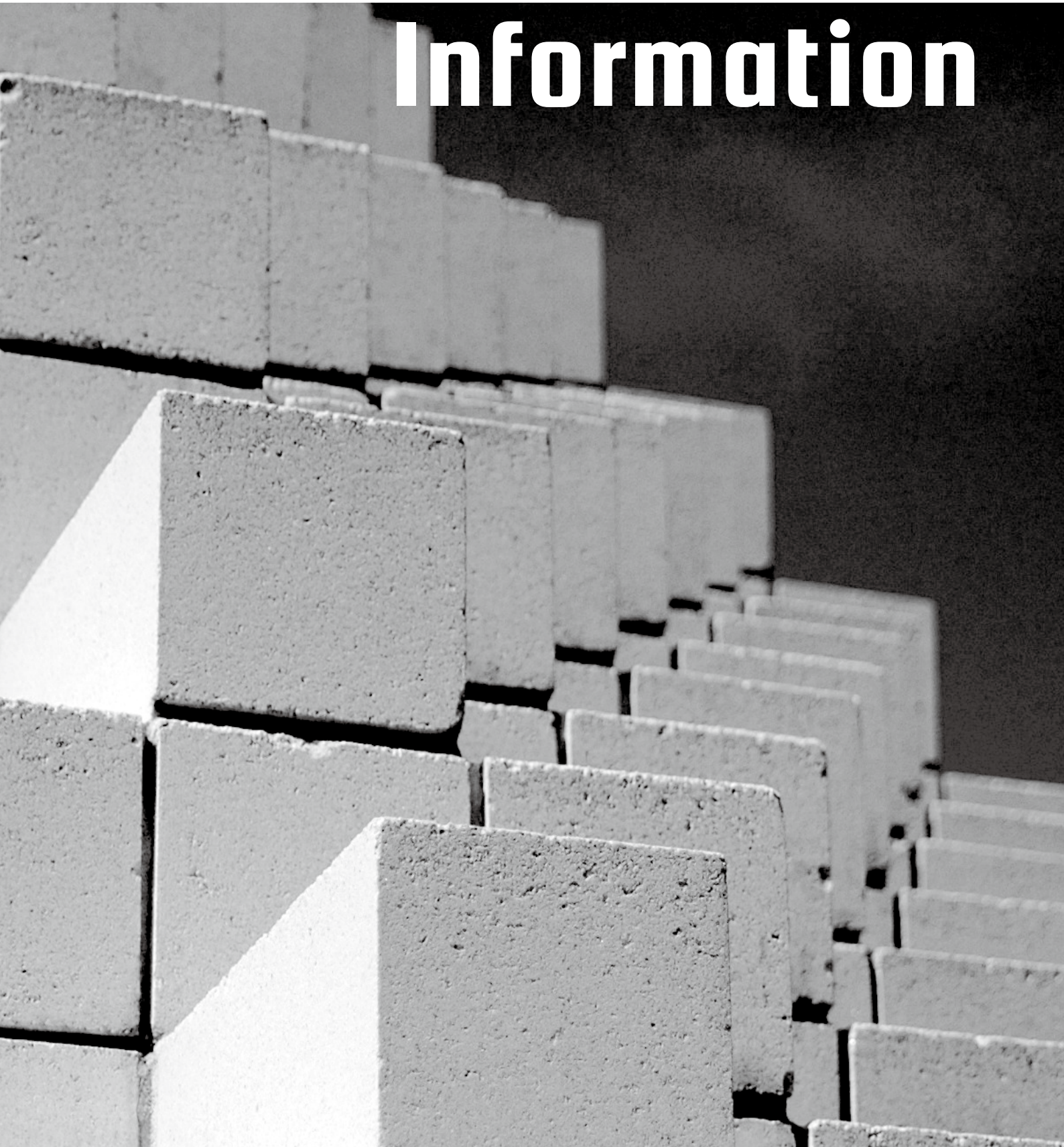
On behalf of the conference organizer, we hope you will find this conference stimulating, enjoyable and productive. We thank you for your participation and contributions to this event, and wish you a wonderful time in Taipei.

Jih-Haw Chou, D.D.S., M.P.H.

Director-General

Centers for Disease Control

Conference Information



Date

Sep. 20-21, 2018

Venue

1F, Cathay Financial Conference Hall (Taipei)

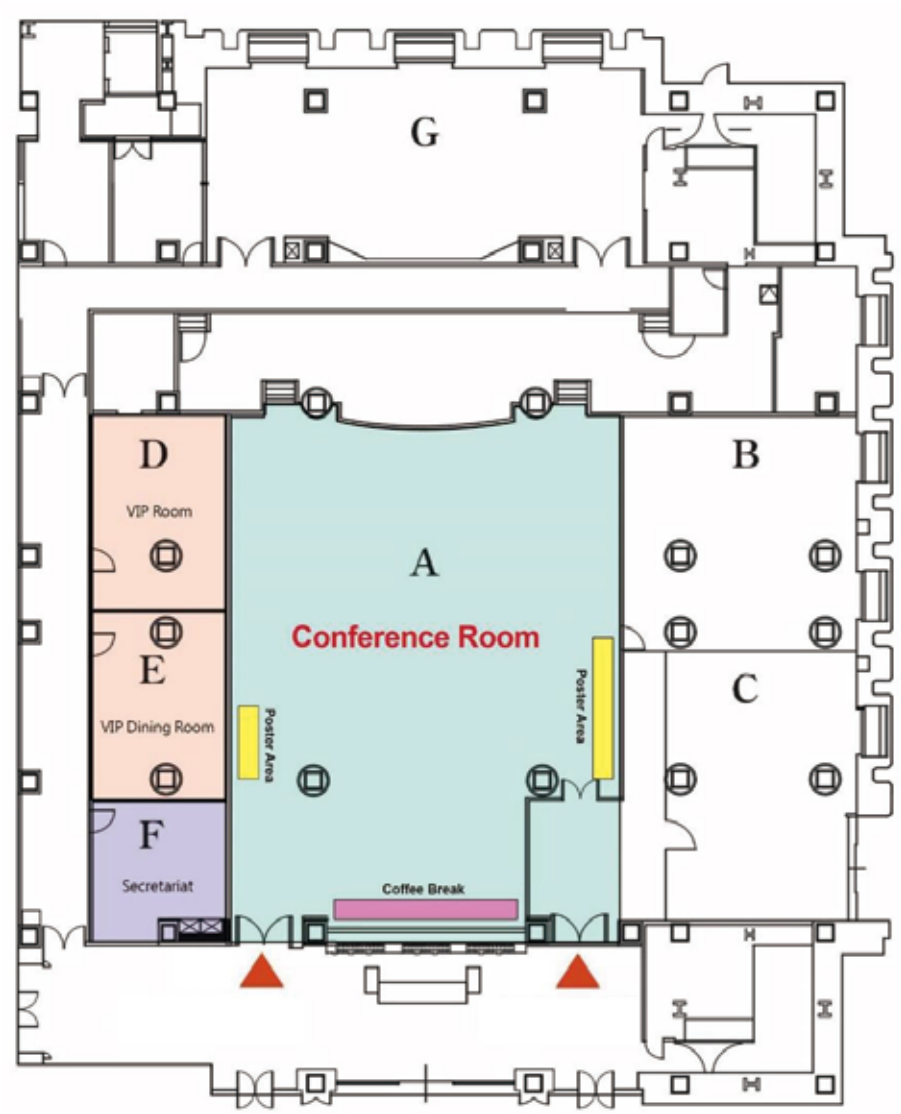
No.9, Songren Rd., Xinyi Dist., Taipei City

Organizer

Centers for Disease Control

Floor Plans

1F, Cathay Financial Conference Hall (Taipei)



Program Agenda

Thursday, 20 September 2018		
Time	**Subject**	**Moderator/ Speaker**
08:20-08:50 (30 mins)	Registration	
08:50-09:00 (10 mins)	Opening Ceremony	
09:00-09:10 (10 mins)	Opening Remarks	**Dr. Shih-Chung Chen** Minister, Ministry of Health and Welfare **Dr. Chin-Cheng Huang** Deputy Minister, Council of Agriculture
09:10-09:25 (15 mins)	Group Photo	
09:25-09:55 (30 mins)	**Keynote Speech I** Chinese Taipei's action plan against antimicrobial resistance	**Moderator** **Dr. Tzou-Yien Lin** Chair of the Board of Directors, National Health Research Institutes **Speaker** **Prof. Shan-Chwen Chang** Dean, College of Medicine, National Taiwan University
09:55-10:25 (30 mins)	**Keynote Speech II** World Veterinary Association's strategy on the prudent use of antimicrobials	**Moderator** **Dr. Tai-Hwa Shih** Deputy Director General, Bureau of Animal and Plant Health Inspection and Quarantine (BAPHIQ) **Speaker** **Dr. Shih- Ming Johnson Chiang** President, World Veterinary Association (WVA)
10:25-10:45 (20 mins)	*Coffee Break*	

Thursday, 20 September 2018		
Time	**Subject**	**Moderator/ Speaker**
Session I	**Strengthening surveillance and laboratory capacity to combat antimicrobial resistance (AMR)**	**Moderator** **Prof. Feng-Yee Chang** Professor, Tri-Service General Hospital, National Defense Medical Center **Dr. Cheng-Hsun Chiu** Professor, Department of Pediatrics, Chang Gung Memorial Hospital
10:45-11:10 (25 mins)	Fighting antimicrobial resistance with rapid, point-of-need diagnostic methods	**Prof. Kazuhiro Tateda** President, Japanese Association for Infectious Diseases
11:10-11:35 (25 mins)	Establish network for AMR surveillance in Asia Pacific region	**Dr. Stephen Sheng-Fong Lin** Regional Medical Therapeutic Area Lead, Anti-infective, Asia-Pacific, PEH, Pfizer Inc.
11:35-12:00 (25 mins)	Longitudinal multicenter surveillance on AMR	**Dr. Tsai-Ling Yang Lauderdale** Investigator, National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes
12:00-12:30 (30 mins)	Panel Discussion	
13:00-14:00 (60 mins)	**Luncheon Session: Strategies to Scale up Patient Access to Novel Antibiotics.**	**Hosted by LSIF**
Session II	**Policies to promote antimicrobial stewardship programs (ASP)**	**Moderator** **Dr. Yao-Shen Chen** Chief, Department of Internal Medicine ,Kaohsiung Veterans General Hospital **Dr. Shu-Hui Tseng** Director, Division of Infection Control and Biosafety, Centers for Disease Control
14:00-14:30 (30 mins)	Antimicrobial Stewardship Programme in Singapore	**Prof. David Chien Boon Lye** Associate Professor, Tan Tock Seng Hospital
14:30-15:00 (30 mins)	The Antibiotic Stewardship Programme in Malaysia	**Prof. Victor Lim** Pro Vice-Chancellor, International Medical University

Thursday, 20 September 2018		
Time	**Subject**	**Moderator/ Speaker**
15:00-15:40 (40 mins)	*Coffee Break & Poster Viewing*	
15:40-16:10 (30 mins)	The Antibiotics Stewardship in Hong Kong	**Prof. Wing Hong Seto** Co-Director, WHO Collaborating Centre for Infectious Disease Epidemiology and Control, The University of Hong Kong
16:10-16:40 (30 mins)	Healthcare-associated Infections in Intensive Care Units in Asia: Recent Trends Based on Healthcare-associated Infections Surveillance Network over an 8-year period	**Prof. Yee-Chun Chen** Professor, Department of Internal Medicine, National Taiwan University Hospital and College of Medicine
16:40-17:10 (30 mins)	Panel Discussion	
18:00-20:00 (120 mins)	Welcome Reception (Invited Only)	

Friday, 21 September 2018		
Time	**Subject**	**Moderator/ Speaker**
08:30-09:00 (30 mins)	Registration	
09:00-09:30 (30 mins)	**Keynote Speech III** WHO strategies to fight antimicrobial resistance	**Moderator** **Prof. Shan-Chwen Chang** Dean, College of Medicine, National Taiwan University **Speaker** **Prof. Didier Pittet** Chief Medical Officer, University Hospitals of Geneva
09:30-10:00 (30 mins)	**Keynote Speech IV** Antimicrobial Resistance Detection and Containment；a current US approach	**Moderator** **Dr. Yi-Chun Lo** Deputy Director-General, Centers for Disease Control **Speaker** **Dr. Michael Bell** Deputy Director, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention
10:00-10:15 (15 mins)	*Coffee Break*	
Session III	**Infection control strategies to contain antimicrobial resistance (AMR)**	**Moderator** **Prof. Yin-Ching Chuang** Professor, Chi Mei Medical Center **Prof. David Chien Boon Lye** Associate Professor, Tan Tock Seng Hospital
10:15-10:40 (25 mins)	Ten years improvement in infection control practice and antimicrobial optimization in the 29 private university hospitals in Japan	**Prof. Satoshi Hori** Professor, Department of Infection Control Science, Juntendo University
10:40-11:05 (25 mins)	Strategies to prevent and control AMR infection in Hong Kong	**Ms. Patricia Ching** Principal Nurse, WHO Collaborating Center For Epidemiology, School Of Public Health, University Of Hong Kong

Friday, 21 September 2018		
Time	**Subject**	**Moderator/ Speaker**
11:05-11:30 (25 mins)	Carrot or stick? Building capacity in ASP and infection control through quality accreditation	**Prof. Marilyn Cruickshank** Professor of Nursing Research, University of Technology Sydney
11:30-12:00 (30 mins)	Panel Discussion	
12:00-12:10 (10 mins)	Closing Remarks	**Dr. Jih-Haw Chou** Director General, Centers for Disease Control
12:10-13:10 (60 mins)	*Lunch Break*	
13:10-14:00 (50 mins)	*Transport to Linkou Chang Gung Memorial Hospital*	
Session IV	**Site Visit to Linkou Chang Gung Memorial Hospital (Invited Only)**	**Moderator** **Prof. Wen-Jin Cherng** Superintendent, Linkou Chang Gung Memorial Hospital **Speaker** **Dr. Cheng-Hsun Chiu** Professor, Department of Pediatrics, Chang Gung Memorial Hospital **Dr. Chun-Wen Cheng** Medical doctor, Division of Infectious Diseases, Linkou Chang Gung Memorial Hospital

Scan this QR code for the most updated version of the agenda and presentation information.

Opening Remarks

Dr. Shih-Chung Chen

Minister, Ministry of Health and Welfare

Dr. Chin-Cheng Huang

Deputy Minister, Council of Agriculture

Dr. Shih-Chung Chen

Position: Minister

Department/organization: Ministry of Health and Welfare

Economy: Chinese Taipei

Education Background

- 1971-1977 D.D.S, School of Dentistry, Taipei Medical College

Professional Career

- 1987-1990 Director, Taipei City Dentists Association
- 1991-1993 Executive director, Taipei City Dentists Association
- 1993-1995 President, Taipei City Dentists Association
- 1995-1996 Commissioner, medical review committee, Taipei City Health Department
- 1995-1999 President, Taiwan Dental Association
- 1993-1998, 1999-2000 Commissioner, Dentist Advisory Committee, DOH
- 1999-2005 Executive director, chief executive officer ,Taiwan Dental Association
- 1996-1999, 2005-2006 Commissioner, National Health Insurance Supervisory Committee, DOH
- 1996-2008 Commissioner, National Health Insurance Medical Expenditure Negotiation Committee, DOH
- 1999-2005, 2009-2017 Consultant, Taipei City Dentists Association
- 1996-2008 Commissioner, National Health Insurance Medical Expenditure Negotiation Committee, DOH
- 1999-2005, 2009-2017 Consultant, Taipei City Dentists Association
- 1999-2005, 2009-2017 Consultant , Taiwan Dental Association
- 2004-2017 Director, Taipei Medical University
- 2016-2017 National Policy Advisor to the President
- 2017- Minister of Health and Welfare

Dr. Chin-Cheng Huang

Position: Deputy Minister

Department/organization: Council of Agriculture

Economy: Chinese Taipei

Education Background

- 1993-1997 Ph. D. University of Wisconsin-Madison, USA
- 1990-1993 M. S. University of Wisconsin-Madison, USA
- 1974-1979 D. V. M. National Chung-Hsing University

Professional Career

- 2012-2016 Director General, Agricultural Biotechnology Park, Council of Agriculture
- 2012 Counselor, Council of Agriculture
- 2009-2012 Director General, Animal Health Research Institute, Council of Agriculture
- 2005-2009 Chief of Biologics Division, A.H.R.I, Council of Agriculture
- 2001 Assistant Professor, National Chung-Hsing University.
- 1998 Postdoctor, Academia Sinica.

Keynote Speech I
Chinese Taipei's Action Plan against Antimicrobial Resistance

Moderator

Prof. Tzou-Yien Lin

Chair of the Board of Directors, National Health Research Institutes

Speaker

Prof. *Shan-Chwen Chang*

Dean, College of Medicine, National Taiwan University

Prof. *Shan-Chwen Chang*

Position: Dean

Department/organization: College of Medicine, National Taiwan University

Economy: Chinese Taipei

Education Background

• 1974-1981	Ph.D., Graduate Institute of Clinical Medicine, National Taiwan University

Professional Career

• 1990 - 1992	Lecturer of Internal Medicine, National Taiwan University
• 1992 - 2000	Associate Professor of Internal Medicine, National Taiwan University
• 1996 – 1999	Chief, Division of Infection, Immunology and Rheumatology, Department of Internal Medicine, National Taiwan University Hospital
• 1999 - 2009, 2011-2013	Chief, Division of Infectious Diseases, National Taiwan University Hospital
• 2006 – 2009	Researcher (joint appointment), Division of Clinical Research, National Health Research Institute
• 2007 - 2008	Vice-director, Department of Internal Medicine, National Taiwan University Hospital
• 2008(May-Sept.)	Director, Department of Internal Medicine, National Taiwan University Hospital
• 2008 - 2009, 2011-2013	Associate Dean, College of Medicine, National Taiwan University
• 2008 - 2009, 2011-2013	Vice-superintendent, National Taiwan University Hospital
• 2009 – 2010	Deputy Minister of Health

Speech Abstract

Chinese Taipei's Action Plan Against Antimicrobial Resistance

Antimicrobial resistance(AMR) is one of the most complex public health threats worldwide; it threatens our ability to treat patients with infectious diseases, resulting in prolonged illness, disability, and death that pose a significant health, economic and social burden on the society. Facing this increasing threat, world leaders in the G7, G20 and the UN General Assembly have declared AMR a global crisis. In 2015, the WHO launched a Global Action Plan on AMR. The action plan underscores the need for an effective One Health approach involving coordination among numerous international sectors and actors, including human and veterinary medicine, agriculture, finance, environment, and well-informed consumers. As the world enters the ambitious new era of sustainable development, world leaders have also adopted universal health coverage (UHC) as a key target under the sustainable development goals. And AMR poses a big challenge to achieving UHC.

In this presentation, the current threats of AMR globally and some critical international action initiatives will be mentioned briefly. Then, Chinese Taipei's framework and strategies to combat AMR will be introduced, which includes establishing surveillance mechanisms, raising awareness and improving knowledge of AMR, and promoting cross-sector cooperation. Finally, the presentation will be concluded with our commitments to addressing AMR.

Chinese Taipei's action plan against antimicrobial resistance

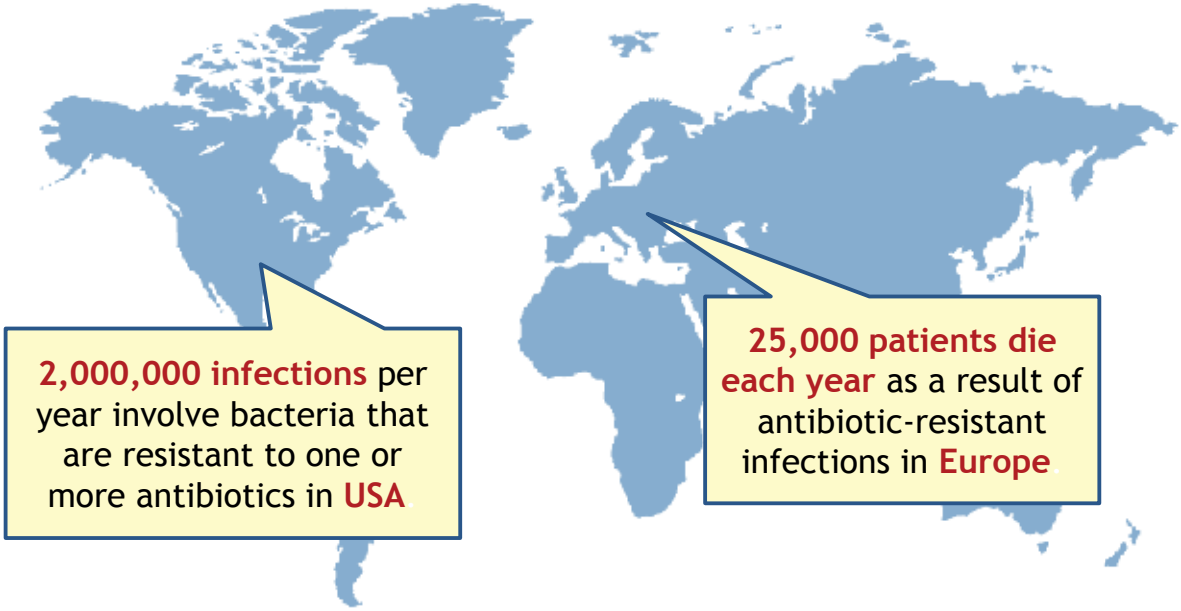
Shan-Chwen Chang, MD, PhD
Dean, College of Medicine
National Taiwan University
20 September 2018

Outline

- Global AMR Threat: Today and Future
- Global Action Initiatives
- Chinese Taipei's Framework and Strategies to Combat AMR
- Prospect: Integrate AMR and UHC

Current Global AMR Threat

Drug-resistant infections cause around 700,000 deaths globally.



http://www.myrolematters.com/amr-infographics.html

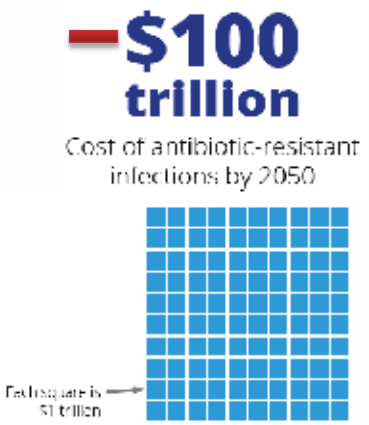
3

Future Global AMR Threat

If the current trend is not altered and no action is taken to counter these threats…

Health and Economic Impact

+10 m deaths by 2050



The world's GDP **2 to 3.5%**

Jim O'Neill. (2016) Tackling Drug-Resistant Infections Globally: Final Report and Recommendations

4

AMR: A Threat to Successful Achievement of the SDGs Targets

AMR strikes hardest on the poor: Treatment of resistant infections is more expensive.

Antibiotic residues from hospitals, pharmaceutical companies, and farms can contaminate waters.

Untreatable infections in animals threaten sustainable food production.

Cost of AMR is predicted to be US$100 trillion by 2050.

Antimicrobials are a fundamental component in all health systems.

It's crucial to balance access, innovation, and conservation of antimicrobials to contain AMR.

All of the above require multi-stakeholder partnerships and a global response. No single country, sector or organization can address this issue alone.

Jasovský et al. Ups J Med Sci. 2016 Aug; 121(3): 159-164.

Global Action Initiatives - United Nations

- Global leaders met at the United Nations General Assembly in New York in September 2016 to commit to fighting AMR together.
- This is only the fourth time in UN history that a health topic is discussed at the General Assembly.

- World leaders pledged to…
  - ✓ **Strengthen regulations**
  - ✓ **Improve knowledge and awareness**
  - ✓ **Promote best practices**
  - ✓ **Foster innovative approaches**

Global Action Initiatives - FAO-OIE-WHO Collaboration

LEGISLATION:
Regulation is mandatory to promote appropriate use of antimicrobials: make sure legislation is implemented.

AWARENESS & EDUCATION:
Raise public awareness and educate all stakeholders

SURVEILLANCE & MONITORING:
Strengthen national AMR and antimicrobial use surveillance systems based on global standards.

RESEARCH:
Support and finance the development of methods for the prevention, diagnosis and treatment of disease, to reduce dependence on antimicrobials.

http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Infographies/EN_AMR-TRIPARTITE-INFOGRAPHIC_2017.pdf

Global Action Initiatives- GHSA

1. Antimicrobial Resistance
2. Zoonotic Disease
3. Biosafety and Biosecurity
4. Immunization

Prevent

5. National Laboratory System
6. Real-Time Surveillance
7. Reporting
8. Workforce Development

Detect

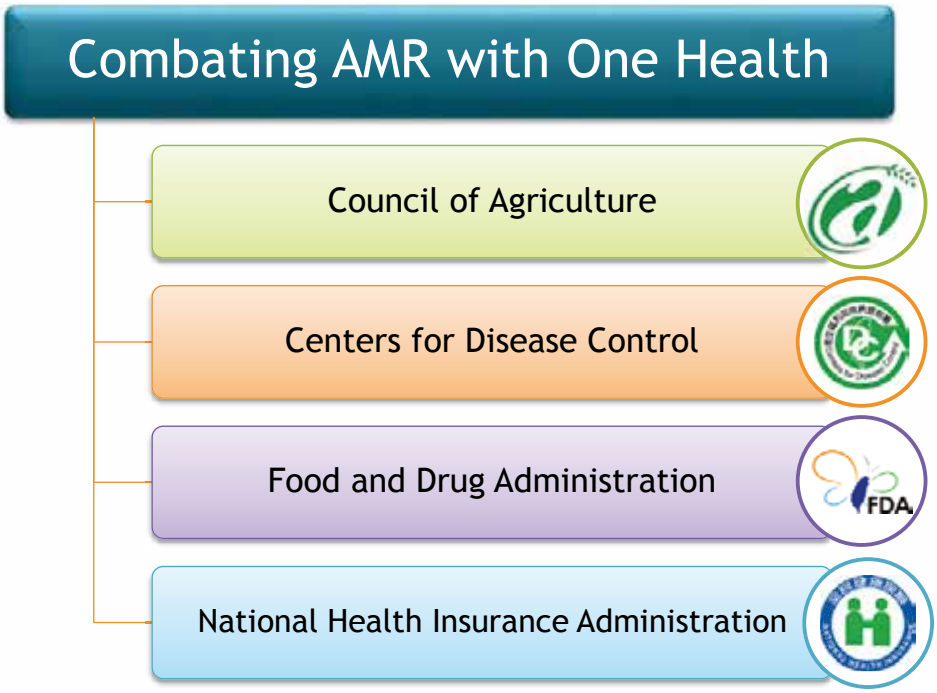
9. Emergency Operations Centers
10. Linking Public Health with Law and Multisectoral Rapid Response
11. Medical Countermeasures and Personnel Deployment

Respond

AMR action package is the first of all 11 action packages.

GHSA emphasizes "**partnership**", "**political commitment**", "**cross-sectoral coordination**", and "**international cooperation**" to strengthen both the global capacity and nations' capacity to prevent, detect, and respond to infectious diseases threats.

Chinese Taipei's Framework to Combat AMR



COA's Strategies to Combat AMR

- Survey and monitor AMR in livestock
- Survey and monitor veterinary medicines used in livestock
- Review and minimize the number of antimicrobials for veterinary use
- Govern veterinary medicine sales and promote appropriate use of antimicrobials in livestock

FDA's Strategies to Combat AMR

- Establish the maximum antimicrobial residue limit for animal products
- Survey and inspect antimicrobial residue in animal products
- Strengthen the detection of illegal sales of antimicrobials
- Promote drug safety education for the general public

NHI's Strategies to Combat AMR

Establish the reimbursement regulations and restrictions for antimicrobials

Review and audit claims for reimbursement of antimicrobials

Survey and monitor indicators for antimicrobial use

Establish incentives for hospitals with good ASP performance

CDC's Framework to Combat AMR

National Level (CDC)	● Formulate AMR policies and strategies ● Establish a national advisory committee ● Promote cross-sectoral cooperation ● Designate qualified and dedicated staffs ● Provide appropriate funds
Local Level (Health Departments)	● Promote AMR related programs and policies ● Evaluate ASP performance of healthcare facilities within their respective jurisdiction
Community Level	● Professional associations and societies: Join task force in promoting AMR strategies ● Healthcare facilities: Comply with related laws and AMR prevention and control regulations ● General public: Raise awareness through education

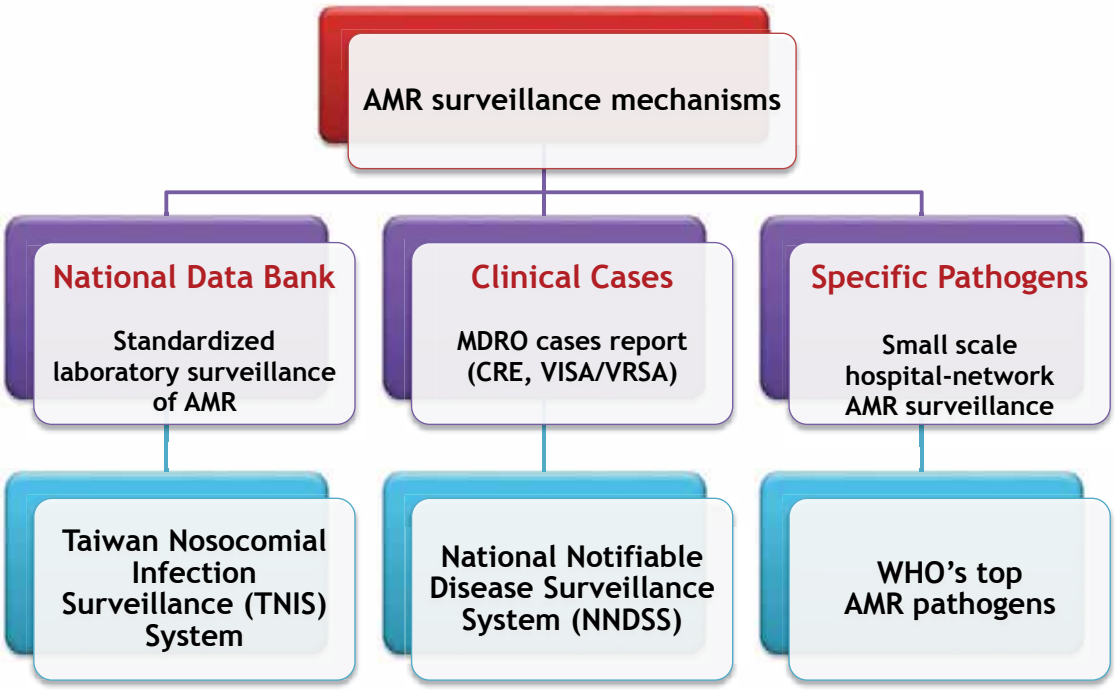
13

CDC's Strategies to Combat AMR

- Establish multi-channel surveillance mechanisms on drug-resistant organisms
- Ensure the appropriate use of antibiotics through AMR-related hospital audits
- Improve awareness and knowledge of AMR through effective communication, education and training
- Promote cross-sectoral cooperation on containing AMR

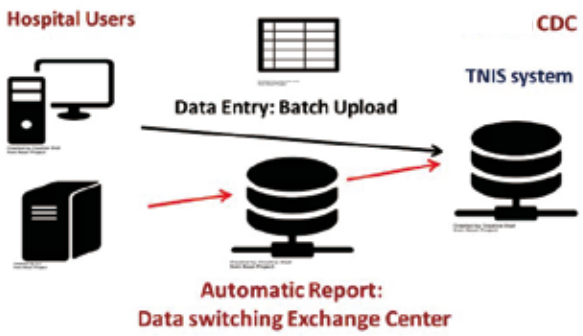
14

Multi-channel surveillance mechanisms



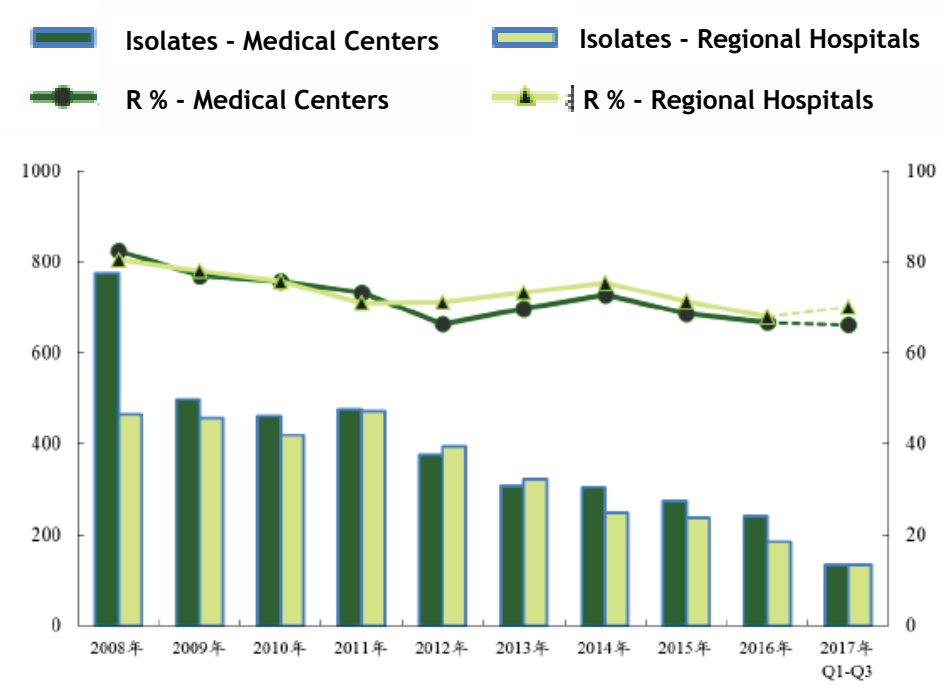
AMR surveillance through TNIS

- Hospitals report individual lab test data of clinical isolates to Antimicrobial Usage and Resistance (AUR) Module within the TNIS system.



Surveillance pathogens	
Escherichia spp.	*Enterococcus spp.*
Klebsiella spp.	*Acinetobacter baumannii*
Enterobacter spp.	*Acinetobacter calcoaceticus*
Proteus spp.	*Acinetobacter calcoaceticus-Acinetobacter baumannii complex*
Salmonella spp.	*Pseudomonas aeruginosa*
Shigella spp.	*Staphylococcus aureus*
Citrobacter spp.	*Streptococcus pneumoniae*
Morganella spp.	*Neisseria gonorrhoeae*
Providencia spp.	*Clostridium difficile*
Serratia spp.	*Helicobacter pylori*
Yersinia spp.	

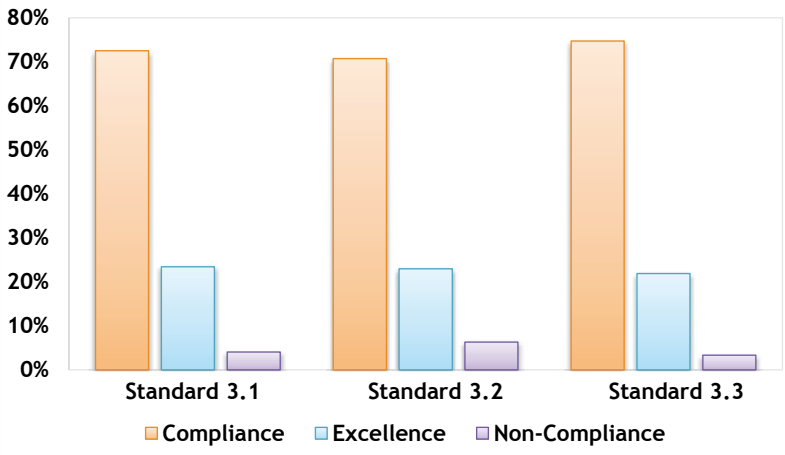
National AMR reports



The percentage of MRSA in ICUs

AMR-related Hospital Audits

Assessment Standards	
3.1	Leadership and responsibilities in Antimicrobial Stewardship program
3.2	Mechanism for surveillance and management of antibiotic use
3.3	Measures for surveillance, diagnosis, and isolation of resistant microbes



A total of 224 hospitals were evaluated in 2017.

AMR Awareness and Education (1)

For General Public

Chinese Taipei CDC has initiated "World Antibiotic Awareness Week" and encouraged general public to respond by signing the pledge online.

AMR Awareness and Education (2)

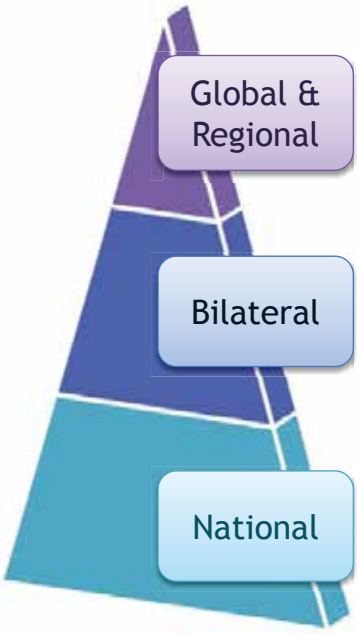
For Healthcare Workers

Guidebooks on CDC website

E-learning courses on CDC website

- Identification, treatment & infection control of common infections
- Rational use of antibiotics
- Healthcare workers' respective roles and responsibilities in ASP
- Infection control of MDROs
- Laboratory diagnosis of infections

Cross-sectoral Cooperation

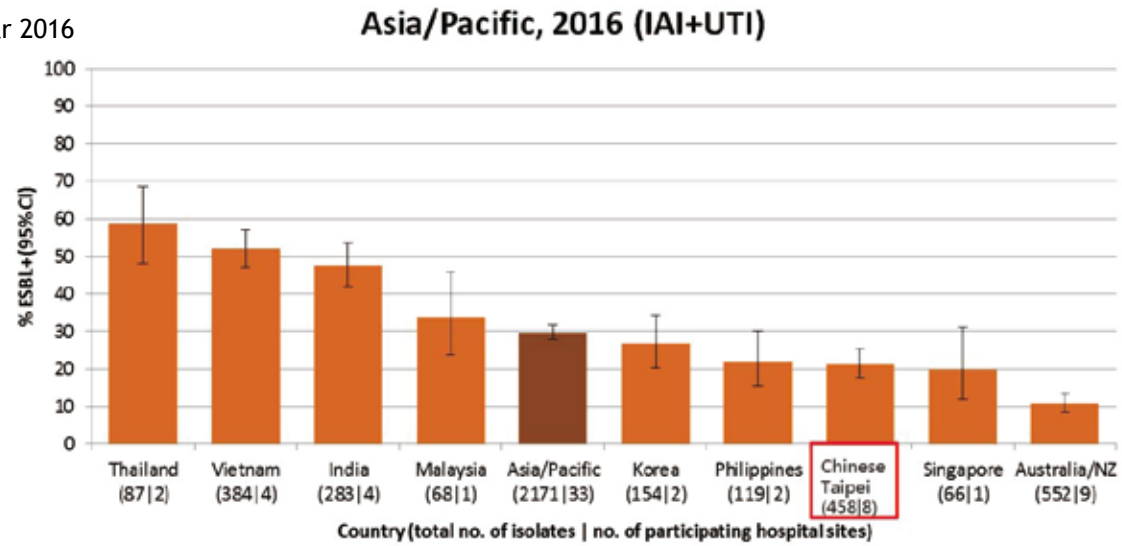


- Host 2018 APEC AMR conference to communicate with APEC economies on AMR prevention, detection, and response strategies
- Collaborate with U.S. CDC to implement active surveillance and isolation for the control of MRSA in our Hospitals
- Communicate with National Institute of Infectious Diseases in Japan on drug-resistant infections related issues
- Establish communication channels, spanning human, animal, and food safety sectors, to discuss the AMR prevention and control strategies

AMR International Comparison(1)

Rate of ESBL production amongst isolates of *E. coli* causing urinary tract infections (UTIs) and Intra-abdominal infection (IAI)

Year 2016



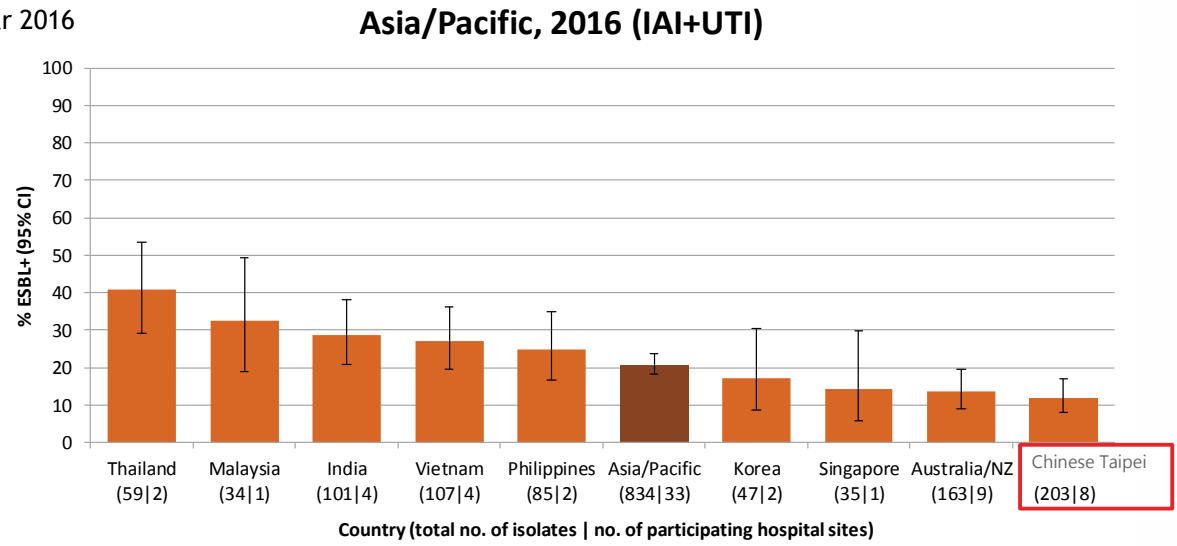
**ESBL: Extended-spectrum ß-lactamases

Data from Study for Monitoring Antimicrobial Resistance Trends (SMART)

AMR International Comparison(2)

Rate of ESBL production amongst isolates of *K. pneumoniae* causing urinary tract infections (UTIs) and Intra-abdominal infection (IAI)

Year 2016

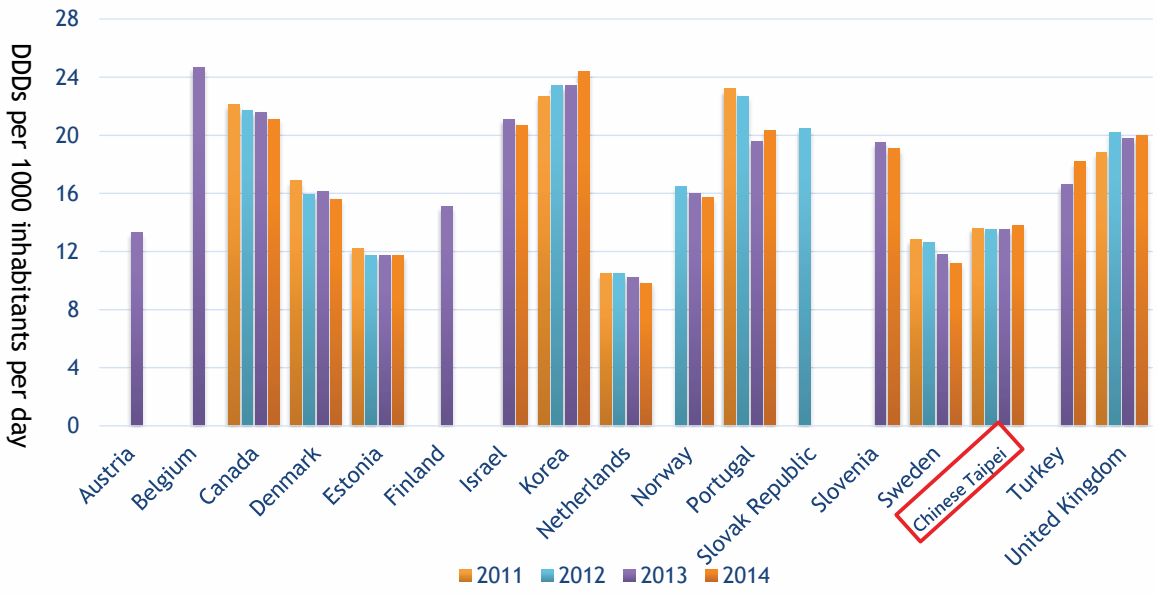


**ESBL: Extended-spectrum ß-lactamases

Data from Study for Monitoring Antimicrobial Resistance Trends (SMART)

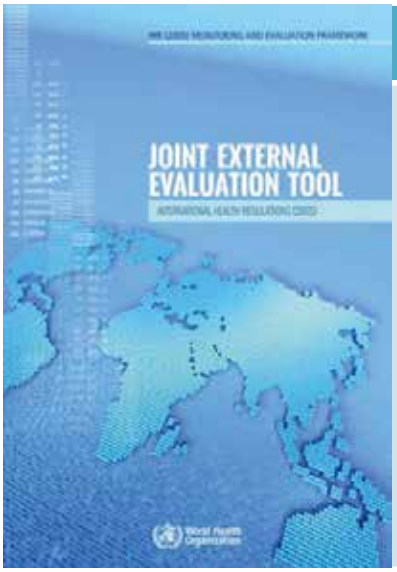
International Comparison of Antimicrobial Consumption

Overall amount of antibiotics prescribed in primary care



International External AMR Capacity Evaluation

Using WHO Joint external evaluation tool: International Health Regulations (2005)



Element	Indicator	Score
Antimicrobial Resistance	P.3.1- Antimicrobial resistance (AMR) detection	5
	P.3.2- Surveillance of infections caused by AMR pathogens	5
	P.3.3- Healthcare-associated infection (HCAI) prevention and control programs	4
	P.3.4- Antimicrobial stewardship activities	4

Score	No Capacity 1	Limited Capacity 2	Developed Capacity 3	Demonstrated Capacity 4	Sustainable Capacity 5

AMR: A Big Challenge on the Path to UHC

Makes 1st and 2nd line antimicrobials ineffective, thus impacting drugs' efficacy and access.

Heavily diverts scarce medical resources, impacting affordability of health systems.

Very expensive to treat, causing affordability issues and financial risks for patients.

Complicates treatments and impacts quality and effectiveness of services.

Making progress towards UHC and delaying the emergence and spread of AMR are interconnected.

http://siapsprogram.org/wp-content/uploads/2016/05/AMR-UHC_USAID-SIAPS_EPN-Forum-2016_Germany_Mohan-Joshi_19May2016.pdf

Prospect: Integrate AMR and UHC

Health System Attributes	Needed UHC Actions to address AMR
	• Strengthen basic public health and prevention • Ensure access to appropriate antibiotics at an affordable cost
	• Regulate the quality of antimicrobials • Include AMR in medical curriculum
	• Alter financial incentives that encourage overuse of antimicrobials • Reduce need for expensive treatment of infections with resistant organisms
	• Provide information on surveillance findings • Provide information on appropriate treatments
	• Strengthen public health services and immunization • Establish partnerships for management of antimicrobials

Bloom G, et al. *BMJ Glob Health* 2017;2

Conclusion

- To combat AMR, Chinese Taipei commit to promoting strategies aligned with WHO.
- To achieve the goal of UHC, Chinese Taipei's actions need to be taken into account regionally and globally.
- Chinese Taipei will continue to fight against AMR and strengthen health security together with the world.


Thank you for your attention!

Keynote Speech II

World Veterinary Association's Strategy on The Prudent Use Of Antimicrobials

Moderator

Dr. Tai-Hwa Shih

Deputy Director General, Bureau of Animal and Plant Health Inspection and Quarantine (BAPHIQ)

Speaker

Dr. Shih- Ming Johnson Chiang

President, World Veterinary Association (WVA)

Dr. Tai-Hwa Shih

Position: Deputy Director General

Department/organization: Bureau of Animal and Plant Health Inspection and Quarantine (BAPHIQ)

Economy: Chinese Taipei

Educational Background

- Master

Professional Career

- Director of Hsinchu Branch, BAPHIQ
- Deputy Director General, BAPHIQ

Dr. Shih- Ming Johnson Chiang

Position: President

Department/organization: World Veterinary Association (WVA)

Economy: Chinese Taipei

Educational Background

- MS, DVM, Veterinary College of National Taiwan University
- EMBA, Management College of National Taiwan University

Professional Career

- President, Taipei Veterinary Medical Association
- President, Taiwan Veterinary Medical Association
- President, Federation of Asian Veterinary Associations (FAVA)
- Vice President, World Veterinary Association (WVA)
- President Elect, WVA
- President, WVA

Speech Abstract

World Veterinary AssOciation's Strategy on The Prudent Use of Antimicrobials

- Introduction WVA

World Veterinary Association (WVA) was formed in 1963. Dr. John Gamgee convened the first International Veterinary Congress in Hamburg, Germany with 103 veterinarians from 10 counties. Nowadays, WVA represents over 500,00 veterinarians through its 95 member associations across six continents.

Our mission is:

"*to assure and promote animal health, animal welfare and public health globally, through developing and advancing veterinary medicine, profession as wells as public and private veterinary services.* "

WVA has 5 strategic priorities: Animal Welfare, Pharmaceutical Stewardship, Veterinary Education, Zoonotic diseases, and Organizational growth and Partnerships. To achieve our mission, WVA collaborates with various international Organizations in the global scales, such as WHO, OIE, WSAVA…etc. Together, WVA is committed to the One-Health concept that to recognize the interconnection between people, animals, plants and their shared environment and aim to achieve optimal health outcomes. Antimicrobial resistance (AMR) is a critical issue in One-health.

- WVA's strategy on the prudent use of antimicrobials

AMR is the ability of a microbe to resist the effects of medication previously used to treat them. AMR occurs naturally in our world, but if no standard usage rules, it will cost enormous problems.

As veterinary professions, WVA's AMR-strategy and initiatives are to have access to a broad range of safe and effective antimicrobials; and to use these medicines in a responsible way with a minimum impact on the development of AMR in animal and human health care. By doing so, WVA are working on disease prevention and establish protocols of pharmaceutical stewardship and global basic principles of antimicrobial use.

In many years, WVA has concerned for AMR issue. In 2015, WVA selected Pharmaceutical Stewardship as one of its key strategic goal. Participating in many international AMR platforms and panels, WVA took several initiatives to raise awareness about the risk for AMR. In 2014 & 2017, WVA held Global Summit meetings together with WHO, FAO and OIE on AMR issue. Again, in 2015 and 2016, WVA/WMA held 1st and 2nd Global One Health conference in Spain and Japan. Also, in 2016 of UN General Assembly on Antimicrobial Resistance and in 2017 of World Veterinary Congress, WVA continuously raised the awareness.

In order to minimis the damage of AMR, WVA develops the Global Basic Principles of Antimicrobial Use, standard codes of using antimicrobial. WVA's main task is to:

- Promote continuing education in the responsible use and disposal of medicines with emphasis on factors involved in decreasing antimicrobial resistance.
- Supports research into further understanding of antimicrobial resistance and the development of new vaccines and medicines to prevent disease and more effectively treat disease.
- Advocate for the availability and access to good quality medicines for veterinarians worldwide

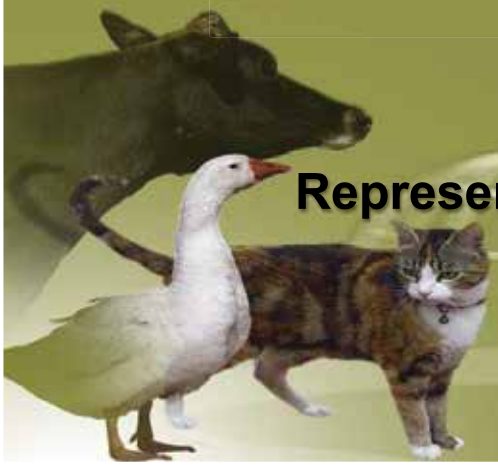
Antimicrobial resistance is a true One-Health issue and defiantly requires a One Health approach thinking. As one of the members of our world, WVA strives to work together with all health professions; and to have access to a broad range of safe and effective antimicrobials, used in a responsible way.

WORLD VETERINARY ASSOCIATION

World Veterinary Association

Since 1863

Representing the Global veterinary Profession



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APEC

Asia-Pacific
Economic Cooperation

APEC Conference
On Strategies Against The Evolving
Threats From Antimicrobial Resistance

Chinese Taipei, September 20-21, 2018

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World Veterinary Association's Strategy on the Prudent Use of Antimicrobials

Dr. Shih Ming, Johnson, CHIANG
President, World Veterinary Association

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- Introduction WVA
- WVA's strategy on the prudent use of antimicrobials
- Conclusions and Recommendations

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WORLD VETERINARY ASSOCIATION

- **Introduction WVA**
- WVA's strategy on the prudent use of antimicrobials
- Conclusions and Recommendations

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WVA's History

In 1863, Dr John Gamgee convened the first International Veterinary Congress in Hamburg, Germany with 103 veterinarians from 10 countries.

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Today

The WVA represents over 500,000 veterinarians through its 95 member associations across six continents:

Veterinary Medical Associations (local, national and regional).

International Associations of Veterinarians working in different areas of veterinary medicine.

Observers – other interested stakeholder associations whether or not they have veterinarians as members (no vote or nominating rights)

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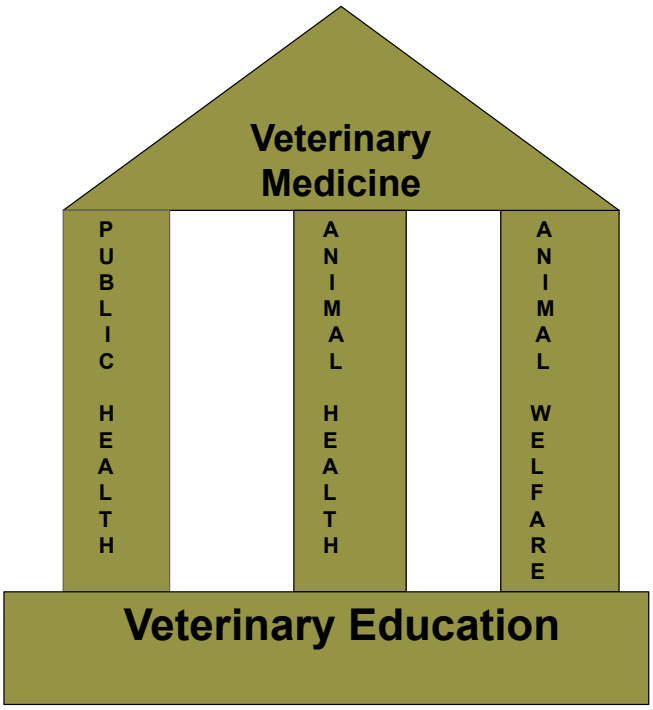
❑WVA Mission

*To assure and promote **animal health** and **welfare** and **public health globally**, through developing and advancing veterinary medicine, the veterinary profession as well as public and private veterinary services.*



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WVA 5 Strategic Priorities

- **Animal Welfare**
- **Pharmaceutical Stewardship**
- **Veterinary Education**
- **Zoonotic Diseases**
- **Organizational Growth and Partnerships**

WVA collaborations with International Organizations

WVA believes in working in partnership.
WVA signed a Memorandum of Understanding and collaborates with relevant **global partners** on various veterinary issues

- Food and Agriculture Organisation of the UN (**FAO**)
- Global Alliance on Rabies Control (**GARC**)
- International Dairy Federation (**IDF**)
- World Animal Health Organization (**OIE**)
- World Health Organisation (**WHO**)
- World Farmers Organization (**WFO**)
- World Medical Association (**WMA**)
- World Small Animal Veterinary Association (**WSAVA**)
- World Animal Protection **(WAP)**
- International Committee on Military Medicine (**ICMM**)

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WVA is committed to the One-Health concept

The **One-Health concept** recognizes that the health of **people** and the health of **animals** and the **environment** are strongly interlinked.

Through a **One-Health approach** veterinarians, physicians, ecologists, and many others work together to learn about how health threats spread among people, animals, and the environment and how to control such threats.

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WVA is committed to the One-Health concept

One-Health initiatives: collaborative, multisectoral, and trans-disciplinary approach, recognizing the interconnection between people, animals, plants, and their shared environment and aiming to achieve optimal health outcomes.

Antimicrobial Resistance is a clear One-Health issue.

The One-Health approach is critical in addressing AMR

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One Health

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WORLD VETERINARY ASSOCIATION

- Introduction WVA
- **WVA's strategy on the prudent use of antimicrobials**
- Conclusions and Recommendations

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AMR Definition

- The WHO defines antimicrobial resistance as a microorganism's resistance to an antimicrobial drug that was once able to treat an infection by that microorganism.
- The ability of a microbe to resist the effects of medication previously used to treat them.

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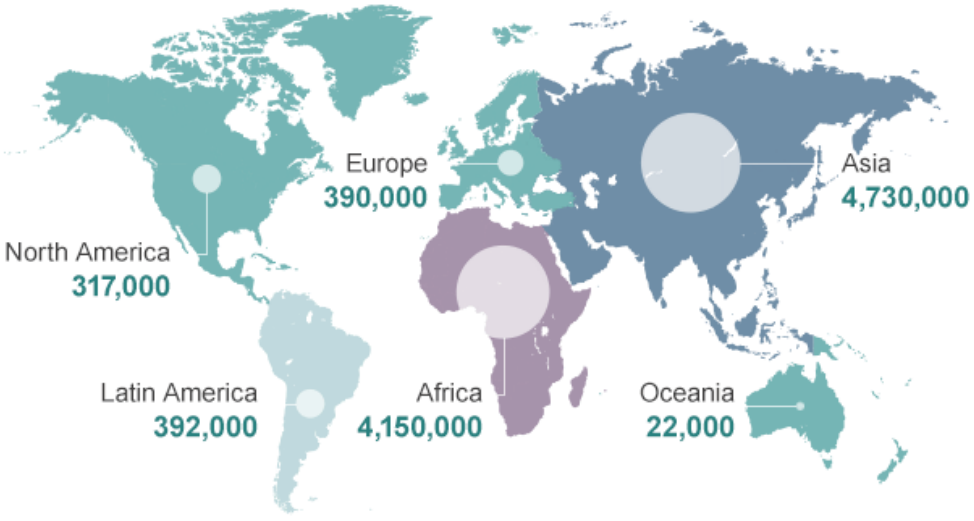
Deaths attributable to antimicrobial resistance every year by 2050



Source: Review on Antimicrobial Resistance 2014

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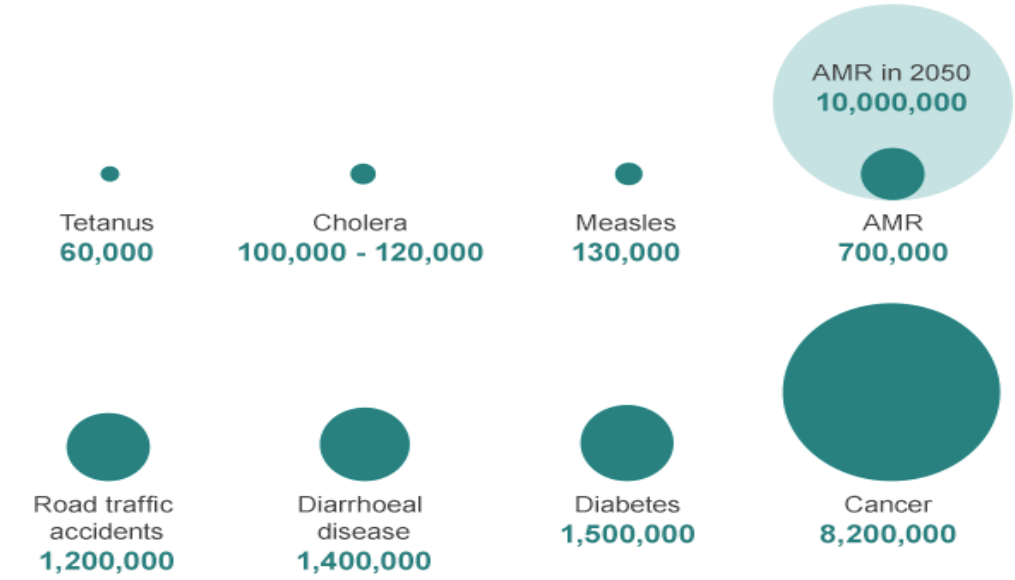
Deaths attributable to antimicrobial resistance every year compared to other major causes of death



Source: Review on Antimicrobial Resistance 2014

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WVA AMR-Strategy and Initiatives

WVA strives for the veterinary profession:

- To have access to a broad range of safe and effective antimicrobials

- To use these medicines in a responsible way with a minimum impact on the development of AMR in animal and human health care.
  - ➢ Disease prevention!
  - ➢ Pharmaceutical Stewardship! (a WVA key strategy topic)
  - ➢ Global Basic Principles of Antimicrobial Use

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WVA AMR-Strategy and Initiatives

- Since many years WVA is active against AMR
- In 2015, WVA selected Pharmaceutical Stewardship as one of its key strategic goals
- Participation in many international AMR platforms and panels

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WVA AMR-Strategy and Initiatives

- WVA also took several initiatives to raise awareness about the risk for AMR
  - 2014 & 2017Global summit on AMR (with WHO, FAO and OIE)
  - 2015 WVA/WMA 1st Global One Health conference in Madrid, Spain
  - 2016 WVA/WMA 2nd Global One Health Conference in Fukuoka, Japan
  - 2016: UN General Assembly on Antimicrobial Resistance
  - 2017: World Veterinary Congress
    ~Global Summit on Antimicrobial Resistance
    ~ Vet Vision 2050

WVA AMR-Strategy and Initiatives

WVA celebrates World Veterinary Day with different themes:

- 2010: One World, One Health
- 2012: Antimicrobial resistance
- 2016: Continuous One Health Education
- 2017: AMR: from awareness to Action

WVA also developed the Global Basic Principles of Antimicrobial Use
(see next slides)

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Global Basic Principles of Antimicrobial Use

- Sick or infected animals should be under the care of a veterinarian, who is responsible for assessing animal health, making a diagnosis, and recommending an effective care program.

- Therapeutic antimicrobials are licensed or registered for the purposes of disease treatment, control, and prevention

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Global Basic Principles of Antimicrobial Use

- Codes of good veterinary practice, quality assurance programs, herd health control and surveillance programs, and education programs should promote the responsible and prudent use of antimicrobials.

- Antimicrobials that are important in human medicine should only be used in animals under veterinary care with a valid veterinarian-client-patient relationship.

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Global Basic Principles of Antimicrobial Use

- The availability of antimicrobials should be based on risk:benefit analysis that considers the importance of the antimicrobial to both veterinary and human medicine.

- Whenever possible, microbiologic diagnosis, including culture and antibacterial sensitivity testing, should be used to make treatment decisions.

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Global Basic Principles of Antimicrobial Use

- Therapeutic antimicrobials should be used for as long as needed but for the shortest duration necessary, and at the appropriate dosage.

- Regional updates of bacterial susceptibility and resistance in human and animal populations should be monitored and made available to practising veterinarians and public health professionals.

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Global Basic Principles of Antimicrobial Use

- Records should be kept when antimicrobials are administered.
- Effective alternative and complementary medicine and practices are needed as an important part of good husbandry practices to minimize or avoid antimicrobial use

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WVA Promotes

- Promote continuing education in the responsible use and disposal of medicines with emphasis on factors involved in decreasing antimicrobial resistance.

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WVA Supports

- Support research into further understanding of antimicrobial resistance and the development of new vaccines and medicines to prevent disease and more effectively treat disease.

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WVA Advocates

- Advocate for the availability and access to good quality medicines for veterinarians worldwide

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- Introduction WVA
- WVA's strategy on the prudent use of antimicrobials
- **Conclusions and Recommendations**

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Conclusions

- Antimicrobial resistance is a true One-Health issue.
- Fighting Antimicrobial Resistance requires an One Health approach.
- WVA strives to work together with all health professions.
- WVA strives to have access to a broad range of safe and effective antimicrobials and to use these in a responsible way.

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Session I
Strengthening Surveillance and Laboratory Capacity to Combat Antimicrobial Resistance (AMR)

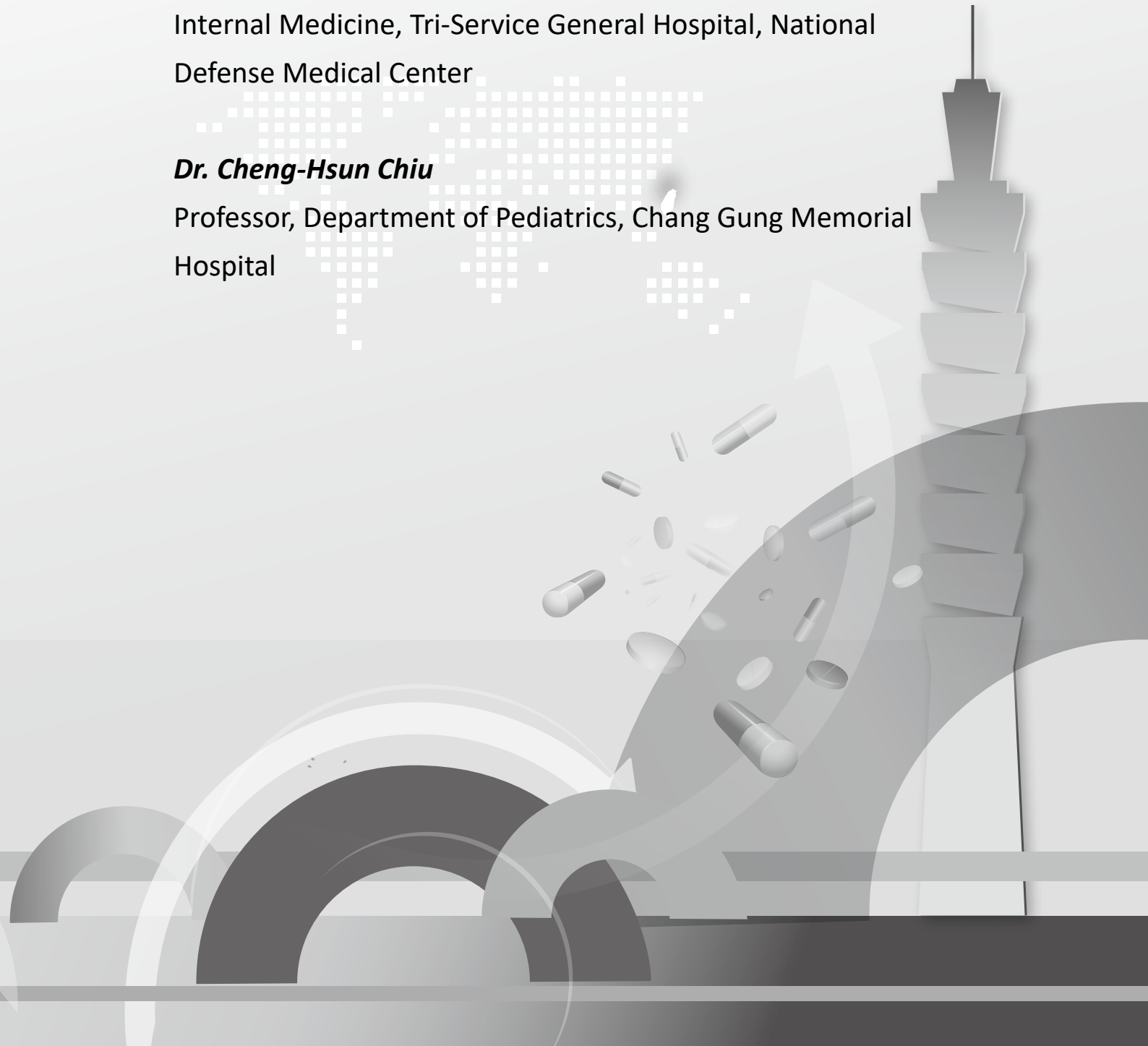
Moderators

Prof. Feng-Yee Chang

Professor, Division of Infectious Diseases, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center

Dr. Cheng-Hsun Chiu

Professor, Department of Pediatrics, Chang Gung Memorial Hospital



Prof. Feng-Yee Chang

Position: Professor
Department/organization: Division of Infectious Diseases, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center
Economy: Chinese Taipei

Education Backgroud

- M.D.,PhD. National Defense Medical Center, Taipei.
- Fellow, Infectious Disease, University of Pittsburgh, the US.

Professional Career

- Attending physician and Professor, Tri-Service General Hospital, National Defense Medical Center
- Director General, CDC
- President, Infection Control Society of Taiwan

Publication

- L. Kristopher Siu, Yu-Kuo Tsai, Jung-Chung Lin, Te-Li Chen, Chang-Phone Fung, Feng-Yee Chang*:Development of a Colloidal Gold-Based Immunochromatographic Strip for Rapid Detection of Klebsiella pneumoniae Serotypes K1 and K2. J Clin Microbiol 2016; 54 (12):3018–3021. doi:10.1128/JCM.01608-16.
- Angela Song-En Huang, Wan-Chin Chen, Wan-Ting Huang, Shih-Tse Huang, Yi Chun Lo, Sung-His Wei, Hung-Wei Kuo, Pei-Chun Chan, Min-Nan Hung, Yu-Lun Liu, Jung-Jung Mu, Jyh-Yuan Yang, Ding-Ping Liu, Jih-Haw Chou, Jen-Hsiang Chuang*, Feng-Yee Chang*: Public Health Responses to Reemergence of Animal Rabies, Taiwan, July16–December 28, 2013. PLOS ONE| DOI:10.1371/journal.pone.0132160 July10,2015.
- Shu-Hui Tseng, Yu-Fen Ke, Feng-Yee Chang*: National action plan to combat antimicrobial resistance in Taiwan. Journal of microbiology, immunology, and infection 04/2014.
- Yu-Kuo Tsai, Ci-Hong Liou, Jung-Chung Lin, Ling Ma, Chang-Phone Fung, Feng-Yee Chang*, L Kristopher Siu*: A Suitable Streptomycin-Resistant Mutant for Constructing Unmarked In-Frame Gene Deletions Using rpsL as a Counter-Selection Marker. PLoS ONE 09/2014; 9(9):e109258. DOI:10.1371/journal.pone.0109258 ·
- Ho-Sheng Wu, Ji-Rong Yang, Ming-Tsan Liu, Chin-Hui Yang, Ming-Chu Cheng, Feng-Yee Chang*: Influenza A(H5N2) Virus Antibodies in Humans after Contact with Infected Poultry, Taiwan, 2012. Emerging Infectious Diseases 2014; 20(5):857-860.

Prof. Cheng-Hsun Chiu

Position: Professor

Department/organization: Department of Pediatrics, Chang Gung Memorial Hospital

Economy: Chinese Taipei

Education Background

- 1989 M.D., Chung Shan Medical and Dental College
- 1997 Ph.D., Graduate Institute of Clinical Medicine, Chang Gung University College of Medicine (Supervisor: Prof. Jonathan T. Ou)
- 1997-1999 Postdoctoral Fellow, Division of Infectious and Immunological Diseases, Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada

Professional Career

- 1993- Attending Physician, Department of Pediatrics, Chang Gung Memorial Hospital
- 2005- Professor, Department of Pediatrics, Chang Gung Memorial Hospital and Chang Gung University

Publication

- Wu PW, Huang CC, Chao WC, Sun CC, Chiu CH (corresponding author), Lee TJ. Impact of influenza vaccine on childhood otitis media in Taiwan: a population-based study. PLoS One 2018; 13:e0190507.
- Chia JH, Wu TS, Wu TL, Chen CL, Chuang CH, Su LH, Chang HJ, Lu CC, Kuo AJ, Lai CH, Chiu CH (corresponding author). Clostridium innocuum is a vancomycin-resistant pathogen that may cause antibiotic-associated diarrhea. Clin Microbiol Infect 2018 Feb 17 [Epub ahead of print].
- Janapatla RP, Chen CL, Hsu MH, Liao WT, Chiu CH (corresponding author). Immunization with pneumococcal neuraminidases NanA, NanB and NanC to generate neutralizing antibodies and to increase survival in mice. J Med Microbiol 2018 March 20 [Epub ahead of print].
- Son S, Thamlikitkul V, Chokephaibulkit K, Perera J, Jayatilleke K, Hsueh PR, Lu CY, Balaji V, Moriuchi H, Nakashima Y, Lu M, Yang Y, Tao K, Kim SH, Song JH, Kim S, Kim MJ, Heininger U, Chiu CH (corresponding author), Kim YJ. Clin Microbiol Infect 2018 April 22 [Epub ahead of print].
- Chen HH, Hsu MH, Wu TL, Li HC, Janapatla RP, Su LH, Chiu CH (corresponding author). Non-typeable Streptococcus pneumoniae infection in a medical center in Taiwan after wide use of pneumococcal conjugate vaccine. J Microbiol Immunol Infect 2018 May 14 [Epub ahead of print].

Session I
Strengthening Surveillance and Laboratory Capacity to Combat Antimicrobial Resistance (AMR)

Speakers

Prof. Kazuhiro Tateda

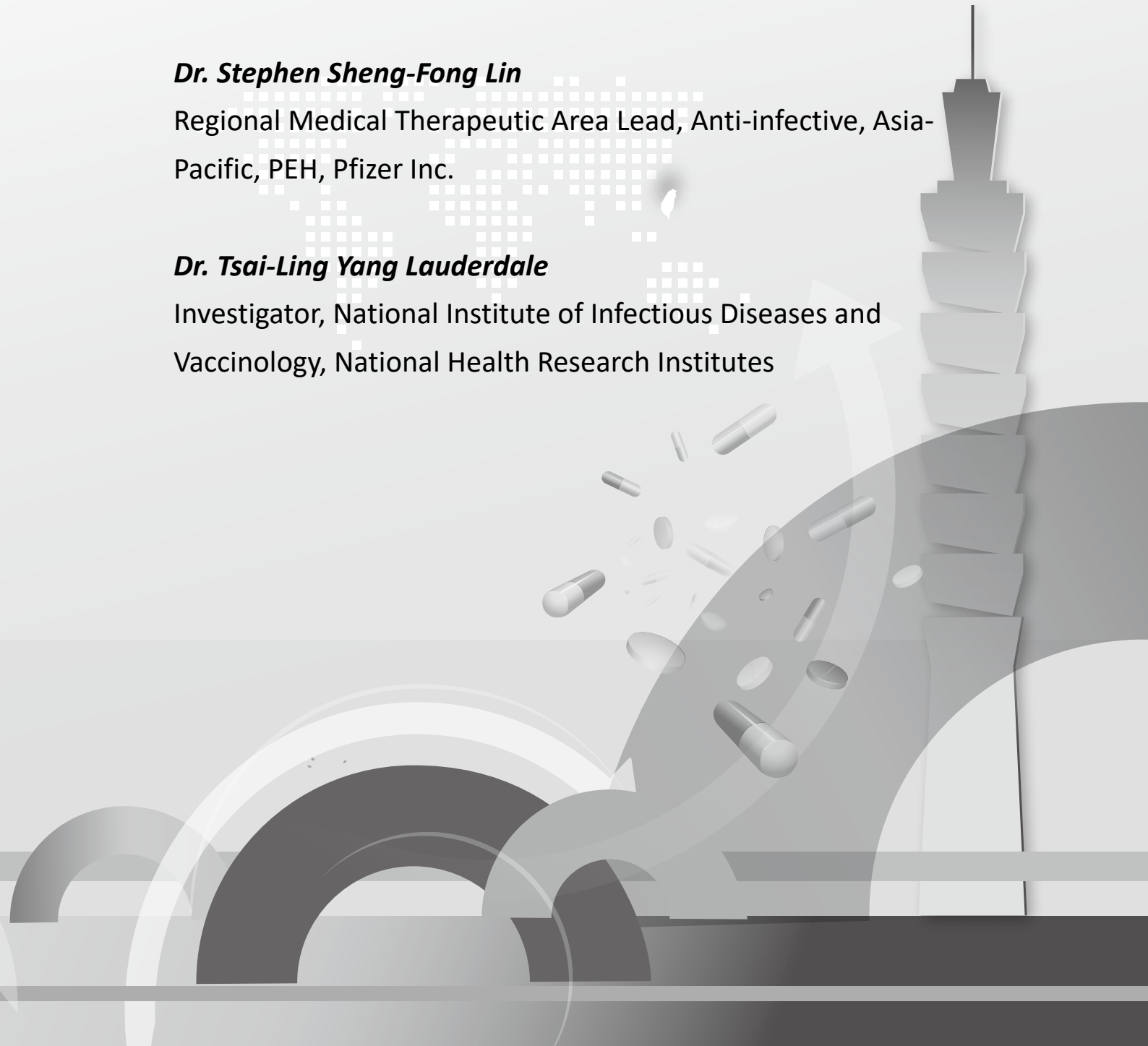
President, Japanese Association for Infectious Diseases

Dr. Stephen Sheng-Fong Lin

Regional Medical Therapeutic Area Lead, Anti-infective, Asia-Pacific, PEH, Pfizer Inc.

Dr. Tsai-Ling Yang Lauderdale

Investigator, National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes



Prof. Kazuhiro Tateda

Position: President

Department/organization: Japanese Association for Infectious Diseases

Economy: Japan

Professional Career

- 1985-1986- Resident in Internal Medicine, Nagasaki University School of Medicine
- 1986-1990 Doctor course, Nagasaki University School of Medicine
- 1990-1995 Assistant professor (1990-1995), Department of Microbiology, Toho University
- 1995-2011 Associate professor, Department of Microbiology, Toho University
- 1999-2001 Visiting professor, Department of respiratory and critical care medicine, University of Michigan Medical School, MI
- 2011- Professor and Chairman, Department of Microbiology and Infectious Diseases, Toho University
- 2017- President, Japanese Association of Infectious Diseases
- 2018- President, Japanese Society of Clinical Microbiology

Speech Abstract

Fighting Antimicrobial Resistance with Rapid, Point-of-Need Diagnostic Methods

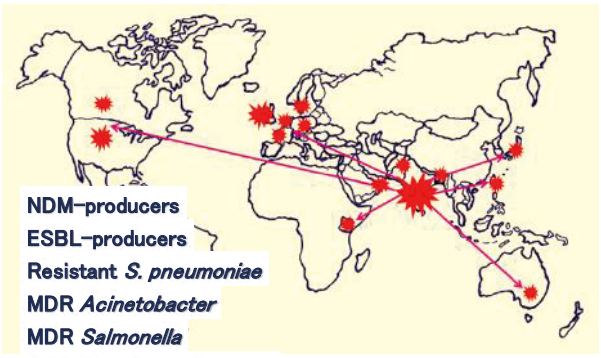
Appearance and spreading of antibiotic resistance (AMR) in bacteria are becoming a world-wide problem. Particularly, community-acquired AMR, such as CA-MRSA and ESBL producers, is in a spot light. Infection control in addtion to appropriate antibiotic uses may be a key factor for prevention of AMR issues. Prompt results in microbiological testing, ideally within 30 min (before prescription of antibiotic), are necessay for wise decision making, antibiotic use or not-use. In this point of view, ordinary PCR techniques are not sufficient, and probably more quick methods are required in recent AMR era. Several diagnostic companies are developing new instruments and technologies to make diagnosis of several infectious diseases. Especially, etiological diagnosis of sepsis and meningitis are hot topics, because suffered individuals are in risk of severe damage and/or death. One of the examples of quick diagnostic methods is an immune-chromatography targeting a variety of pathogenic antigens, such as polysaccharide and ribosomal proteins. Another is nucleic acid amplification-dependent chromatographic approaches. By using these methods, several infectious diseases will be made diagnosis within 30 min. In this presentation, recent progress of novel and unique diagnostic technologies will be reviewed. Further, advantages of these techniques, how we can use these methods for our patients, will be discussed with audiences.

Asia-Pacific Economic Cooperation
20 September, 2018
Taipei

Fighting Antimicrobial Resistance with Rapid, Point-of-Need Diagnostic Methods

Kazuhiro Tateda, MD, PhD
Department of Microbiology and Infectious Diseases
Toho University School of Medicine, Tokyo, Japan

We are in "Epicenter" of Antibiotic Resistant Bacteria



Int J Antimicrob Agents 37: 291, 2011

National Action Plan on Antimicrobial Resistance (AMR)

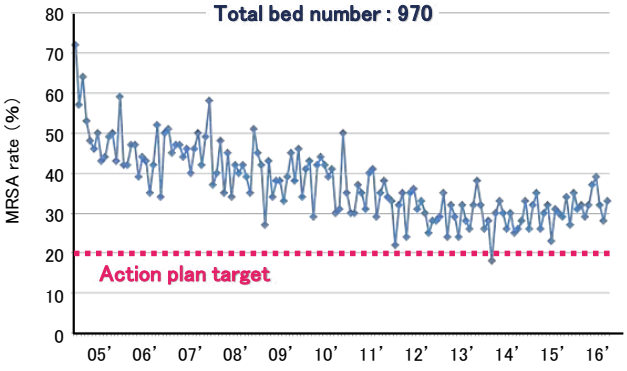
2016-2020

"Mt Fuji Action Plan"

Higher Goal is good, but ・・・・

April 5, 2016
The Government of Japan

Percentage of MRSA in total *S. aureus* (all spesimens)
– Toho University Hospital 2005～2016 –



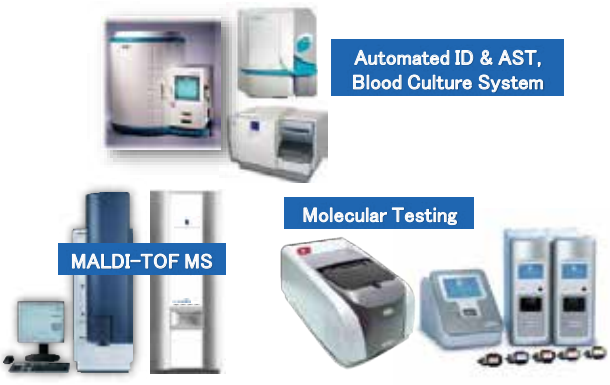
Toho University Hospital

Six Areas and Goals for Countermeasures on AMR

1. Public Awareness and Education
2. Surveillance and Monitoring
3. Infection Prevention and Control
4. Appropriate Use of Antimicrobials
5. Research and Development
6. International Cooperation

National Action Plan on AMR in Japan 2016

"Top 3" Innovation
in routine microbiology laboratory



FilmArray® ・・・・ A Game Changer !?

1 Hour

Identify Pathogens from Positive Blood Cultures in About 1 Hour

The FilmArray Blood Culture Identification Panel (BCID) tests for a comprehensive list of 24 pathogens and 3 antibiotic resistance genes associated with bloodstream infections. With just one test you can identify pathogens in 9 out of 10 positive blood cultures in about an hour with only 2 minutes of hands-on time.

Verigene® ・・・・ A Game Changer !?

5 min handling

and wait for 2.5 hours !

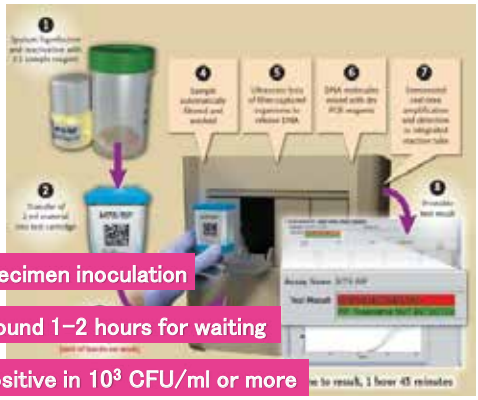
Gram Positive Panel

- 12 species
- Drug Resistance Genes (mecA, vanA, vanB)

Gram Negative Panel

- *K. pneumoniae*
- *K. oxytoca*
- *E. coli*
- *P. aeruginosa*
- *Acinetobacter* spp.
- *Enterobacter* spp.
- *Proteus* spp.
- *Citrobacter* spp.

GeneXpert® ・・・・ A Game Changer !?



Specimen inoculation

Around 1–2 hours for waiting

Positive in 10^3 CFU/ml or more

Boehme CC et al. N Engl J Med 363: 1005, 2010

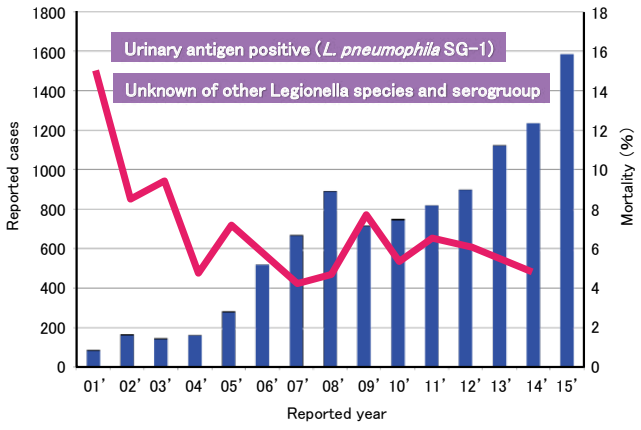
Ideal Diagnostic Methods in AMR era

- "Within 30 min" (Before ABX treatment)
- ID for species and AST
- Correlation to severity and/or pathogen load
- Differentiation between Infection and Contamination
- Cost, Cost, Cost, Cost ・・・

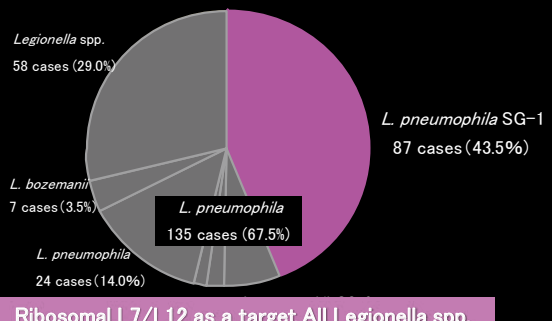
Improvement for survival ・・・

Annual Changes of Legionella Pneumonia Cases and Mortality Rate

NIID in Japan



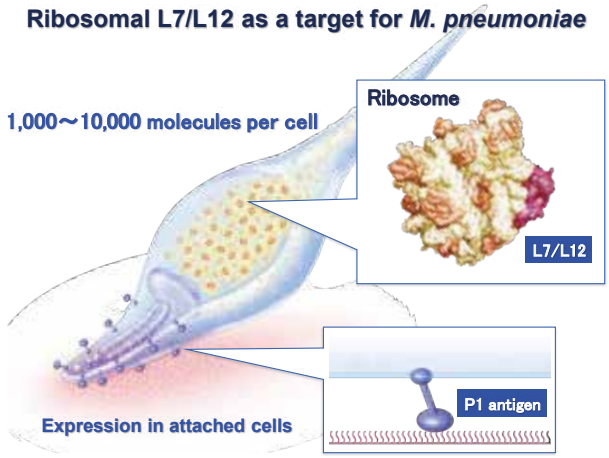
Causative Organisms of Legionella Pneumonia (200 cases)



Ribosomal L7/L12 as a target All Legionella spp.

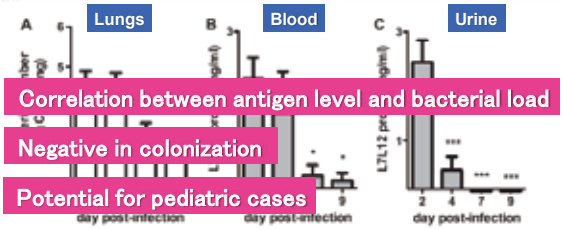
Department of Microbiology and Infectious Diseases
Toho University School of Medicine

Ribosomal L7/L12 as a target for *M. pneumoniae*



JCM

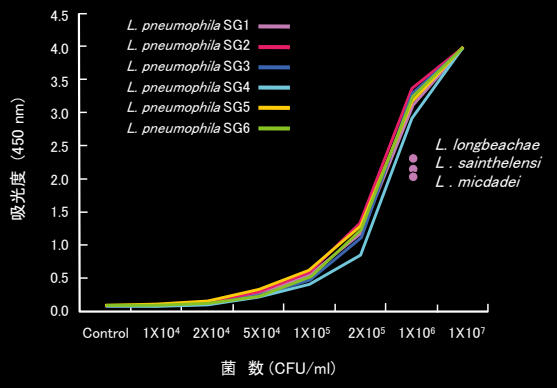
Diagnostic Usefulness of Ribosomal Protein L7/L12 for Pneumococcal Pneumonia in a Mouse Model



- Correlation between antigen level and bacterial load
- Negative in colonization
- Potential for pediatric cases

Sawa T et al. J Clin Microbiol 51: 70, 2013

L7/L12蛋白によるレジオネラの検出



Immuno-, DNA-Chromatography Method

Urine specimens

- *S. pneumoniae*
- *Legionella* spp.
- *S. aureus*
- *P. aeruginosa*

Stool specimens

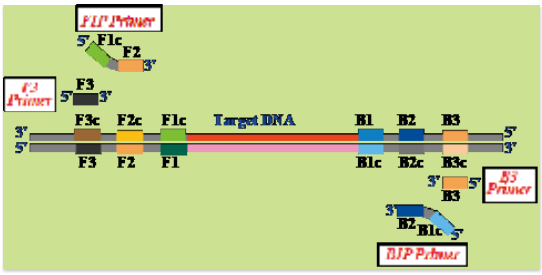
- Noro virus
- Adeno virus
- *E. coli* O-157
- *C. difficile*

Respiratory specimens

- *S. pyogenes*
- Adeno virus
- Influenza virus
- RS virus
- *S. pneumoniae*
- *M. pneumoniae*
- *B. pertussis*
- TB and NTM

LAMP Method Loop-mediated isothermal amplification

- 4 primers for 6 specific sequences
- Isothermal amplification under lead replacement reaction (65℃)
- 10^9～10^{10} amplification in 15～60 min



Courtesy of Notomi T (Eiken Kagaku Co.)

Detection of LAMP Positive Results by Naked Eye

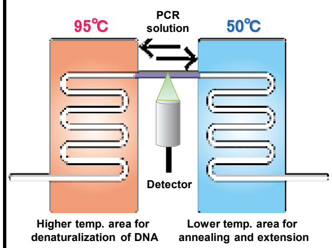
200 100 50 0 CFU/mL

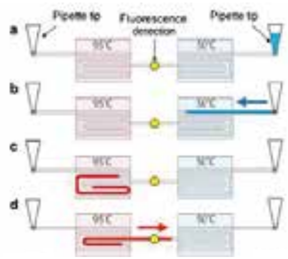
Positive results were observed in 50 CFU/mL or over of *M. tuberculosis* by naked eye

Courtesy of Notomi T (Eiken Kagaku Co.)

Rapid qPCR system "within 10 min"

①Microfluidics ②Miniaturized fluorescence detector





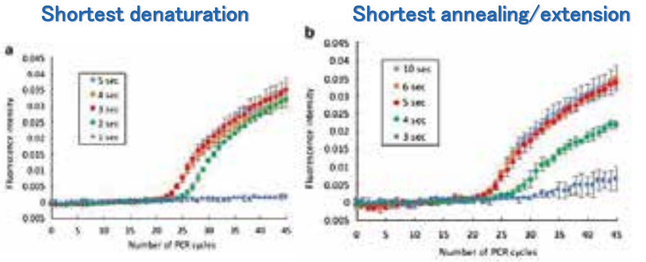
Detectable a small amount of virus and bacteria within approximately 10 min.

Furutani, S. et al. Anal Bioanal Chem 408: 5641, 2016

Furutani, S. et al. Meat Science 131: 56, 2017

Rapid qPCR system "within 10 min"

Shortest denaturation Shortest annealing/extension

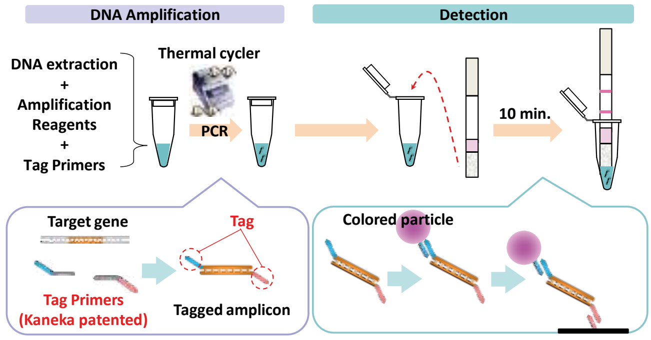


2 sec for denaturation 5 sec for annealing/extension

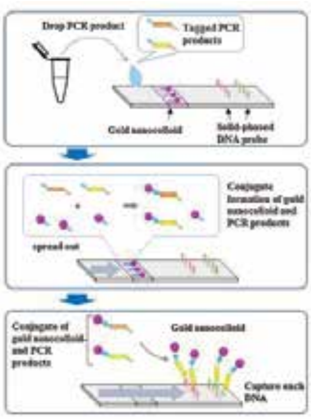
Furutani, S. et al. Anal Bioanal Chem 408: 5641, 2016

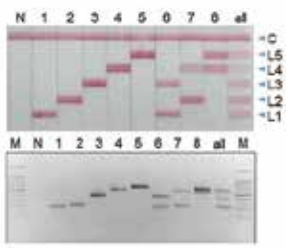
DNA Chromatography Chip (Kaneka)

"Fast & visual detection device" for multiplex PCR amplicons



DNA Chromatography Chip (Kaneka)





After PCR, 5 min for detection

High sensitivity (100 times)

Multiplex application available

Nagai S et al. Harmful Algae 51: 97, 2016

"Electronic-Nose" Technology

J Clin Microbiol. 2010 Nov;48(11):4235-8. Epub 2010 Aug 18.

Electronic-nose technology using sputum samples in diagnosis of patients with tuberculosis.

Kolk A, Hoelscher M, Maboko L, Jung J, Kuijper S, Cauchi M, Bessant C, van Beers S, Dutta R, Gibson T, Reither K.

Curr Opin Pulm Med. 2012 May;18(3):228-32.

Developments in novel breath tests for bacterial and fungal pulmonary infection.

Chambers ST, Scott-Thomas A, Epton M.

aDepartment of Pathology, University of Otago, Christchurch bDepartment of Infectious Diseases cDepartment of Respiratory Medicine, Christchurch Hospital, Christchurch, New Zealand

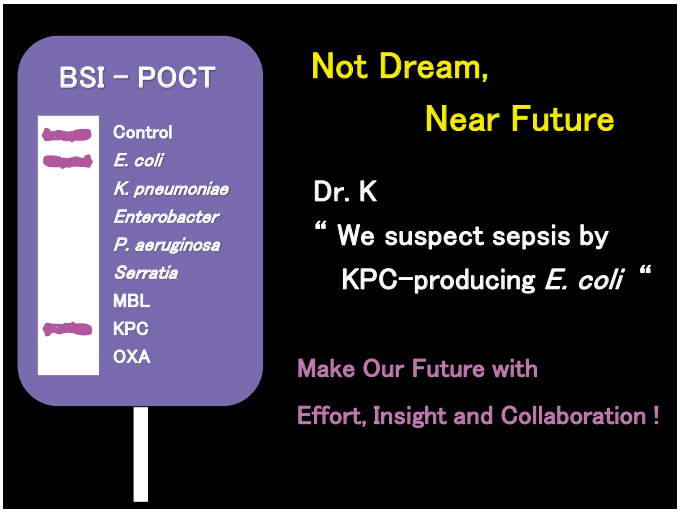
M. tuberculosis → Nicotinic acid → Gas Chromatography

Aspergillus → 2-pentylfuran → Gas Chromatography Mass Spectroscopy

New Diagnostic Methods in "AMR era"

1. Diagnostic Methods
   - "within 30 min" to Guide Antibiotic Use
   - Bacteria or Virus
   - AMR Mechanisms and Antibiotic Choice

2. Development of Novel Antimicrobials
   - Narrow, but Potent (Pathogen-directed Therapy)
   - Anti-Virulence or Anti-Resistance Therapy
   - Immuno-Modulatory Therapy



Dr. Stephen Sheng-Fong Lin

Position: Regional Medical Therapeutic Area Lead Department/ organization: Anti-infective, Asia-Pacific, PEH, Pfizer Inc.
Economy: Chinese Taipei

Educational Backgroud

LLM, Postgraduate Law School, Suchou University,
Medical Doctor, Medical School, National Taiwan University
Dilpoma, Trainee of Taiwan Infectious Disease Training Program

Professional Career

- 1996-1997 Attending physician, Infectious Division, Internal Medicine Department, National Taiwan University Hospital
- 1998-2000 Attending physician, Sun-Yat Sen Cancer Center Hosptial
- 2000-2004 Director of Infectious Disease Department, Far East Memorial Hosptial
- 2004-2006 Product Physician, Pfizer Inc.
- 2006-2007 Associate Medical Affairs Director, Pfizer Inc.
- 2007-2009 Country Medical Director, Pfizer Inc.
- 2009- Senior Regional Medical Director, Anti-infective, APAC Region, Pfizer Inc.

Publications

- Update of contemporary antimicrobial resistance rates across China: reference testing results for 12 medical centers. Diagnostic Microbiology and Infectious Disease 2013: 258–266
- Regional Resistance Surveillance Program Results for 12 Asia-Pacific Nations (2011), Antimicrobial Agents and Chemotherapy, 2013, 57(11): 5721–5726
- Echinocandins for management of invasive candidiasis in patients with liver disease and liver transplantation. Infection and Drug Resistance 2018:11 805–819
- Antimicrobial stewardship for acute-care hospitals: An Asian perspective. Infection Control & Hospital Epidemiology (2018), (In press)5.

Speech Abstract

Establish Network for AMR Surveillance in Asia Pacific Region

Antimicrobial agents were recognized the most important innovation to address the critical challenges of human morbidity and mortality when penicillin was discovered and manufactured in the era of World War II. However, more consumption of antimicrobial agents would trigger the emergence of challenges from microbial organisms' resistance. Less innovation of new antimicrobial agents with dry pipeline was another critical situation when we moved into the 21st century. Although there seems to be revitalized trend of antimicrobial agents development, the battle between human and microorganism would be an endless story. To ensure human can sustain the advantageous strength in this confrontation, several strategies and actions plans should be adopted and surveillance is one of the most important strategic pillars.

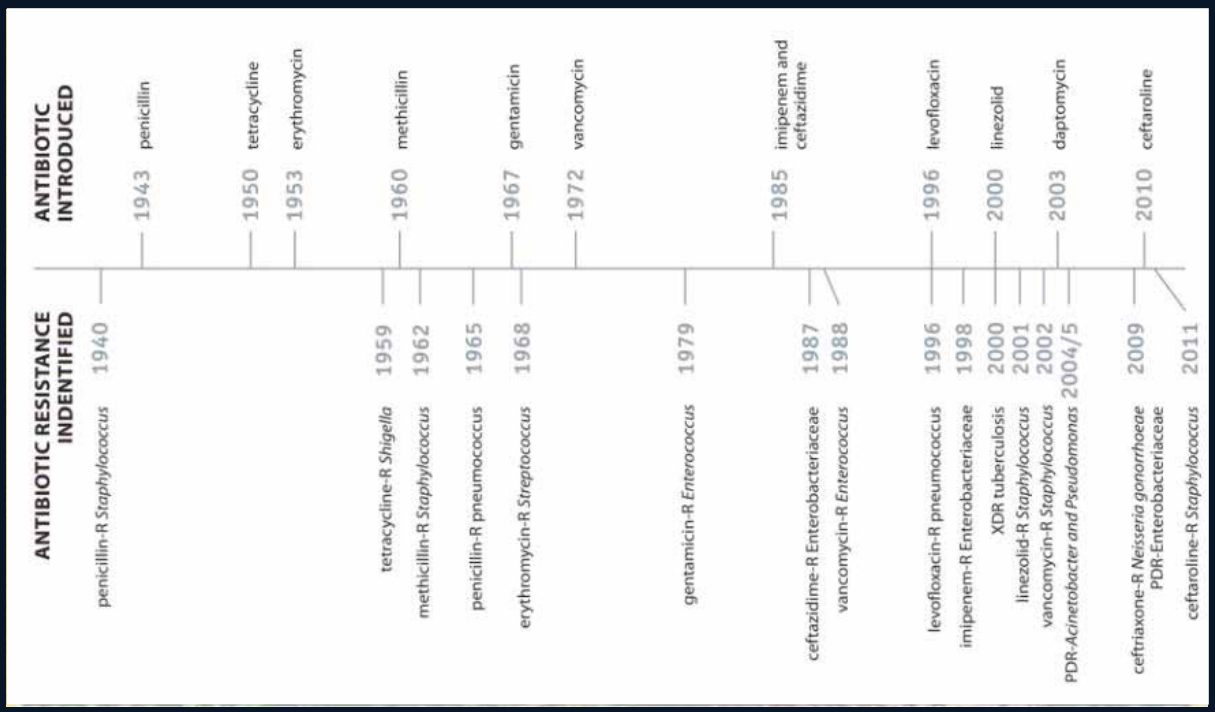
Surveillance is the system to help human to identify the emergence of antimicrobial resistance and its possible mechanism, guide the appropriate treatment of infections, and create the trend of innovative antimicrobial agent development. There will be review of readiness variation of effective surveillance system among APAC countries in this presentation. Furthermore, we will also go through several international surveillance programs sponsored by government institutes, academia body, and industries. In this review, we would also learn some lessons about the caveats in development of international surveillance system and trigger the insights of cross boundary collaborations to address the critical needs.

Establish network for AMR surveillance in Asia Pacific region

STEPHEN S. F. LIN, MD, LLM

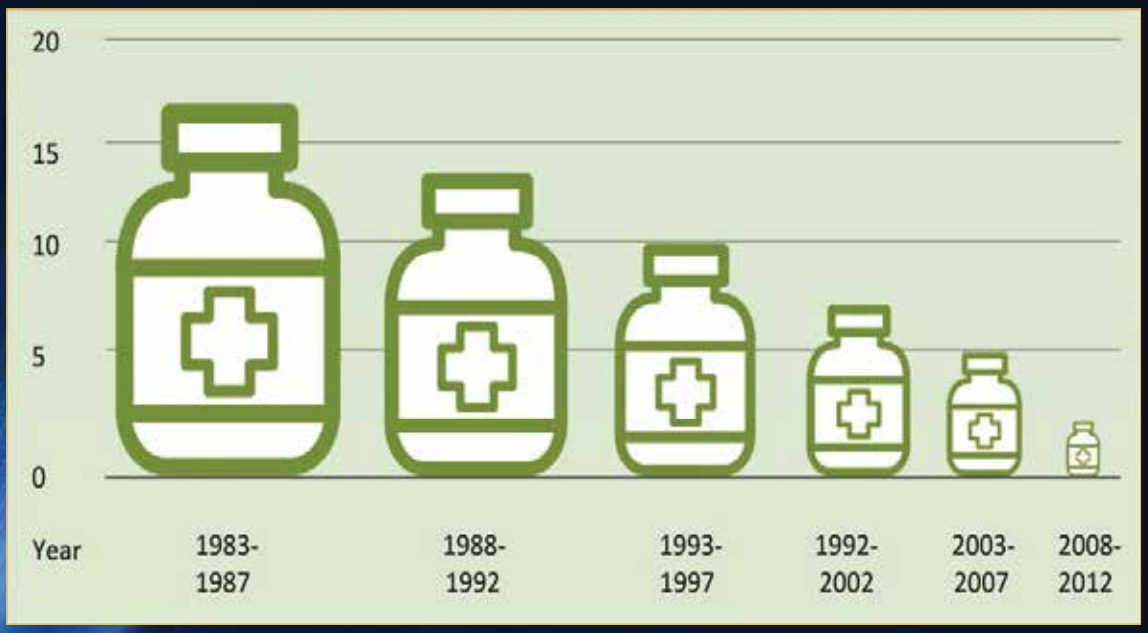
APAC REGIONAL MEDICAL THERAPEUTIC AREA LEAD, ANTI-INFECTIVES, *PFIZER INC.*

It would be an endless story ....



https://www.cdc.gov/drugresistance/about.html

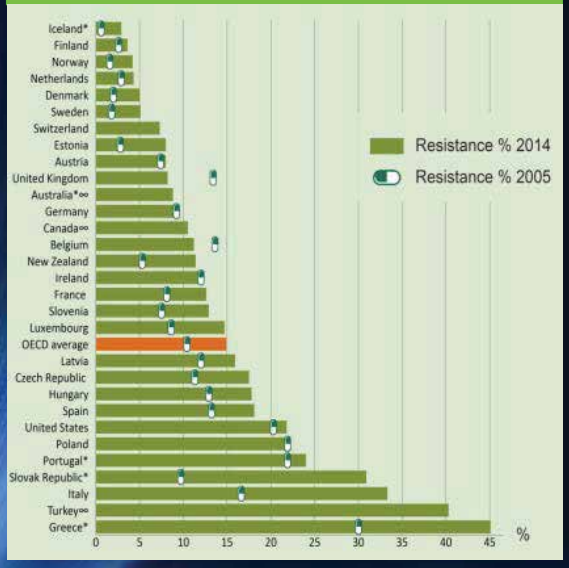
Number of new antimicrobials approved by the United States Food and Drug Administration since 1983



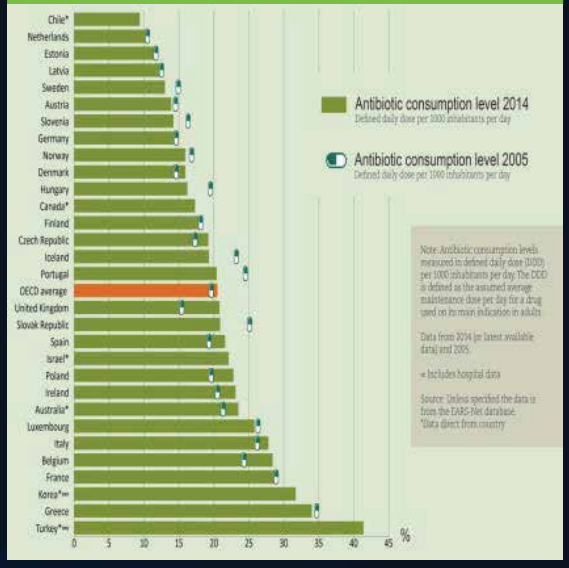
Source: OECD (2015). Antimicrobial resistance in G7 countries and beyond: economic issues, policies and options for action.

Antimicrobial resistance is a growing challenges across countries

TREND ACROSS OECD COUNTRIES ANTIBIOTICS RESISTANCE IS GROWING

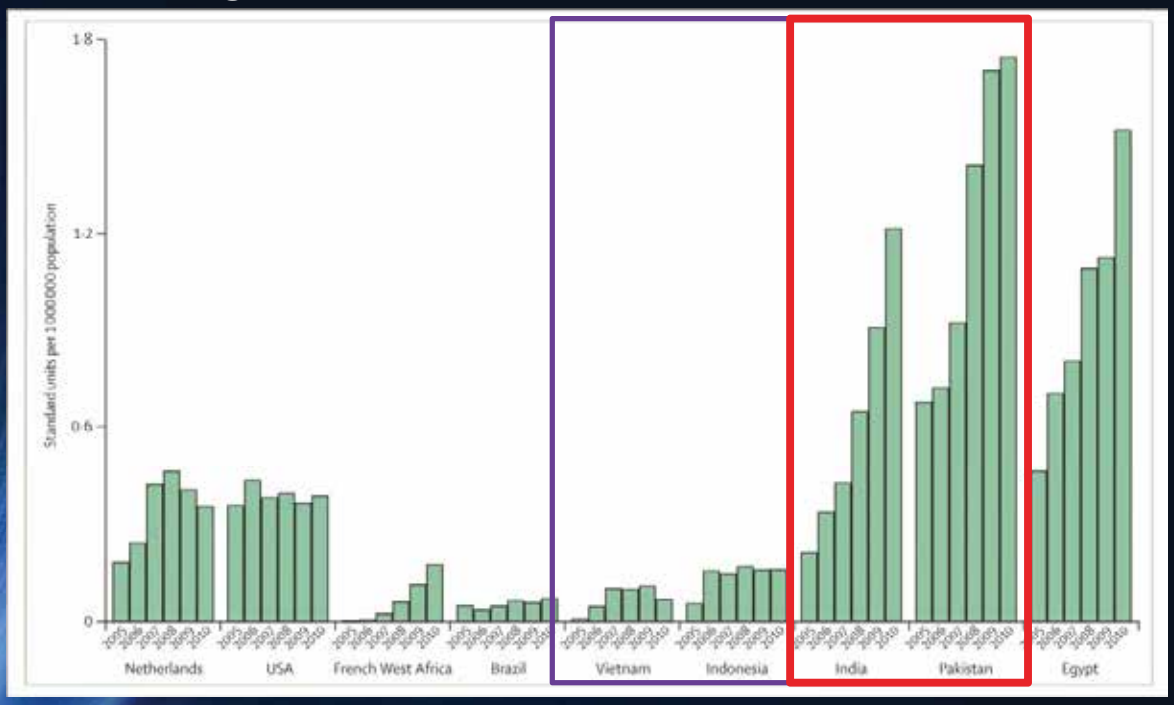


HUMAN CONSUMPTION OF ANTIBIOTICS REMAINED SUBSTANTIALLY STABLE BETWEEN 2005 AND 2014



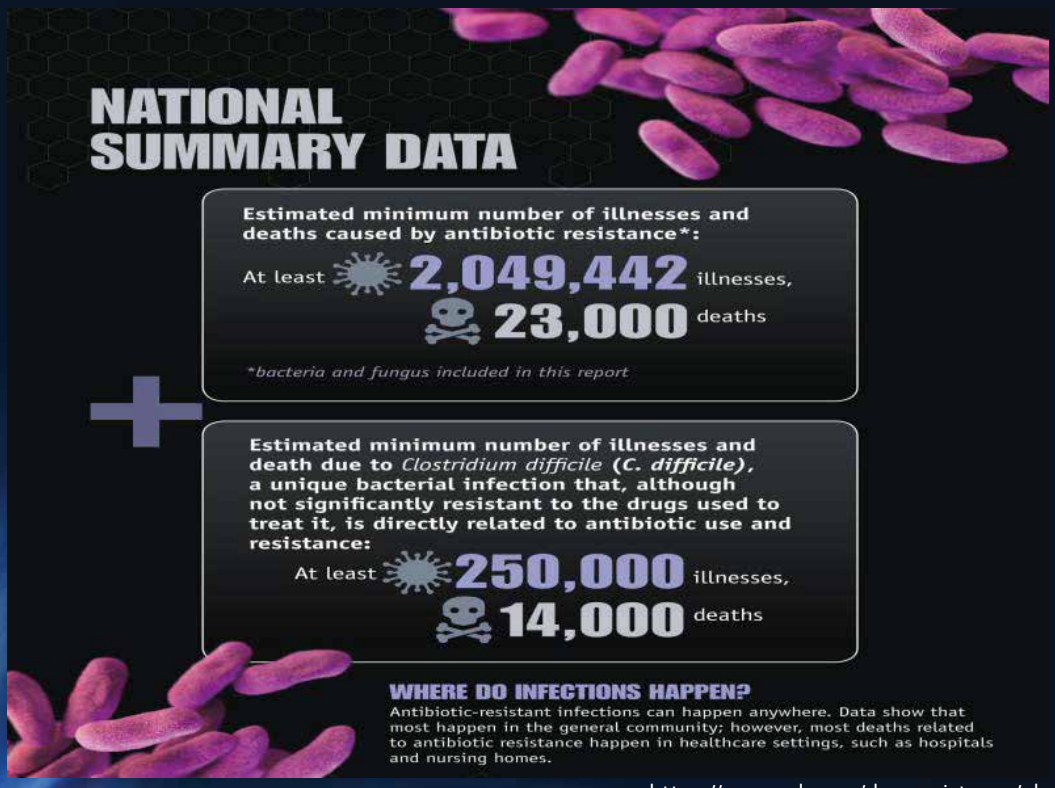
www.oecd.org/health/antimicrobial-resistance.htm © OECD 2016

Trends in retail sales of carbapenem antibiotics for Gram-negative bacteria in different countries



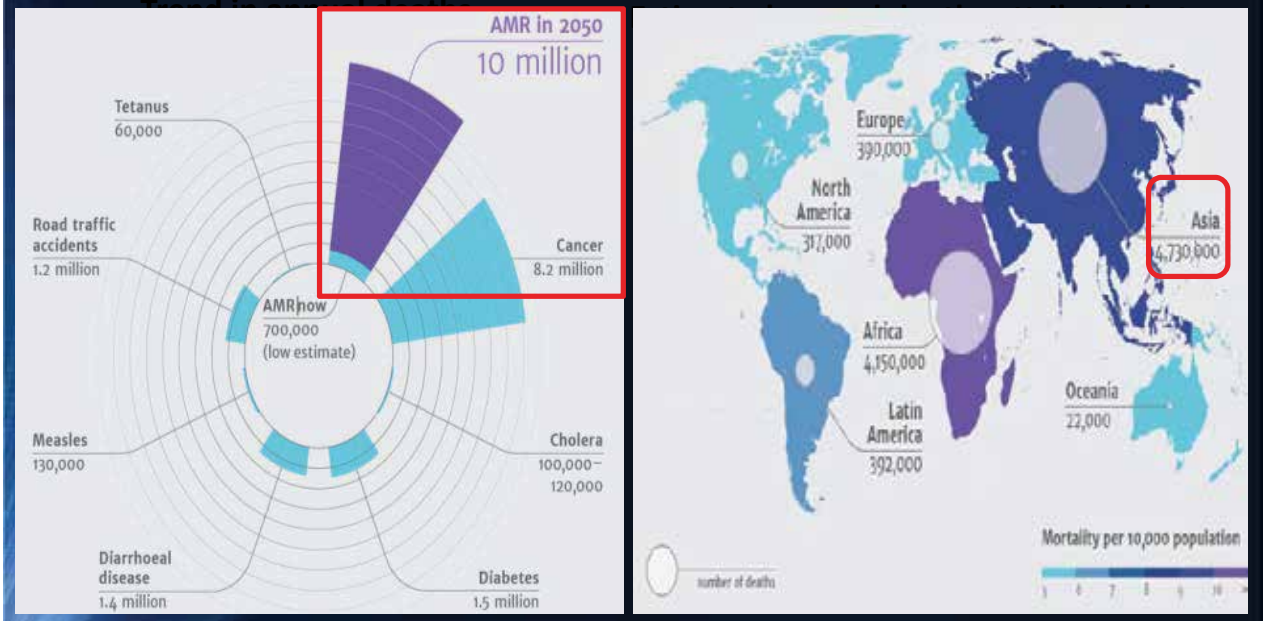
Based on data obtained from IMS Health's MIDAS™ database.
Ramanan Laxminarayan *et al Lancet Infect Dis* 2013 Nov. *at* http://dx.doi.org/10.1016/S1473-3099(13)70318-9

Impact of AMR to human community



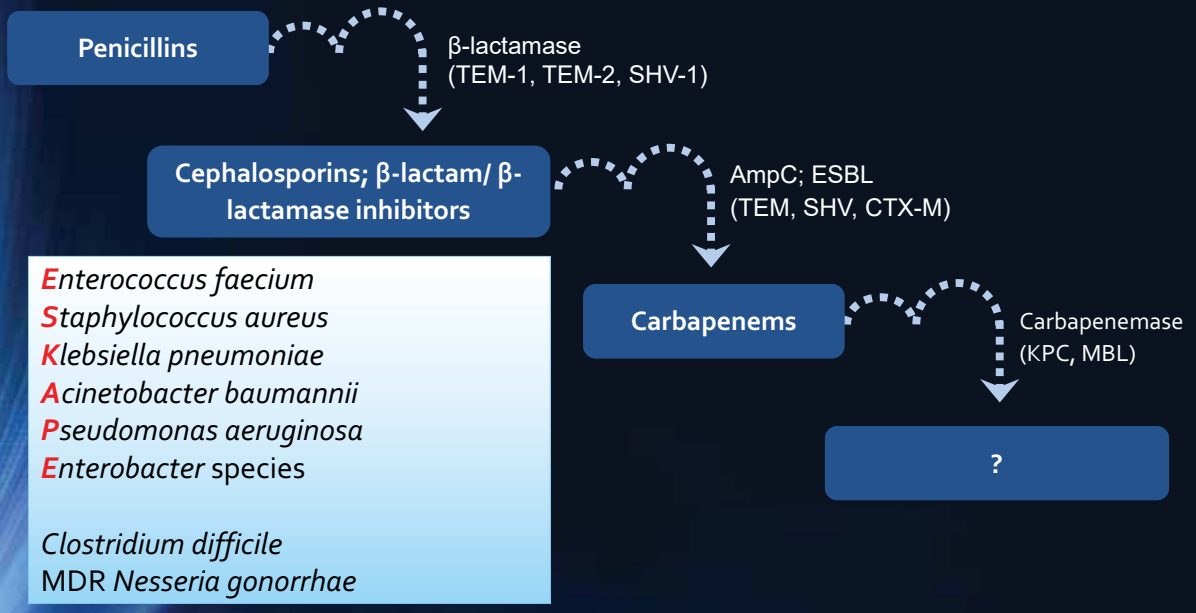
https://www.cdc.gov/drugresistance/about.html

Increasing Antibiotic Resistance Has the Largest Impact in Emerging Markets



Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. January 2016. Available at: http://amr-review.org/sites/default/files/Tackling%20drug-resistant%20infections%20-%20An%20overview%20of%20our%20work_LR_NOCROPS.pdf (accessed 18 Feb 2016)

Development of Antibiotics in Response to Resistance Due to β-Lactamases



MBL=metalllo-β-lactamase; TEM-1, TEM-2, SHV-1, TEM, SHV, CTX-M=types of β-lactamases.

Burgess DS, et al. *Am J Health-Syst Pharm*. 2008;65(suppl 2):S4-S15.

Mortality rate associated with resistant and MDR ESKAPE bacteria.

Authors	Hospital Wards	Bacteria	Mortality rate	P-value	References
Al Jarousha et al. (2009)	Neonatal ICU	MDR-*A. baumannii* (15/40)	37.5%	0.001	[54]
		Susceptible *A. baumannii* (12/100)	12%		
Anunnatsiri et al. (2011)	ICU	MDR-*A. baumannii* (22/24)	91.7%	0.001	[41]
		Susceptible *A. baumannii* (12/25)	48%		
Amer et al. (2015)	Emergency ICU /Pediatric ICU	CR-MBLP-*P. aeruginosa* (14/32)	43,8%	0.2	[64]
		CR-MBLN-*P. aeruginosa* (2/8)	25%		
Furtado et al. (2009)	ICU	Imipenem-resistant *P. aeruginosa* (31/63)	49%	0.02	[31]
		Imipenem-susceptible *P. aeruginosa* (61/182)	33%		
Marra et al. (2006)	ICU	ESBL-producing *K. pneumoniae* (18/56)	32.14%	0.042	[46]
		Non-ESBL *K. pneumoniae* (8/52)	15.38%		
Moreira et al. (2008)	ICU	ORSA (11/29)	37.9%	0.41	[47]
		OSSA (8/32)	25%		
Serefhanoglu et al. (2009)	ICU	MDR-ESBL-producing-*E. coli* and *K. pneumoniae* (7/30)	23.3%	0.606	[32]
		Non-MDR-ESBL-producing-*E. coli* and *K. pneumoniae* (12/64)	18.8%		
Tuon et al. (2012)	ICU	Carbapenem-resistant *P. aeruginosa* (13/29)	54.2%	0.043	[22]
		Carbapenem-susceptible *P. aeruginosa* (26/48)	44.8%		
Chen et al. (2012)	ICU	MRSA (25/75)	33%	0.01	[48]
		MSSA (8/43)	18.6%		
Fu et al. (2015)	ICU	XDR *A. baumannii* (31/39)	79.5%	0.1	[49]
		Non-XDR *A. baumannii* (38/86)	44.2%		
Jia et al. (2015)	ICU	Linezolid non-susceptible Enterococci (3/44)	6.8%	0.521	[50]
		Linezolid-susceptible Enterococci (2/44)	4.5%		
		Un-infected Control patients (3/176)	1.7%		
Yao et al. (2015)	ICU	MRSA (12/57)	21%	0.002	[35]
		MSSA (9/116)	8%		
Gomez Rueda et al. (2014)	ICU	Carbapenem resistant *K. pneumoniae* (31/61)	50.8%	0.042	[36]
		Carbapenem-susceptible *K. pneumoniae* (20/61)	32.7%		
		Un-infected control patients (25/122)	20.4%		
Kumar et al. (2014)	ICU	Carbapenem-resistant *A. baumannii* (9/33)	27.3%	0.074	[37]
		Carbapenem-susceptible *A. baumannii* (3/32)	9.4%		
Nazer et al. (2015)	ICU	MDR-*A. baumannii* (118/161)	73.3%	0.015	[53]
		Non-MDR-*A. baumannii* (142/232)	61.2%		
Deris et al. (2011)	ICU	Imipenem-resistant -*A. baumannii* (6/15)	42.9%	0.201	[39]
		Imipenem-susceptible *A. baumannii* (9/41)	24.3%		
Inchai et al. (2015)	ICU	MDR-*A. baumannii* (10/72)	13.9%	0.001	[44]
		XDR- *A. baumannii* (88/220)	40%		
		PDR-*A. baumannii* (7/12)	58.3%		
Jamulitrat et al. (2009)	ICU	Imipenem-resistant-*A. baumannii* (35/67)	52.2%	0.001	[59]
		Imipenem-susceptible *A. baumannii* (26/131)	19.9%%		
Thatrimontrichai et al. (2016)	ICU	Carbapenem-resistant *A. baumannii* (10/63)	15.9%	0.01	[19]
		Carbapenem-susceptible *A. baumannii* (1/13)	7.7%		
		Un-infected control patients (0/25)	0%		
Topeli et al. (2000)	ICU	MRSA (15/46)	32.6%	0.02	[21]
		MSSA (7/55)	12.7%		

RC Founou *et al* PLOS ONE https://doi.org/10.1371/journal.pone.0189621 December 21, 2017

Foster the development of new innovative antimicrobial agents

U.S. Department of Health & Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

GAIN Act and Qualified Infectious Disease Product Program (QIDP)

	Year initiated	Benefits	Data required	Antibacterial examples and approval year	Notes
Accelerated Approval Pathway	1992	• FDA approval based on surrogate end point, offering shorter development time • Clinical trials must be conducted post-approval to confirm clinical benefit	• Not specified, however must show advantage over existing therapies and effect on surrogate end point likely to predict clinical efficacy • Sponsor must discuss this pathway possibility with FDA during development	• Quinupristin/dalfopristin 1999 • Bedaquiline 2012	• Inception due to AIDS epidemic and need for zidovudine (AZT) on market • Majority of drugs approved by this pathway include oncological agents
Fast Track Designation	1997	• More frequent meetings with FDA • More frequent written communication from FDA • Rolling NDA review	• Preliminary nonclinical, mechanistic, or clinical data • Of note, typical Phase 3 data still required for FDA approval • Can be requested upon IND submission; FDA has 60 days to respond	• Ceftaroline 2010 • Fidaxomicin 2011 • Bedaquiline 2012 • Dalbavancin[a] 2014 • Oritavancin[a] 2014 • Tedizolid[a] 2014 • Ceftolozane/tazobactam[a] 2014 • Ceftazidime/avibactam[a] 2015	• Addresses broad range of diseases, including but not limited to HIV/AIDS, Alzheimer's, cancer, epilepsy, cardiovascular, endocrine • GAIN Act of 2012 enables QIDP designated drug candidates to receive Fast Track Designation
Priority Review	1992	• Shortens review of NDA from 10 months to 6 months	• Data contained in NDA submission • Must show significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of a serious condition	• Fidaxomicin 2011 • Bedaquiline 2012 • Dalbavancin[a] 2014 • Oritavancin[a] 2014 • Tedizolid[a] 2014 • Ceftolozane/tazobactam[a] 2014 • Ceftazidime/avibactam[a] 2015	• GAIN Act of 2012 enables QIDP designated drug candidates to have Priority Review
Breakthrough Therapy Designation	2012	• More frequent meetings with FDA • More frequent written communication from FDA • Rolling NDA review • Intensive guidance on efficient development program • Involvement of FDA to expedite development	• Preliminary clinical data • Must show substantial improvement on clinically significant end point(s) over available therapies	None	• Largely oncology and orphan diseases • Several new agents for Hepatitis C infection have received this designation • Microbiome therapeutic (SER-109) and microbiome restoration therapy (RBX2660) for recurrent *Clostridium difficile* infection and monoclonal antibody for *Staphylococcus aureus* infections have received status (pipeline agents)

EXPERT REVIEW OF ANTI-INFECTIVE THERAPY, 2017 VOL. 15, NO. 00, 425–433
http://dx.doi.org/10.1080/14787210.2017.1308251

Antibiotic Drug Details, Development Milestones, and ESKAPE Status: FDA-Approved Antibiotics, 2010-2015

Drug	IND Filed	NDA Filed	Approval Date	Current Manufacturer	Drug Class (Year of Discovery)	Method of Administration	Novel Mechanism of Action	Indications	In Vitro Activity Against ESKAPE Pathogens?
Ceftaroline	December 2004	December 2009	29 October 2010	Actavis	Cephalosporin (1928)	Intravenous	No	ABSSSI; CABP	Yes
Fidaxomicin	August 2003	November 2010	27 May 2011	Cubist Pharmaceuticals (subsidiary of Merck)	Macrolide (1948)	Oral	No	CDAD and prevention of recurrences	No*
Bedaquiline	November 2006	June 2012	28 December 2012	Janssen Research and Development (Johnson & Johnson)	Diarylquinoline (1997)	Oral	Yes	Pulmonary tuberculosis caused by multidrug-resistant tuberculosis	No†
Dalbavancin	July 2000	September 2013	23 May 2014	Actavis	Lipoglycopeptide (1953)	Intravenous	No	ABSSSI	No
Tedizolid	November 2007; August 2009	October 2013	20 June 2014	Cubist Pharmaceuticals (subsidiary of Merck)	Oxazolidinone (1955)	Oral; intravenous	No	ABSSSI	No
Oritavancin	August 1996	December 2013	6 August 2014	The Medicines Company	Glycopeptide (1953)	Intravenous	No	ABSSSI	No
Ceftolozane-tazobactam	July 2009	April 2014	19 December 2014	Cubist Pharmaceuticals (subsidiary of Merck)	Cephalosporin (1928) + β-lactamase inhibitor	Intravenous	No	CIAI; CUTI	Yes
Ceftazidime-avibactam	January 2008	June 2014	25 February 2015	AstraZeneca/ Actavis	Cephalosporin (1928) + β-lactamase inhibitor	Intravenous	No	CIAI; CUTI	Yes

ABSSSI = acute bacterial skin and skin-structure infection; CABP = community-acquired bacterial pneumonia; CDAD = *Clostridium difficile*-associated diarrhea; CIAI = complicated intra-abdominal infection; CUTI = complicated urinary tract infection; ESKAPE = *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species; IND = investigational new drug; NDA = new drug application.
* *Clostridium difficile* is a Centers for Disease Control and Prevention urgent-threat pathogen.
† Multidrug-resistant tuberculosis is a global health priority.

Ann Intern Med. 2016;165:363-372. doi:10.7326/M16-0291

Global action plan on antimicrobial resistance from WHO

- Alert to this crisis, the May 2015 World Health Assembly adopted a global action plan on antimicrobial resistance, which outlines five objectives:
- to **improve awareness and understanding** of antimicrobial resistance through effective communication, education and training;
- to strengthen the knowledge and evidence base through **surveillance and research**;
- to reduce the incidence of infection through effective **sanitation, hygiene and infection prevention measures**;
- to **optimize the use of antimicrobial medicines** in human and animal health; and
- to develop the economic case for **sustainable investment** that takes account of the needs of all countries and to increase investment in **new medicines, diagnostic tools, vaccines and other interventions.**

http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/

Four Core Actions to Fight Resistance

US CDC

https://www.cdc.gov/drugresistance/about.html

The key objective of AMR surveillance system

- To providing early warning of emerging problems
  - monitoring changing patterns of resistance,
  - targeting and evaluating prevention and control measures
- Assisting researchers in developing new drugs
- Providing good patient care
  - Development of clinical guidance of empirical treatment of infectious diseases
- Improve understanding of the relationship between drug use and resistance, identify and anticipate gaps in availability of existing drugs, and help identify preventive interventions.

https://www.cdc.gov/drugresistance/actionplan/surveillance1.html

Lancet Infect Dis 2018: 18 e99-e106

The key directives of impact by well established surveillance system

- Therapy guidelines *
- Antibiotic formulary *
- Antibiotic stewardship programmes *
- Public health interventions
- Infection control policies
- Antimicrobial development.

***The elementary and starting goals of surveillance program**

Lancet Infect Dis 2018: 18:e99-106

The key merits of well functioned AMR surveillance system to address the objectives

- Accurate
- Reliable
- Flexible access
- Timely updated

Difference of various surveillance program

- **Isolate based**
  - Data on resistance patterns within the **bacterial population**
    - Percentage of resistance to a variety of antimicrobial agents
    - Clinical driven and impacted by clinical behavior
    - Potentially biased with under- or over -estimated of AMR challenges
- **Sample based***
  - Data of both basic insight into patterns and the extent of AMR in **the tested populations**
    - Incidence of stratified tested population
    - allows detecting the most frequent type of resistant infections within that population and it allows stratification to identify AMR patterns and strategic foci

2018 GLASS report
* Preferred program by GLASS

Difference of various surveillance program (cont'd)

Passive surveillance	Active surveillance	Sentinel surveillance*
data from **voluntary reporting** without stimulating report by reminder or controlled protocol.	Driven by **protocol** with active monitoring of reporters' performance and data quality (protoocl-driven)	data collection from **selected** , either randomly or intentionally**, a small group** of health workers with protocol guidance
requested of each health worker is minimal	specific feedback to improve their performance	Sentinel reporters should be trained
few incentives for reporters	stimulus to reports in the form of individual feedback or other incentives	Incentives for reporters
data would be **incomplete**	**more complete** data collection	more detailed data on cases of illness
least costly	substantially more time and resources needed	requires more time and resources

* may be the best type of surveillance if more intensive investigation of individual case is needed

http://conflict.lshtm.ac.uk/page_02.htm

Snapshot of AMR surveillance system across APAC countries (I)

Country	Surveillance program	accessibility	Key natures
Japan	JANIS https://janis.mhlw.go.jp/english/about/index.html	Website access of the annual report (since 2013)	Passive surveillance 1000+ sites send the report to repository monthly
Korea	KONSAR since 1997	Publication of specific analysis report	Passive surveillance
Philippines	http://arsp.com.ph/ (25 years)	Annual report since 2014 to 2017	24 sentinel sites to send results to central lab with WHONET
Thailand	NARST since 1998 http://narst.dmsc.moph.go.th/	Website access of annual report and AMR data	Passive surveillance guided with well structured manual

Snapshot of AMR surveillance system across APAC countries (II)

Country	Surveillance program	Accessibility	Key natures
Hong Kong	CHP https://www.chp.gov.hk/en/statistics/data/10/641/697/3345.html	Website access of the annual report of antimicrobial susceptibility data of targeted pathogens (since 2014))	Passive surveillance
Australia	AURA https://www.safetyandquality.gov.au/antimicrobial-use-and-resistance-in-australia/about-aura/	Website access of the annual report of since 2011 (updated to 2017)	Passive surveillance

Snapshot of AMR surveillance system across APAC countries (III)

Country	Surveillance program	Accessibility	Key nature
Indonesia		Assessment Tool for Laboratory and Antimicrobial Resistance (ATLASS) kicked off in Oct. 2017	
Malaysia	NSAR since 2002 http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html	Website access of the annual report of since 2002	Passive surveillance
Singapore*	Driven by NAT in 2011, NARCC in 2014, and National Strategic Action Plan on Antimicrobial Resistance in 2015	Publications	Passive surveillance among public hospitals

*NAT: the National Antimicrobial Taskforce ; NARCC: National Antimicrobial Resistance Control Committee . It is integrated surveillance for antimicrobial resistance and antimicrobial utilization across sectors for human, animals, food and environment.

Snapshot of AMR surveillance system across APAC countries (IV)

Country	Surveillance program	Accessibility	Key nature
Vietnam	National Action Plan to Combat Antimicrobial Resistance since 2017#	NA yet	sentinel surveillance system involving 16 laboratories and six model hospitals.
India	NCDC	Access report at website	10 Network laboratories to initiate antimicrobial resistance surveillance on four common bacterial pathogens*
	ICMR - ICMR's surveillance network at http://14.139.60.53/iamrsn/	Accessible report at website since 2014 and published articles	Isolates driven

US CDC collaborates with WHO-Vietnam, Oxford Clinical Research Unit, American Society for Microbiology, Association of Public Health Laboratories, and PATH to directly support implementation of Vietnam's National Action Plan to Combat Antimicrobial Resistance

* *Klebsiella*, *Escherichia coli*, *Staphylococcus aureus*, *and Enterococcus* species

GLASS Report- Early implementation 2016-17

Great variation of the status of country implementation of surveillance system

- Bangladesh, Bhutan, India, Indonesia, Maldives, and Myanmar are at the early stage of surveillance set up, and surveillance guidelines have been developed but not fully implemented. AMR surveillance data exist but are not centralized, with limited analysis and representativeness.
- Three countries (Nepal, Sri Lanka, and Thailand) possess standardized national AMR surveillance data. However, surveillance development is at an early stage and the scope of antibiotics under surveillance is limited
- 11 countries, including Australia, Cambodia, China, Fiji, Japan, Malaysia, Mongolia, New Zealand, Philippines, Republic of Korea and Viet Nam have already developed their National Action Plans, with Viet Nam currently undertaking its first review of its plan

On 22 October 2015 WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS)

The GLASS objectives

- Foster national surveillance systems and harmonise global standards;
- Estimate the extent of AMR globally by monitoring selected indicators;
- Collect surveillance data needed to inform and estimate AMR burden;
- Routinely analyse and report global data on AMR;
- Detect emerging resistance and its international spread;
- Assess the impact of interventions.

Global Antimicrobial Resistance Surveillance System (GLASS) Report- Early implementation 2016-17

GLASS

- GLASS is a system that enables standardised global reporting of official national AMR data. It collaborates with **existing regional and national AMR surveillance networks** to produce timely and comprehensive data.
- GLASS **relies upon countries to conduct their own national surveillance**. GLASS promotes the use of globally agreed and standardised methods for compiling data both locally and nationally, and the gathering of information on selected AMR indicators in a harmonised way across and within countries.

Global Antimicrobial Resistance Surveillance System (GLASS) Report- Early implementation 2016-17

GLASS Enrolment map in 2017

Global Antimicrobial Resistance Surveillance System (GLASS) Report- Early implementation 2016-17

Asian Network for Surveillance of Resistant Pathogens(ANSORP)

- ANSORP is the first and only international study group for the surveillance of AMR in the Asian region and over the past 18 years
- It is a very unique model worldwide, given that it was **voluntarily organised by physicians,** specifically focuses on AMR and infectious diseases
  - 14 hospitals from 11 Asian countries in 1996
  - 120 hospitals in 14 countries or areas in 2014
- **A series of international studies – 20 publications found at PubMed**
  - ***Streptococcus pneumoniae***
  - **MRSA**
  - **MDR GNB (metallo β lactamase producers)**
  - **VRE**

APFID_Intl_Innovation_149_Research_Media

SENTRY Antimicrobial Surveillance Program

- Establishment by JMI Laboratory in 1997
- Monitors worldwide pathogens and the changes in resistance patterns over time through **centralized testing** and **utilizing reference susceptibility methods**
- Sites submitting organisms through a **prevalence based approach** across a number of different types of infections, including bloodstream, skin and soft tissue, respiratory, urinary tract, pathogens from patients hospitalized with pneumonia, intra-abdominal and invasive fungal infections.
- New compounds and other agents can easily be integrated into the SENTRY platform by establishing agreements at the beginning of the calendar year and transferring the client compound and request to be incorporated into the panel production process.
- There are over 200 sites worldwide that participate annually.
- 2019 publications, including 497 full articles searched at PubMed and other posters and abstracts

https://www.jmilabs.com/sentry-surveillance-program/
sentry-mvp.jmilabs.com

Study for Monitoring Antimicrobial Resistance Trends (SMART)

- SMART monitors the in vitro susceptibility of clinical bacterial isolates to antimicrobials in **intra-abdominal** and **urinary tract infections** worldwide since 2002 and 2009, respectively.
- The program is sponsored by Merck & Co., *Inc.*, Started in 2002 and 198 countries are involved
- **Isolates based surveillance**:
  - Each site need to collect up to 100 consecutive aerobic and facultative gram-negative bacilli from patients with intra-abdominal infections and Record the duration of hospitalization (<48 hours or ≥8 hours) at time of isolate recovery
- A total of 21,584 clinical bacterial isolates were collected in 2011.
  - 13,356 were intra-abdominal infection isolates
  - 7,989 were urinary tract infection isolates
- 39 published articles and 56 congress posters were developed up to 2012
- Data is accessible at website (http://www.globalsmartsite.com/smart/index.aspx) by registered visitors

http://partnerships.ifpma.org/partnership/study-for-monitoring-antimicrobial-resistance-trends-smart

Antimicrobial Testing Leadership and Surveillance (ATLAS)

- ATLAS includes a fully-searchable database initially built since 2004 with data from the TEST (Tigecycline Evaluation Surveillance Trial) surveillance program, but now also encompassing data from the AWARE (Assessing Worldwide Antimicrobial Resistance Evaluation) and INFORM (International Network for Optimal Resistance Monitoring) programs.
- **Isolates based surveillance**
  - Each site will collect, identify, store, and ship fresh clinical Gram-positive and -negative aerobic isolates from documented cIAI, cUTI, cSSSI, LRTI and blood sources with information of sources (ICU, wards, etc.). All isolates will be sent to International Health Management Associates, Inc. (IHMA's) central laboratory, in Schaumburg, Illinois where the isolates will be further evaluated (phenotyping and genotyping) and stored. Only isolates considered to be the potential causative agent of the patient's infection should be included in this study.
- The registered user is able to analyze the data from either or both programs, and produce reports in tabular and graphical formats by visiting the website at https://atlas-surveillance.com
- The ATLAS database will be regularly updated (every 6 to 8 months).

Antimicrobial Testing Leadership and Surveillance (ATLAS)

	TEST	INFORM/AWARE	Combined
Total Number of Isolates	415,388	218,432	631,680
Total Number of Countries Contributing Data	70	40	73*
Total Number of Sites Contributing Data	689	234	780*
Total Number of Pathogens	196	146	287
Total Number of Antimicrobials	21	40	44
Years Contributing Data	2004-2017	2012-2017	2004-2017

* There are duplicates of countries and sites between TEST and INFORM/AWARE

- 650 posters and 63 full articles were developed up to 2017

The differences among the international surveillance programs

	GLASS	ANSORP	SENTRY	SMART	ATLAS
Sponsor	WHO	Academia (APFID)	JMI Lab	Merck &Co. Inc.	Pfizer Inc.
Nature	Passive	Passive	Passive	Passive	Passive
Surveillance types	Variable	Isolates based	Protocol driven	Protocol driven	Protocol driven
Specific diseases focus	none	Project driven	Variable per client's needs	cIAI cUTI	cIAI , cUTI, cSSSI, LRTI, BSI
Accessibility	Annual report	publications	Publications	Website and publications	Website and publications
Validation process	absent	absent	Central laboratory validation	Central laboratory validation	Central laboratory validation
Timely update	Annual	variable	Annual report	Annual report	Every 6-8 months

cIAI: complicated intra-abdominal infections, cUTI: complicated urinary tract infection, cSSSI: complicated skin and skin structure infection, LRTI: lower respiratory tract infection, BSI: blood stream infection

Value of international surveillance programs

- Provide reliable global in vitro susceptibility data
- Identify changes in the resistance rates of global, regional and local pathogens
- Recognize the emergence of new resistance mechanisms
- Detect trends in multidrug resistance by analysing data longitudinally over time

Features of 42 European national and regional surveillance systems on antimicrobial resistance included in review

Despite the efforts of European Centre for Disease Control and Prevention (ECDC) and other organizations, wide heterogeneity in procedures and indicators still exists.

Characteristic	Variable	*n* (%)
Source of data	Laboratory only	33 (78.5)
	Laboratory and patients' charts	8 (19.0)
	Unknown/not reported	1 (2.3)
Duplicates policy	Duplicates excluded	25 (59.5)
Case definition	Isolates from clinical samples	22 (52.3)
	Infections	10 (23.8)
	Unknown/not reported	10 (23.8)
Indicators	Proportion of resistant isolates[a]	27 (64.2)
	Cumulative incidence[a]	11 (26.1)
	Incidence density[a]	12 (28.5)
	Unknown/not reported	8 (19.0)
Pathogens specified	*Streptococcus pneumoniae*	32 (76.1)
	Staphylococcus aureus	41 (97.6)
	Enterococcus spp.	31 (73.8)
	Escherichia coli	38 (90.4)
	Klebsiella pneumoniae	36 (85.7)
	Pseudomonas aeruginosa	34 (80.9)
	Acinetobacter baumannii	35 (83.3)
	Clostridium difficile	22 (52.3)

[a] Not mutually exclusive.

M. Núnez-Núnez *et al.* *Clinical Microbiology and Infection* 24 (2018) 105 - 109

Limitations of surveillance program

Lessons learned from EARS-Net (ECDC)

Structural Problems

- **Different objectives**
- **Insufficient coordination and sharing of information**
- **Inadequate standardization** of data collected and methods of microbiological testing (including susceptibility testing), and data sharing policies
- **Delay in publication** and insufficient publication for food surveillance data

Laboratory-based surveillance issues

- **Insufficient associated** and relevant epidemiological, clinical, and outcome data
- **Genetic typing** and characterization not routinely included
- **Biases** introduced by sample collection protocols

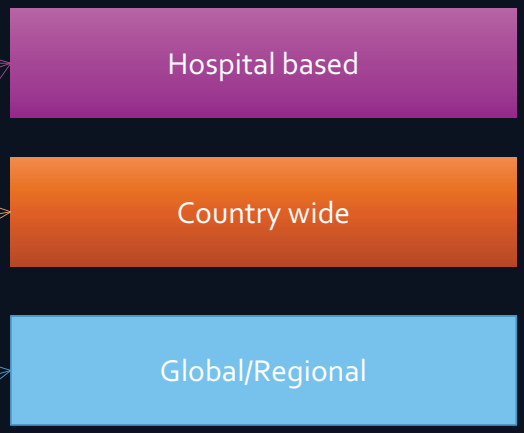
Insufficient coordination between human, animal, and food systems

- Data collection in animals directed at disease eradication and not detection of resistance to either animal or human drugs
- Coverage of only veterinary pathogens and antibiotics in animal and food surveillance systems

Lancet Infect Dis 2018: 18 e99-e106
http://dx.doi.org/10.1016/S1473-3099(17)30485-1

The key utility of different surveillance programs

- Therapy guidelines
- Antibiotic formulary
- Antibiotic stewardship programmes
- Public health interventions
- Infection control policies
- Identify emergence of resistant bugs with warning system
- Antimicrobial development.



Necessity of surveillance program across levels: Hospital based, country wide, international (region or global)

The key elements of collaborative surveillance programs

- Standardized methodology of susceptibility tests
- Common objectives with key foci
- Unified protocol of isolates collections
- Timely updated data accessibility to guide the treatment and antimicrobial stewardship
- Generation of clinical impact
  - Enhancement the benefits and minimize for patients
  - Changes of clinicians' behavior
  - Impact on appropriate uses of antimicrobial agents in agricultures and veterinary industry

It is critical to have collaboration among all stakeholders

- Government
- Academia
- Clinical institutes
- Pharmaceuticals
- Industries

Dr. Tsai-Ling Yang Lauderdale

Position: Investigator

Department/organization: National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes

Economy: Chinese Taipei

Educational Background

- Ph.D. Graduate School of Medicine, Juntendo University, Tokyo, Japan. Doctor of Medical Science.
- M.S. State University of New York (SUNY) Upstate Medical University, Syracuse, NY. Medical Technology specializing in Microbiology.
- B.S. SUNY Upstate Medical University, Syracuse, NY. Medical Technology.

Professional Career

- 2014- Investigator. National Institute of Infectious Diseases and Vaccinology (NIIDV), National Health Research Institutes (NHRI).
- 2006-2014 Associate Investigator. NIIDV, NHRI.
- 2001-2006 Assistant Investigator. NIIDV (formerly Division of Infectious Diseases/ Division of Clinical Research), NHRI.

Publications

- Kuo SC, Huang WC, Huang TW, Wang HY, Lai JF, Chen TL, Lauderdale TL. Molecular epidemiology of emerging blaOXA-23-like and blaOXA-24-like-carrying Acinetobacter baumannii in Taiwan. Antimicrob Agents Chemother. 2018;62:pii: e01215-17.
- Wu CJ, Lai JF, Huang IW, Hsieh LY, Wang HY, Shiau YR, Lauderdale TL. Multiclonal emergence of levofloxacin-resistant group B Streptococcus,. J Antimicrob Chemother. 2017;72:3263-71.
- Wang JT, Huang IW, Chang SC, Tan MC, Lai JF, Chen PY, Lauderdale TL. Increasing resistance to fusidic acid among clinical isolates of MRSA. J Antimicrob Chemother. 2017;72:616-618.
- Chen YT, Lai YC, Tan MC, Hsieh LY, Wang JT, Shiau YR, Wang HY, Lin AC, Lai JF, Huang IW, Lauderdale TL. Prevalence and characteristics of pks genotoxin gene cluster-positive clinical Klebsiella pneumoniae isolates in Chinese Taipei. Sci Rep. 2017;7:43120.
- Kuo SC, Huang WC, Wang HY, Shaiu YR, Cheng MF, Lauderdale TL. Colistin-resistance gene mcr-1 in E. coli isolates from human and retailed meats, Chinese Taipei. J Antimicrob Chemother 2016;71:2327-9.

Speech Abstract

Longitudinal Multicenter Surveillance on AMR

Antimicrobial resistance (AMR) is a global public health threat. Longitudinal multicenter surveillance plays an important role in the control of AMR by helping to define the extent of the problem, detect emerging resistance, and identify specific problems that exist locally. These data can be used to advocate for intervention measures and then assess the impact of intervention. In 1998 NHRI implemented a multicenter AMR surveillance program, called TSAR, to monitor antibiotic resistance of clinical bacterial isolates recovered from inpatients and outpatients. Report of high rates of resistance to first-line agents found in TSAR I (1998) lead to a government policy to restrict antibiotic use for outpatients with acute upper respiratory infections. Ten rounds of TSAR have been completed to date and TSAR has expanded to include not only phenotypic surveillance but also genotypic studies on selected AMR species. Since 2002, TSAR isolates have been collected from the same 25-28 medical centers and regional hospitals located in the 4 regions following similar collection protocols. TSAR data showed that, following the 2001 policy to restrict antibiotic use, significant decrease in erythromycin resistance occurred in Group A *Streptococcus*. However, multidrug-resistance is prevalent in many other species of isolates from hospital inpatients as well as those from outpatients. In addition, significant increase in resistance to broad-spectrum agents have occurred, including extended-spectrum ß-lactam resistance in *E. coli* from outpatients, carbapenem resistance in *Acinetobacter baumannii* and *Klebsiella pneumoniae*, vancomycin resistance in *Enterococcus faecium* and MRSA prevalence remains high albeit stable. Plasmid-mediated colistin resistance, *mcr*-1, has also been detected. Emergence and increase of fluoroquinolone (FQ) resistance in both Gram-positive and Gram-negative organisms have also been observed, which lead to investigations on FQ consumption and usage. These findings will be discussed at this presentation.

Longitudinal Multicenter Surveillance on AMR

Tsai-Ling Yang Lauderdale (楊采菱)
National Institute of Infectious Diseases and Vaccinology (NIIDV)
National Health Research Institutes (NHRI)

Why?

- Antimicrobial resistance (AMR) is a global public health threat
- "Determining the scope of the problem is essential for formulating and monitoring an effective response to AMR"

  from WHO Antimicrobial Resistance: global report on surveillance 2014

Background

- In 1998, **Dr. Monto Ho** established the "Microbial Infections Reference Laboratory (MIRL)" to carry out the mission of "Research and control of antimicrobial resistance"
- Aims of MIRL: **Surveillance, Research, Service, and Advocacy**
- To attain the first aim, Dr. Ho also instituted the Taiwan Surveillance of Antimicrobial Resistance (**TSAR)** program in 1998
- Objective of TSAR: Systematically document, store, and track pathogenic microbes and their antimicrobial susceptibilities
- Targets of TSAR study: Bacterial isolates recovered from clinical samples of inpatients and outpatients by hospitals

Stages of TSAR Related Work

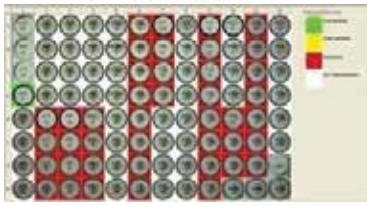
Isolate Collection
- Hospitals
  - Isolates
  - Basic info.
- NHRI
  - Isolate bank
  - Database

Centralized AST (Antimicrobial Susceptibility Testing) **at NHRI**
- AST
  - Confirm species
  - Determine MIC
  - Additional tests
- Data analysis
  - WHONET

Epidemiological Studies
- Mechanisms of AMR
- Strain typing
- Clonality
- Risk groups

Follow-up Activities
- Report to hosp.
- Symposium
- Advocacy

CLINICAL AND LABORATORY STANDARDS INSTITUTE



First MIRL Symposium, July 1999

- Report of excessive resistance to "first-line antibiotics" (TSAR I data)
- National Health Insurance Administration issued a policy to restrict antibiotic use for acute upper respiratory tract infections (URI) effective Feb 2001
- Antimicrobial consumption for URI decreased by 55.8% from 2000 to 2001

(Ho M, Hsiung CA *et al.*, Int J Antimicrob Agents. 2004)

TSAR Progress

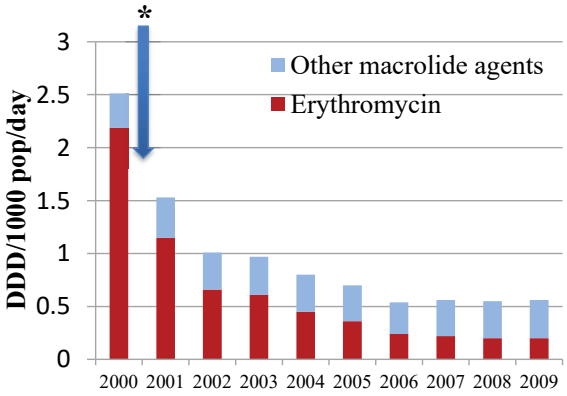
TSAR	Collection time	No. of Hospitals	No. of isolates
I	Oct-Dec 1998	44	~6000
II	Mar-May 2000	21	~3200
III	**Jul-Sep 2002**	**26**	**~6000**
IV	**Jul-Sep 2004**	**26**	**~6500**
V	**Jul-Sep 2006**	**25**	**~6300**
VI	**Jul-Sep 2008**	**26**	**~7300**
VII	**Jul-Sep 2010**	**26**	**~7400**
VIII	**Jul-Sep 2012**	**27**	**~8000**
IX	**Jul-Sep 2014**	**26**	**~7600**
X	**Jul-Sep 2016**	**25**	**~7600**
XI	**Jul-Sep 2018**	**25**	**Ongoing**

TSAR III – XI: Similar isolate collection protocol & participating hospitals

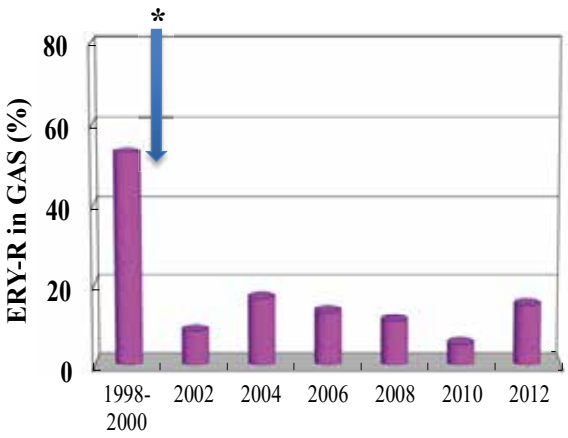
Impact of Restriction on Antibiotic Use

- Erythromycin use in outpatients decreased by nearly 50% between 2000 and 2001 (*), from 2.19 to 1.15 DDD/1000 pop/day.

- Resistance to erythromycin in Group A *Streptococcus* (GAS) was >50% in 1998-2000, but has remained at around 20% since 2002.



NHI data (Provided by Institute of Population Health Sciences/NHRI)



TSAR data (J Clin Microbiol 2014)

WHO priority pathogens list for R&D of new antibiotics

Priority 1: CRITICAL

- *Acinetobacter baumannii*, carbapenem-resistant ★
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing ★

Priority 2: HIGH

- *Enterococcus faecium*, vancomycin-resistant ★
- *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant ★
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter* spp., fluoroquinolone-resistant
- *Salmonellae*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant ★
- *Shigella* spp., fluoroquinolone-resistant

http://www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed

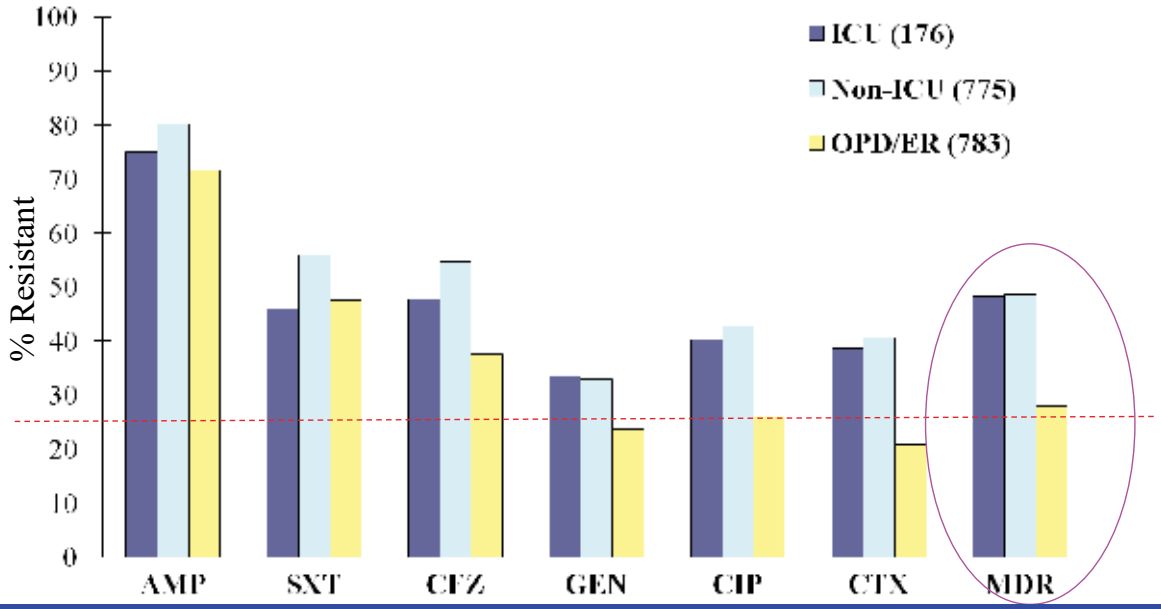
Data to be presented

★ Highlighted pathogens
Plus

- *mcr-1* in human and retail meat *E. coli*
- Fluoroquinolone (FQ)-resistant GN and GP pathogens & FQ consumption

MDR is Prevalent in Hospitals & Community

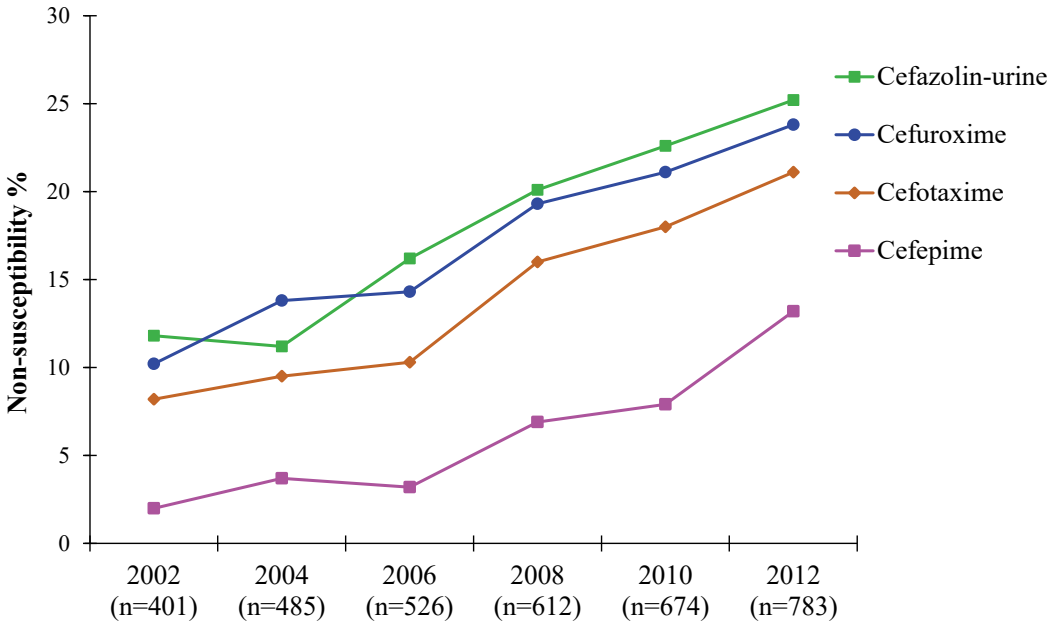
TSAR VIII (2012) *E. coli* data



MDR (Multidrug resistance), resistant to ≥ 3 of the agents in this figure

AMP, ampicillin; SXT, trimeth/sulfa; CFZ, cefazolin; GEN, gentamicin; CIP, ciprofloxacin; CTX, cefotaxime.

Increased Extended-Spectrum ß-Lactam Resistance in *E. coli* from Outpatients

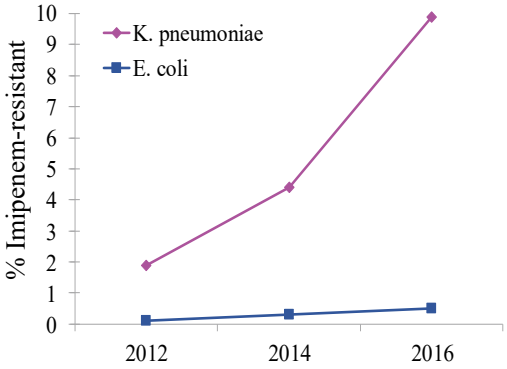


Due to increase of ESBL (mostly CTX-M) and AmpC ß-lactamase (mostly CMY-type) producers.

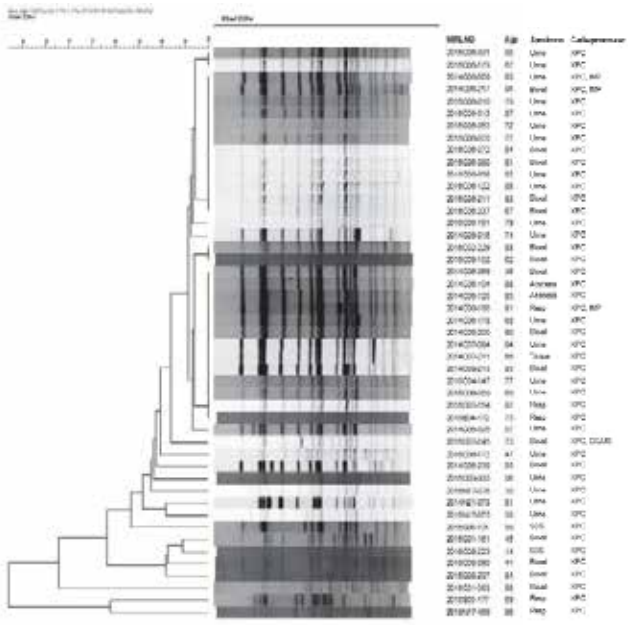
Modified from Wang JT et al., PLoS One 2015

Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP)

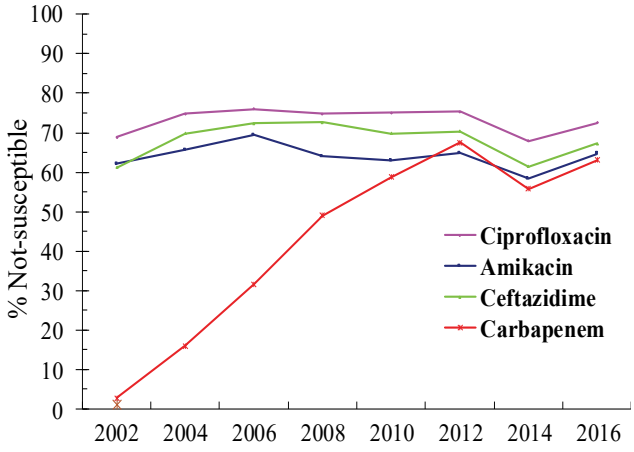
Increase of CRKP

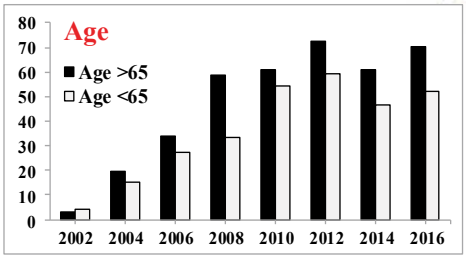


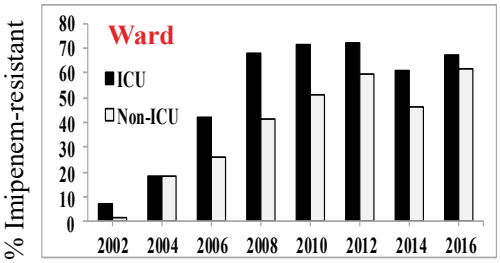
Dendrogram of KPC-Pos CRKP

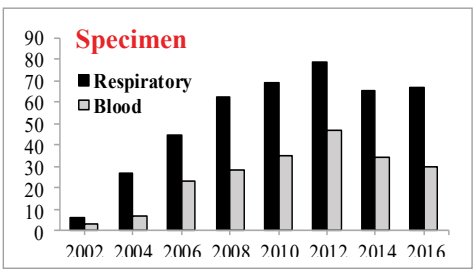


Carbapenem-Resistant *Acinetobacter baumannii** - Secular Trend & Risk Factors









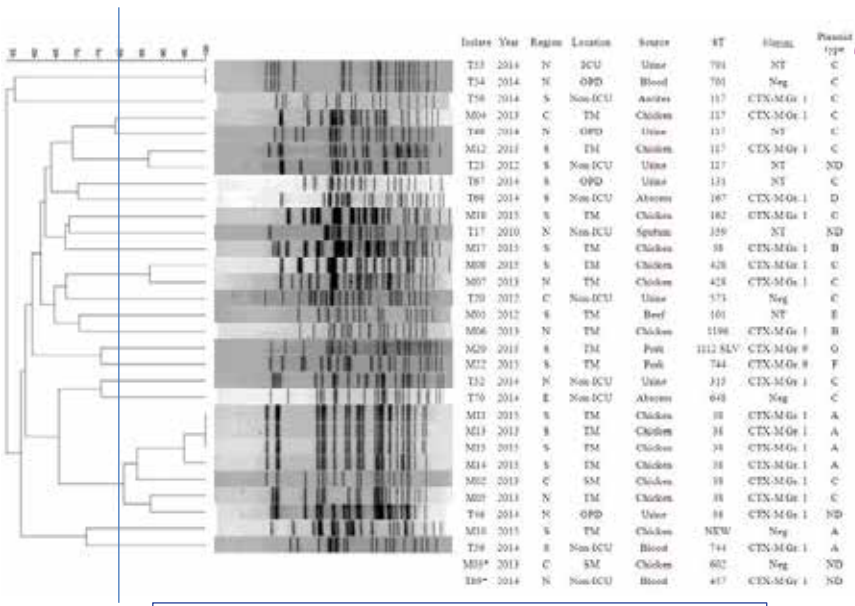
**Acinetobacter calcoaceticus-A. baumannii* complex*

mcr-1 in *E. coli* isolates from Humans & Retail Meat

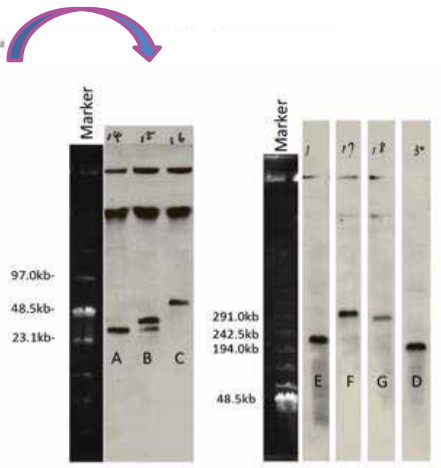
- Colistin (& polymyxin B):
  - Old agents from the 1960s shelved for decades because of toxicities.
  - Increase of XDR GN bacteria in recent years lead to their renewed use.
- *mcr-1*: The first plasmid-mediated colistin resistance gene, was reported from China in late 2015.

- *mcr-1* prevalence
  - TSAR: 0.1%, 0.1%, and 0.6% of 2010, 2012, & 2014 collection, respectively.
  - Retail meat: 1.1%, 6.6%, and 8.7% of 2012, 2013, & 2015 isolates, respectively.

mcr-1 positive *E. coli* from Humans & Retail Meat



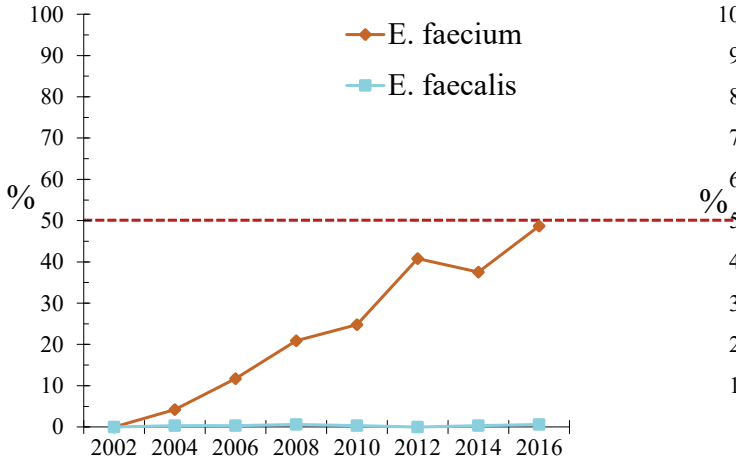
PFGE of XbaI digested genomic DNA.
Isolate: T=TSAR; M=Meat



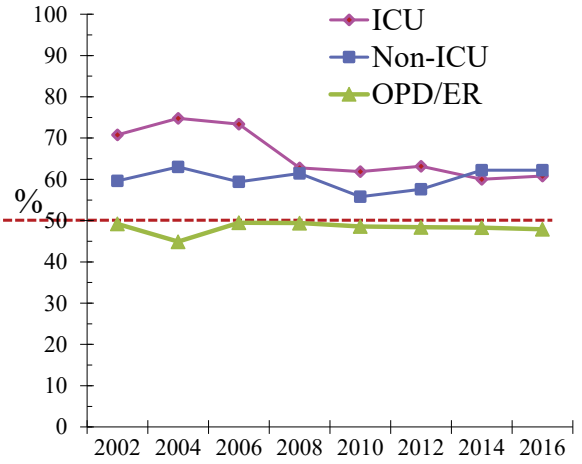
Plasmid profiles from S1 nuclease assay

Kuo SC et al., J Antimicrob Chemother 2016

VRE and MRSA Prevalence



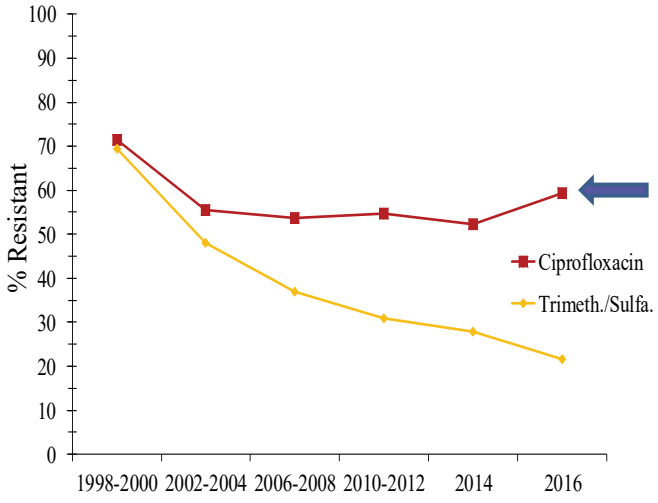
VRE in *Enterococcus faecalis & E. faecium*



MRSA in ICU, non-ICU, and OPD/ER

Changing MRSA Resistance

Non-β-lactams	% Resistant (TSAR VIII – X combined)	
	MRSA	MSSA
Ciprofloxacin	56.5	4.2
Clindamycin	73.6	11.4
Erythromycin	86.3	20.8
Gentamicin	57.6	14.5
Tetracycline	49.7	34.2
Trimeth./Sulfa (SXT)	27.3	1.0
Vancomycin	0.1 (I)	0

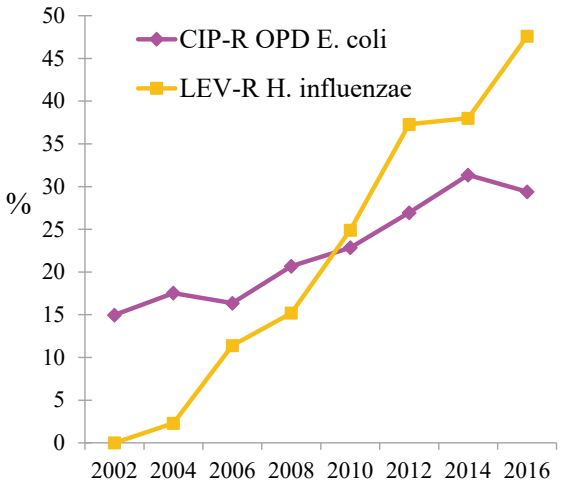


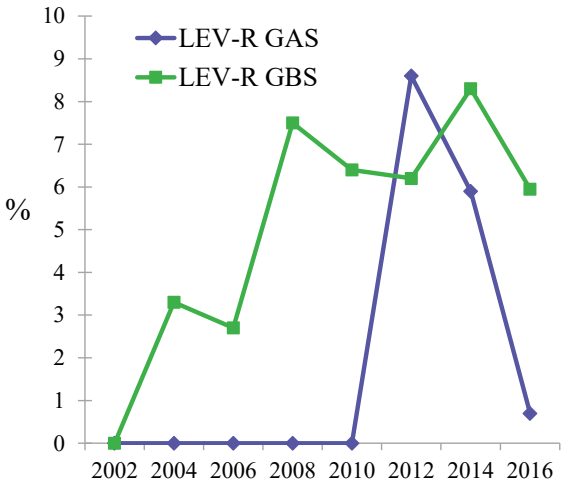
Changing resistance to non-β-lactams in MRSA due to changes in major clones

Emergence and Increase of Fluoroquinolone (FQ) Resistance

Secular Trend of Fluoroquinolone Resistance

CIP (ciprofloxacin), LEV (Levofloxacin)

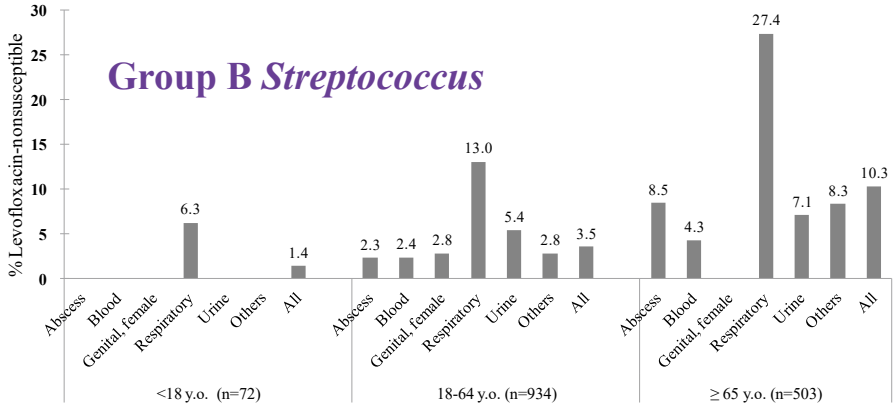




- Data modified and updated from:
  - Kuo SC, et al., EID 2014 (*Haemophilus influenzae*)
  - Lauderdale TL et al., ICAAC 2015 (Group A *Streptococcus*)
  - Wang JT et al. PLoS One 2015 (*E. coli* from outpatients)
  - Wu CJ et al., JAC 2017 (Group B *Streptococcus*)

Factors Associated with FQ-R Organisms (2002 -2012 data)

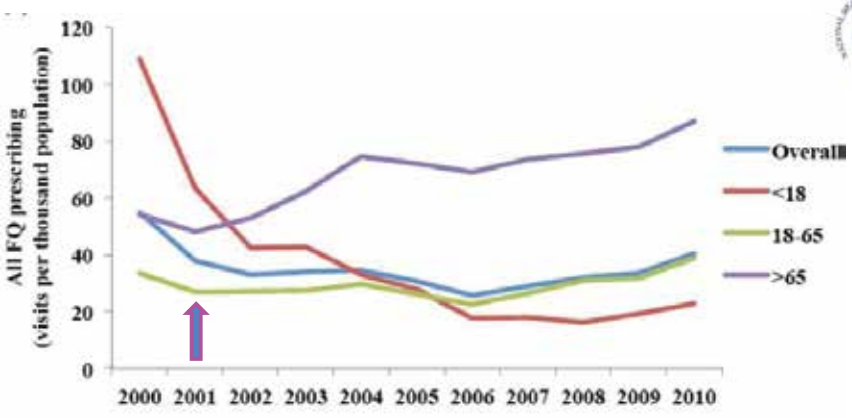
H. influenzae	N (%) levofloxacin		*P*[a]	OR[b]	95%CI[b]	*P*[b]
	Susceptible	Resistant				
Total	1280 (87.5)	182 (12.5)				
Patient age > 65 y	591 (80.8)	140 (19.2)	<0.001	3.601	2.435-5.325	<0.001
Resp. tract specimen	1123 (86.5)	175 (13.5)	<0.001			NS
Regional hospital	766 (85.0)	135 (15.0)	<0.001	2.054	1.379-3.059	<0.001



Investigation of FQ use in National Health Insurance (NHI) database

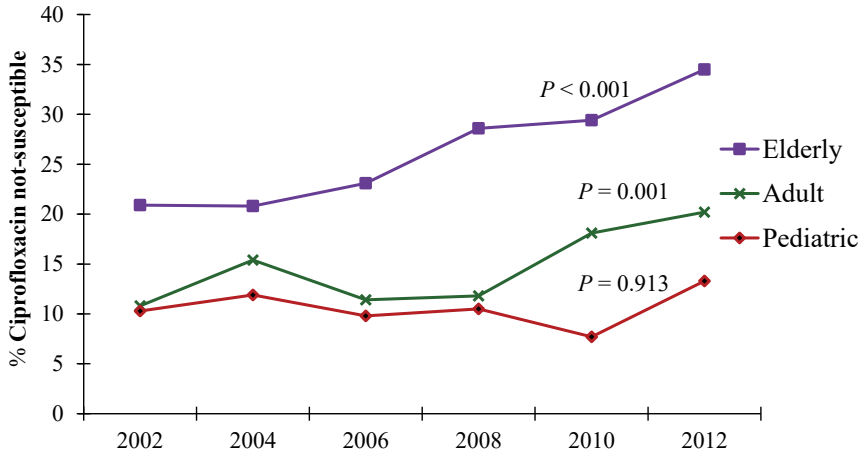
Estimated annual prescriptions of all FQs in NHI system

(Modified from J Microbiol Immunol Infect; In press)



Ciprofloxacin resistance in outpatient *E. coli*

(Modified from PLoS One 2015)



Closing Remarks

- Longitudinal multicenter AMR (phenotypic and genotypic) surveillance plays an important role in AMR control by helping to
  - Monitor AMR trends in different patient groups
  - Identify risk groups associated with AMR organisms
  - Detect emerging resistance
  - Pinpoint specific AMR problems that exist locally
  - Increase understanding of changing epidemiology

  - Provide data for intervention measure & advocacy decisions
  - Measure the impact of intervention measures

- However, AMR control requires a multifaceted approach, one of which is better understanding of antibiotic consumption and usage from human and non-human sectors

Acknowledgements

- **TSAR Hospitals**

- Microbial Infections Reference Laboratory (**MIRL**) Steering Committee
  - Dr. Shan-Chwen Chang (Chair); Dr. Feng-Yee Chang
  - Dr. Ying-Ching Chuang; Dr. Chang-Phong Fung; Dr. Yao-Shen Chen

- TSAR Studies:
  - Dr. Jann-Tay Wang (Enterococci, OPD *E. coli*)
  - Dr. Shu-Chen Kuo (*Acinetobacter, H. influenzae, mcr*-1)
  - Dr. Chi-Jung Wu (Gr. B *Streptococcus*)

- Antibiotic Consumption Studies:
  - Dr. Chao A. Hsiung
  - Dr. Yee-Chun Chen
  - Dr. Shu-Chen Kuo

Thank You for Your Attention

Session II
Policies to Promote Antimicrobial Stewardship Programs (ASP)

Moderators

Dr. Yao-Shen Chen

Chief, Department of Internal Medicine, Kaohsiung Veterans General Hospital

Dr. Shu-Hui Tseng

Director, Division of Infection Control and Biosafety, Centers for Disease Control

Dr. Yao-Shen Chen

Position: Chief

Department/organization: Department of Internal Medicine, Kaohsiung Veterans General Hospital

Economy: Chinese Taipei

Educational Background

- 1979-1986 Bachelor Degree, Medical College, National Yang-Ming University
- 2010-2012 Master Degree, Graduate of Healthcare Administration, Kaohsiung Medical Universit

Professional Career

- 1993- Attending physician, Kaohsiung Veterans General Hospital
- 2006-2013 Chief, Div. of Infectious Diseases, KVGH
- 2013- Chief, Department of Internal Medicine
- 2013- Associate Professor, Department of Medicine, National Yang-Ming University

Publications

- Hsueh PT, Lin HH, Wang HH, Liu CL, Ni WF, Liu JK, Chang HH, Sun DS, Chen YS, Chen YL. Immune imbalance of global gene expression, and cytokine, chemokine and selectin levels in the brains of offspring with social deficits via maternal immune activation. Genes Brain Behav 2018 Epub 2018/04/16.
- Chen YS, Chen BC, Chang JT, Huang TS, Chang TH. Human parechovirus infection in children in Taiwan: a retrospective, single-hospital study. Jpn J Infect Dis 2018 Epub 2018/05/02
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- Chen YS, Lin HH, Hsueh PT, Ni WF, Liu PJ, Chen PS, Chang HH, Sun DS, Chen YL. Involvement of L-selectin expression in Burkholderia pseudomallei-infected monocytes invading the brain during murine melioidosis. Virulence 2017;8(6):751-766.

Dr. Shu-Hui Tseng

Position: Director

Department/organization: Division of Infection Control and Biosafety, Centers for Disease Control

Economy: Chinese Taipei

Educational Background

- Doctor Program in the Graduate Institute of Clinical Medical Science, Chang Gung University (PhD)
- Clinical Medical Science, National Taiwan University (Msc)
- National Yang-Ming Medical University (MD)

Professional Career

- Director, infection control and biosafety, CDC
- Deputy Director, Fifth Division, CDC
- Acting Director, Fifth Division, CDC
- Branch Director, South Branch, CDC
- Section Chief, Immunization Section, CDC
- Director, Tao-Yuan City Health Center
- Attending Physician, Tao-Yuan Veteran General Hospital

Publications

- Chih-Cheng Lai, Chun-Ming Lee, Hsiu-Tzy Chiang, Ching-Tzu Hung, Ying-Chun Chen, Li-Hsiang Su, Zhi-Yuan Shi, Jein-Wei Liu, Chang-Pan Liu, Min-Chi Lu, Yin-Ching Chuang, Wen-Chien Ko, Shu-Hui Tseng, Yen-Hsu Chen, Po-Ren Hsueh. Implementation of a national bundle care program to reduce catheter-associated urinary tract infection in high-risk units of hospitals in Taiwan. Journal of Microbiology Immunology and Infection. vol. 50, no. 4: 464-470, 2017.
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Session II
Policies to Promote Antimicrobial Stewardship Programs (ASP)

Speakers

Prof. David Chien Boon Lye

Associate Professor, Tan Tock Seng Hospital

Prof. Victor Lim

Pro Vice-Chancellor, International Medical University

Prof. Wing Hong Seto

Co-Director, WHO Collaborating Centre for Infectious Disease Epidemiology and Control, The University of Hong Kong

Prof. Yee-Chun Chen

Professor, Department of Internal Medicine, National Taiwan University Hospital and College of Medicine

Prof. David Chien Boon Lye

Position: Associate Professor

Department/organization: Tan Tock Seng Hospital

Economy: Singapore

Educational Background

- 1996 MBBS, University of Melbourne, Australia
- 2004 Fellow of Royal Australasian College Physicians
- 2009 Fellow, Academy of Medicine, Singapore,
- 2016 Fellow, Royal College of Physicians, Edinburgh

Professional Career

- 2011-2015 Chair, Chapter of Infectious Diseases, College of Physicians, Singapore
- 2012-2014 Treasurer, College of Physicians, Singapore
- 2014- Vice President, College of Physicians, Singapore
- 2015- President, Society for Infectious Diseases (Singapore)
- 2016- Bursar, Academy of Medicine, Singapore
- 2016- Board member, College of Clinician Scientists, Academy of Medicine, Singapore

Publications

- A Versporten, P Zarb, I Caniaux, M-F Gros, N Drapier, M Miller, V Jarlier, D Nathwani, H Goossens, on behalf of the Global-PPS network. First web-based Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (GLOBAL-PPS) in 53 Countries: results on hospitalized adults. Lancet Global Health 2018, in press.
- HL Htun, TW Yeo, CC Tam, J Pang, YS Leo, DC Lye. Metformin use and severe dengue in diabetic adults. Scientific Reports 2018, in press.
- K Saeed, S Esposito, I Gould, T Ascione, M Bassetti, E Bonnet, E Bouza, M Chan, JS Davis, G De Simone, M Dryden, T Gottlieb, K Hijazi, DC Lye, P Pagliano, C Petridou, E Righi, J Segreti, S Unal, AN Yalcin. Hot topics in necrotising skin and soft tissue infections. Int J Antimicrob Agents 2018, in press.

Speech Abstract

Antimicrobial Stewardship Programme in Singapore

Antimicrobial resistance has emerged as a major public health problem with significant economic cost and impact on human health. The potential burden on human health is greatest in Africa and Asia. Many countries are responding the global call for action by World Health Organisation, and putting in place national action plans. In Singapore, a One Health Coordination Committee oversees a One Health Antimicrobial Resistance Workgroup in developing a national action plan. Already in place is national infection control programme which emphasises enhanced hand hygiene and active surveillance of MRSA with resultant decrease in MRSA incidence. Antimicrobial stewardship is funded in all public hospitals, led by infectious disease physicians and pharmacists. A combination of regularly updated hospital antibiotic guidelines, prospective review and feedback on targeted broad-spectrum antibiotics, computerised decision support and bi-annual national reporting with feedback to hospital administration has produced some sustained results but also new emerging issues. The ongoing One Health Antimicrobial Resistance national action plan aims to broaden the scope beyond hospitals, by engaging the public and multi-sectoral stakeholders via education, surveillance and risk assessment, research, prevention of infections and optimising antibiotic use.

Antimicrobial stewardship programme in Singapore

David Lye FRACP, FAMS, FRCP

Senior consultant, Tan Tock Seng Hospital
Associate professor, Yong Loo Lin School of Medicine,
National University of Singapore
Associate professor, Lee Kong Chian School of Medicine,
Nanyang Technological University, Singapore

Outline

- Burden of antimicrobial resistance in Singapore
- National strategic action plan on antimicrobial resistance
- Antimicrobial stewardship in Singapore hospitals

ST22 and ST239 MRSA duopoly in Singaporean hospitals: 2006–2010

J. TEO[1], T. Y. TAN[2], P. Y. HON[3], W. LEE[1], T. H. KOH[4], P. KRISHNAN[5], L. Y. HSU[3]* AND the Network for Antimicrobial Resistance Surveillance (Singapore)

Epidemiol. Infect. (2013), **141**, 153–157.

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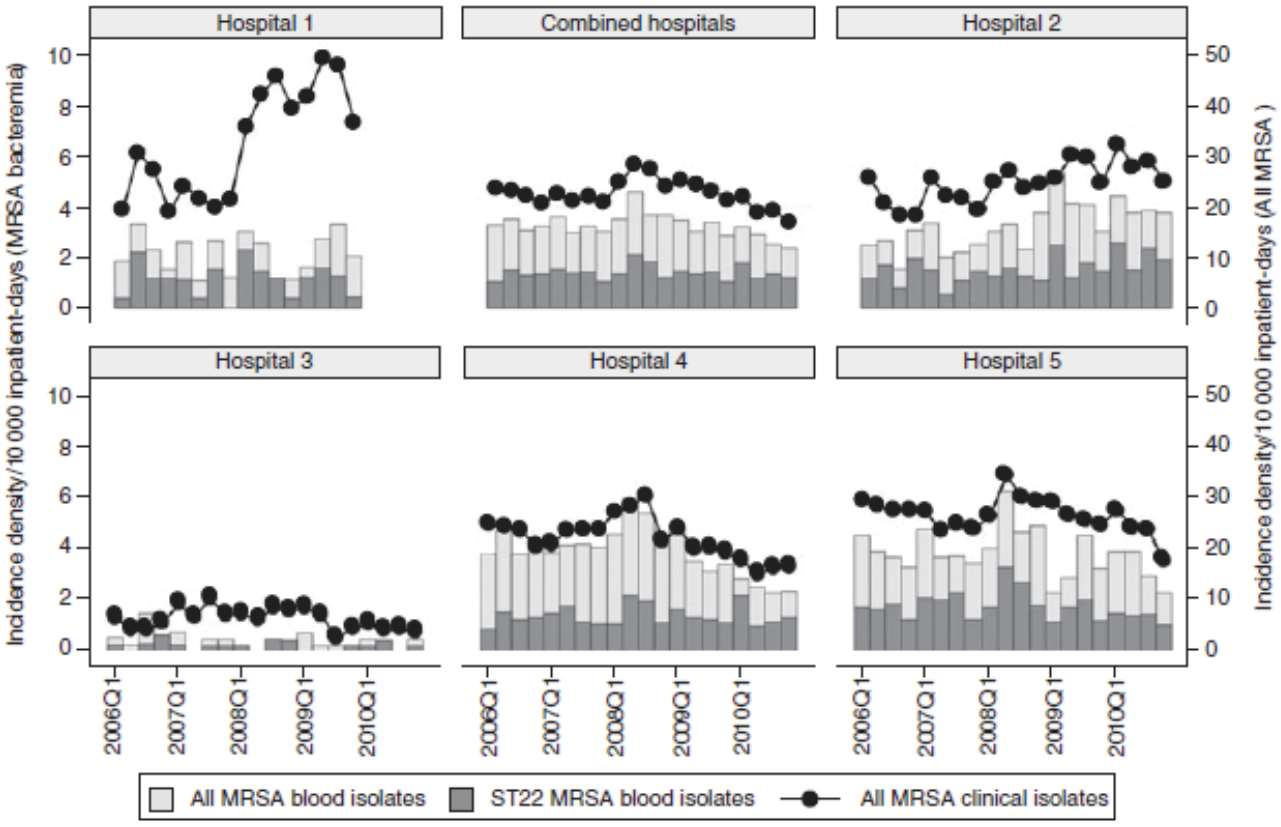
Rising trend in 2, decreasing in 2



Sustained meticillin-resistant *Staphylococcus aureus* control in a hyper-endemic tertiary acute care hospital with infrastructure challenges in Singapore

D. Fisher[a,b,c,*], P.A. Tambyah[a,b], R.T.P. Lin[b,c,d], R. Jureen[b,c,d], A.R. Cook[e,f,g], A. Lim[b,h], B. Ong[a,b], M. Balm[c,d], T.M. Ng[c], L.Y. Hsu[a,b,e]

Journal of Hospital Infection 85 (2013) 141–148

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- Active MRSA surveillance, NAG, chromogenic agar
- Hand hygiene
- Isolation and cohorting
- Education and feedback

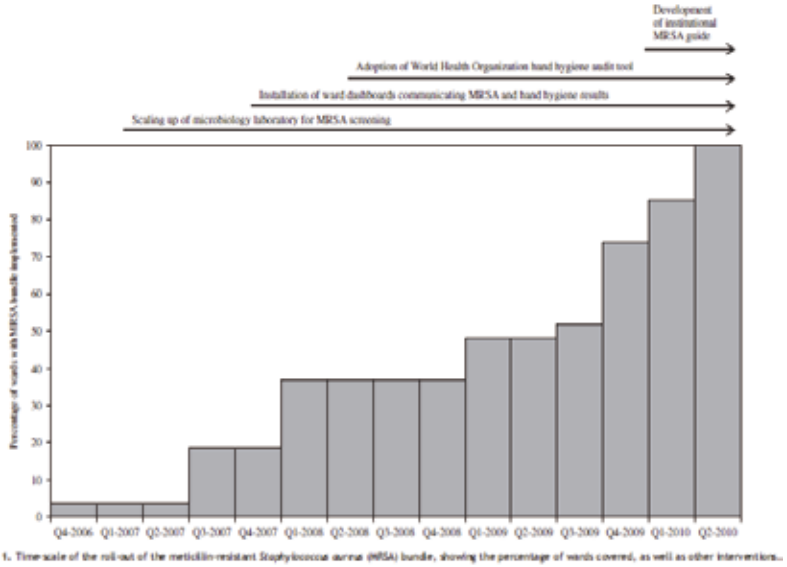


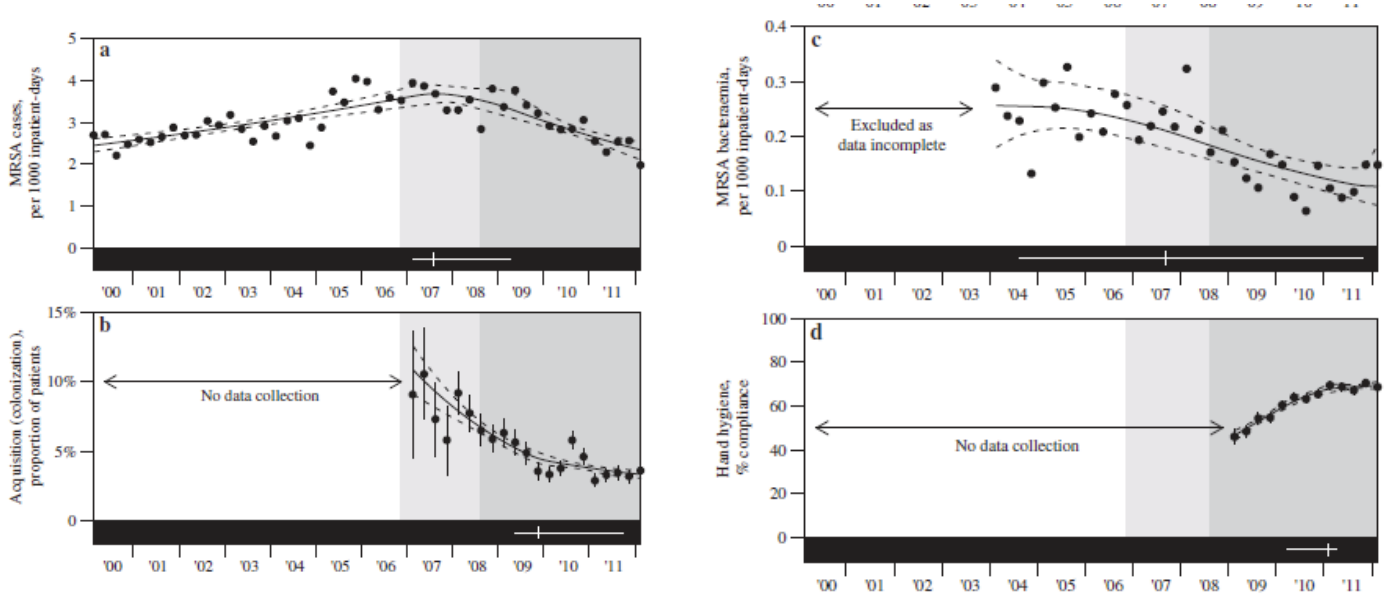
Figure 1. Time-scale of the roll-out of the meticillin-resistant *Staphylococcus aureus* (MRSA) bundle, showing the percentage of wards covered, as well as other interventions.

Sustained meticillin-resistant *Staphylococcus aureus* control in a hyper-endemic tertiary acute care hospital with infrastructure challenges in Singapore

IIDE Institute of Infectious Diseases and Epidemiology

D. Fisher [a,b,c,*], P.A. Tambyah [a,b], R.T.P. Lin [b,c,d], R. Jureen [b,c,d], A.R. Cook [e,f,g], A. Lim [b,h], B. Ong [a,b], M. Balm [c,d], T.M. Ng [c], L.Y. Hsu [a,b,e]

Journal of Hospital Infection 85 (2013) 141–148



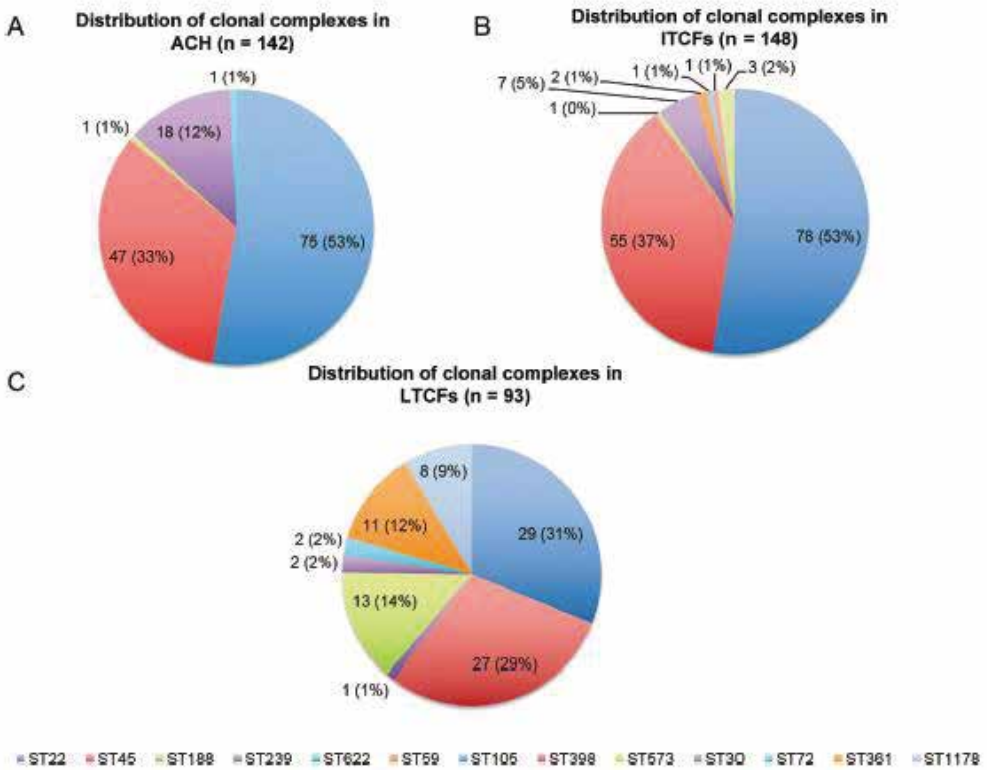
All temporal trends significant reduction

MRSA Transmission Dynamics Among Interconnected Acute, Intermediate-Term, and Long-Term Healthcare Facilities in Singapore

IIDE Institute of Infectious Diseases and Epidemiology

Angela Chow,[1,5] Vanessa W Lim,[1] Ateeb Khan,[9] Kerry Pettigrew,[9] David C. B. Lye,[2,6] Kala Kanagasabai,[7] Kelvin Phua,[8] Prabha Krishnan,[3] Brenda Ang,[2,6] Kalisvar Marimuthu,[2,6] Pei-Yun Hon,[3] Jocelyn Koh,[8] Ian Leong,[4] Julian Parkhill,[10] Li-Yang Hsu,[2,5] and Matthew T. G. Holden[9]

Clinical Infectious Diseases® 2017;64(S2):S76-81



MRSA Transmission Dynamics Among Interconnected Acute, Intermediate-Term, and Long-Term Healthcare Facilities in Singapore

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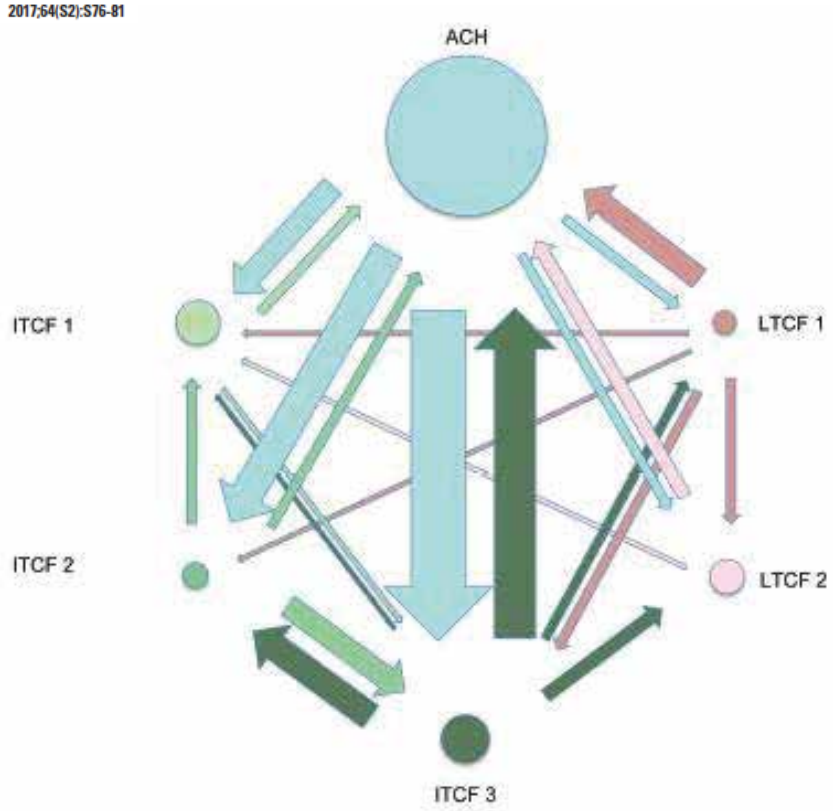
Clinical Infectious Diseases® 2017;64(S2):S76-81



Vancomycin-resistant Enterococci in Singaporean Hospitals: 5-year results of a Multi-centre Surveillance Programme

Yiying Cai,[1] BSc (Pharm), Joey PJ Chan,[2] FRCPath, Dale Andrew Fisher,[3] FRACP, Li Yang Hsu,[3] MPH, Tse Hsien Koh,[4] FRCPath, Prabha Krishnan,[5] FRCPath, Andrea LH Kwa,[1] PharmD, Thean Yen Tan,[6] MRCPath, Nancy WS Tee,[7] FRCPA

Ann Acad Med Singapore 2012;41:77-81

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Rising in 1, decreasing in 1

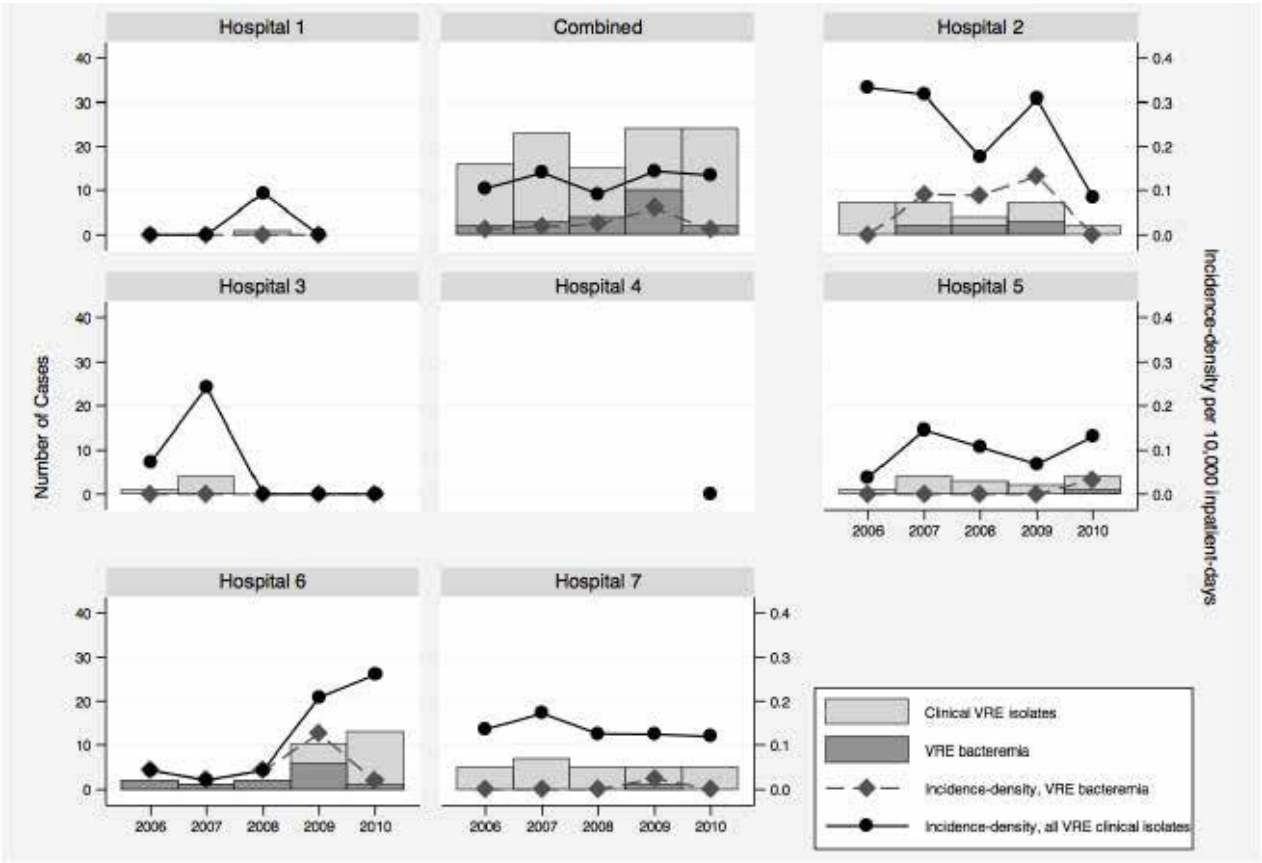


Fig. 1. Incidence-density and number of vancomycin-resistant enterococci isolates from clinical and blood cultures, by hospital, 2006-2010.

Control of a hospital-wide vancomycin-resistant *Enterococci* outbreak

Asok Kurup, MRCP,[a] M. P. Chlebicki, ABIM,[b] M. L. Ling, FRCPA,[a] T. H. Koh, FRCPA,[c] K. Y. Tan, RN,[a] L. C. Lee, RN,[a] and K. B. M. Howe, RN[a]

Am J Infect Control 2008;36:206-11

(1) formation of a VRE task force, (2) hospital-wide screening, (3) isolation of carriers, (4) physical segregation of contacts, (5) surveillance of high-risk groups, (6) increased cleaning, (7) electronic tagging of VRE status, and (8) education and audits. This is a

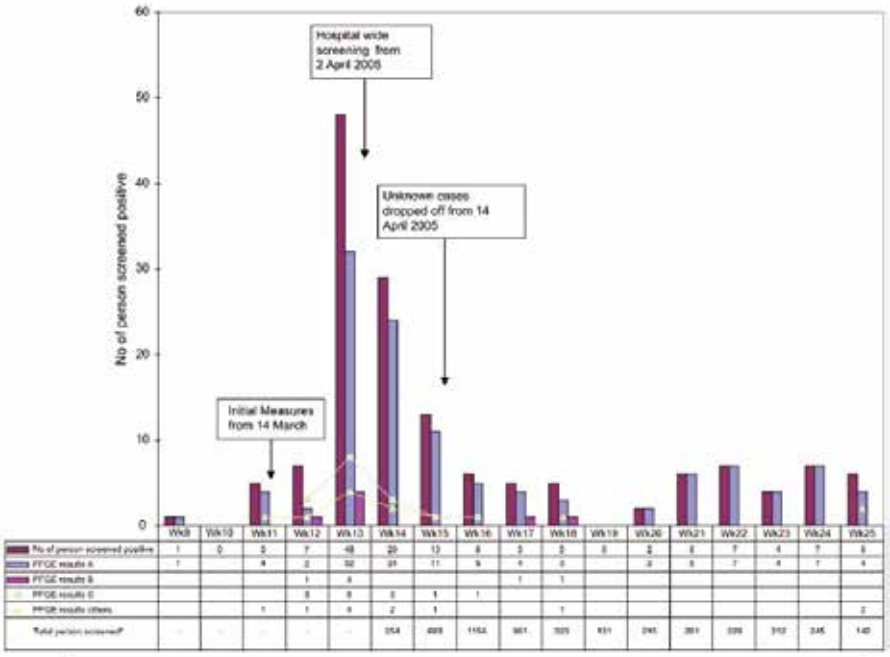


Fig 2. Time series showing distribution of positive cases with PFGE clone types interposed. *Data for total persons screened available only after hospital-wide screening was started at week 14.

Surveillance and Correlation of Antibiotic Prescription and Resistance of Gram-Negative Bacteria in Singaporean Hospitals[▽]†

Li-Yang Hsu,[1]* Thean-Yen Tan,[2] Vincent H. Tam,[1,3] Andrea Kwa,[4] Dale Andrew Fisher,[1] Tse-Hsien Koh,[5] and the Network for Antimicrobial Resistance Surveillance (Singapore)

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 2010, p. 1173–1178

TABLE 2. Incidence density and percentage of antimicrobial-resistant Gram-negative bacteria in Singapore hospitals, 2006 to 2008

Organism(s), drug susceptibility, and isolate type	No. of resistant isolates	% Resistance	Median incidence density of resistant isolates/1,000 inpatient-days (range)
Escherichia coli			
Ceftriaxone			
All isolates	6,629	20.0	1.87 (1.61–2.17)
Blood isolates	854	21.7	0.24 (0.18–0.30)
Ciprofloxacin			
All isolates	12,081	38.7	3.37 (3.18–3.74)
Blood isolates	1,285	31.0	0.36 (0.31–0.40)
Klebsiella pneumoniae			
Ceftriaxone			
All isolates	6,321	32.3	1.76 (1.42–2.27)
Blood isolates	685	27.4	0.19 (0.15–0.24)
Ciprofloxacin			
All isolates	6,285	30.1	1.72 (1.32–2.39)
Blood isolates	610	24.0	0.16 (0.13–0.25)
Acinetobacter spp., imipenem			
All isolates	2,000	46.2	0.56 (0.43–0.72)
Blood isolates	184	56.0	0.05 (0.03–0.08)
Pseudomonas aeruginosa, imipenem			
All isolates	1,139	7.5	0.32 (0.24–0.41)
Blood isolates	119	12.8	0.03 (0.02–0.07)

A prospective observational study of the prevalence and risk factors for colonization by antibiotic resistant bacteria in patients at admission to hospital in Singapore

Barnaby E Young[1*], David C Lye[1,2], Prabha Krishnan[3], Siew Pang Chan[1,4] and Yee Sin Leo[1,2]

BMC Infectious Diseases 2014, **14**:298

IIDE Institute of Infectious Diseases and Epidemiology

Results: 1006 patients were screened. 124 (12.4%) were colonized by ESBL-E, 18 (1.8%) by MRSA while no VRE was detected. Antibiotic use within the past month was the only significant predictor for ESBL-E colonization in the regression model, with an adjusted odds ratio (AOR) of 2.58 (1.04 to 6.42). In participants recently prescribed antibiotics and hospitalized in the previous 3 months, 29.4% were colonized by ESBL-E. This represented 20.2% of the total ESBL-E burden, and ESBL-E was also detected in 6.3% of participants with no healthcare contact. Hospitalization and outpatient hospital visits predicted MRSA colonization in the univariate analysis. Neither was statistically significant in the logistic regression model, with AORs for MRSA colonization following hospitalization in the past 3 and 12 months of 3.81 [95% CI 0.84-17.28] and 3.48 [0.64-18.92] respectively.

Extended-Spectrum Beta-Lactamase-Producing *Enterobacteriaceae* in Retail Chicken Meat in Singapore

IIDE Institute of Infectious Diseases and Epidemiology

Eugene JZ Lim*, [1], Si Xian Ho*, [1], Delphine YH Cao, [2BSc], Quek Choon Lau, [1PhD], Tse Hsien Koh, [2PhD], Li Yang Hsu, [3,4MPH]

AAMS 2016;45:557

Table 1. Distribution of CTX-M Genes and *Enterobacteriaceae* Isolates from 15 Chicken Samples According to Type of Chicken and Country of Origin

Country of Origin	Type of Chicken	Poultry Farming	*Enterobacteriaceae* (Number of Isolates)	CTX-M Group (Number of Isolates)
Malaysia	Black (ayam cemani†)	Conventional	*Escherichia coli* (2)	1 (2)
Malaysia	Ordinary	Conventional	*E. coli* (2)	1 (1)
				9 (1)
Malaysia	Ordinary	Conventional	*E. coli* (2)	9 (2)
Malaysia	Ordinary	Conventional	*E. coli* (4)	9 (3)
				2 and 9 (1)
Malaysia	Ordinary (ayam kampong‡)	Conventional	*E. coli* (2)	1 (1)
				9 (1)
Malaysia (France)*	Yellow chicken	Conventional	*E. coli* (2)	1 (2)
Malaysia	Ordinary	Antibiotic-free (probiotic)	*E. coli* (3)	1 (3)
Malaysia	Ordinary	Antibiotic-free (probiotic)	*E. coli* (3)	2 and 9 (2)
				9 (1)
Malaysia	Ordinary	Antibiotic-free (probiotic)	*E. coli* (1)	1 (1)
			Proteus mirabilis (1)	9 (1)
			Klebsiella pneumoniae (2)	CTX-M negative
Malaysia	Ordinary	Antibiotic-free (probiotic)	*E. coli* (2)	1 (2)
			P. mirabilis (5)	9 (5)
			K. pneumoniae (2)	1 (2)
Brazil	Ordinary	Conventional	*E. coli* (5)	2 (2)
				8 (3)
Brazil	Ordinary	Conventional	*E. coli* (4)	2 (4)
France	Ordinary	Conventional	*E. coli* (4)	1 (4)
France	Yellow chicken	Conventional	*E. coli* (5)	1 (5)
France	Yellow chicken	Antibiotic-free	*E. coli* (5)	1 (5)

Decline in *Clostridium difficile*-associated disease rates in Singapore public hospitals, 2006 to 2008

Li-Yang Hsu[1*], Thean Yen Tan[2], Tse Hsien Koh[1,3], Andrea L Kwa[4], Prabha Krishnan[5], Nancy W Tee[6], Roland Jureen[7]

BMC Research Notes 2011, **4**:77

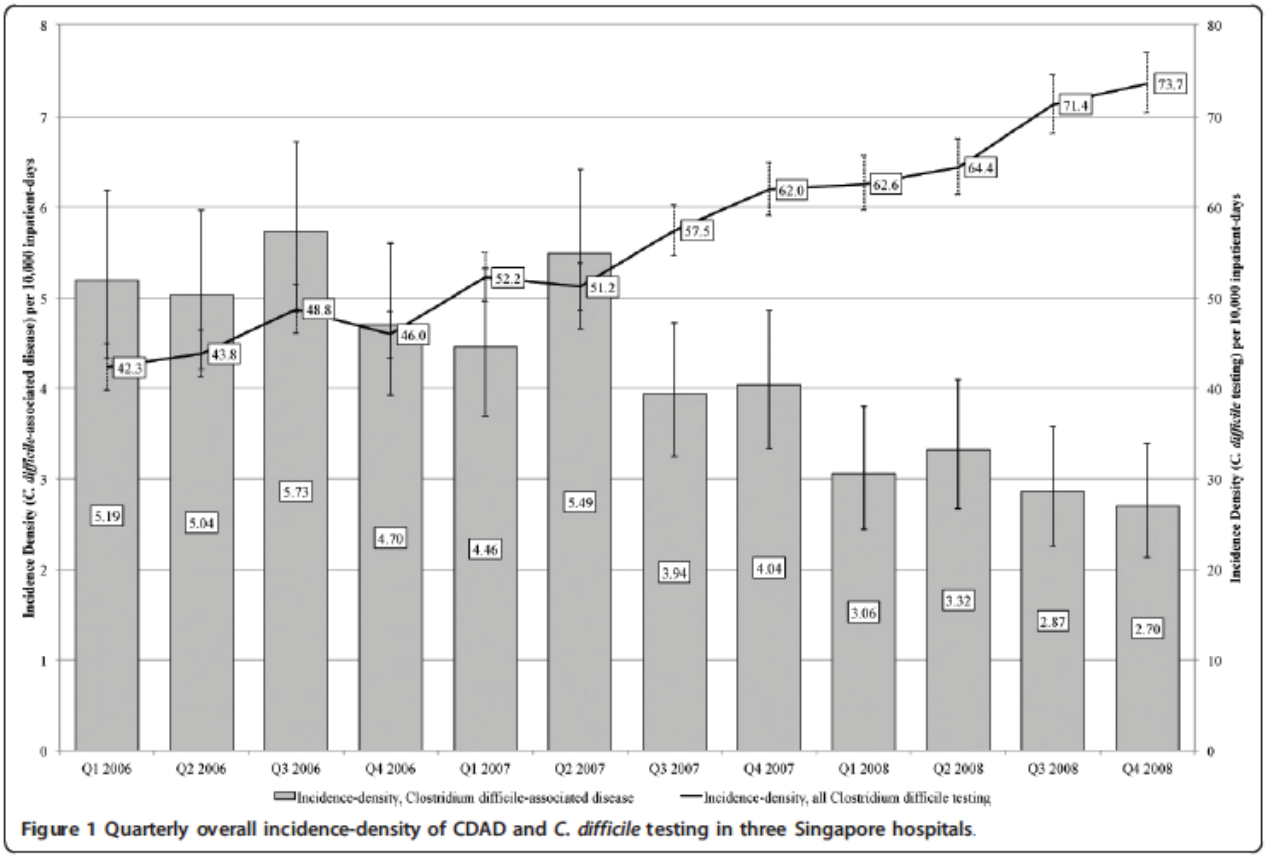


Figure 1 Quarterly overall incidence-density of CDAD and *C. difficile* testing in three Singapore hospitals.

Isolation of the first three cases of *Clostridium difficile* polymerase chain reaction ribotype 027 in Singapore

Lim P L, Ling M L, Lee H Y, Koh T H, Tan A L, Kuijper E J, Goh S S, Low B S, Ang L P, Harmanus C, Lin R T P, Krishnan P, James L, Lee C E

Singapore Med J 2011; 52(5) : 361

Methods: From September 2008 to December 2009, all non-duplicate toxin-positive stool samples from the three largest public hospitals in Singapore were collected for culture and further analysis.

Results: Out of the 366 samples collected, 272 viable isolates were cultured. Of these, 240 tested toxin-positive and ten tested positive for the binary toxin gene; 35 different PCR ribotypes were found. Three isolates that tested positive for binary toxin contained the same PCR ribotyping pattern as the *C. difficile* 027 control strain. All three had the 18-bp deletion and single nucleotide *tcdC* deletion at position 117. Susceptibility testing was performed, demonstrating susceptibility to erythromycin and moxifloxacin.

Acquired carbapenemases in *Enterobactericeae* in Singapore, 1996–2012

Tse Hsien Koh*†, Delphine Cao†, Quek Yen Shan†, Anna Bacon§, Li-Yang Hsu* and Eng Eong Ooi‡

Pathology (October 2013) **45**(6), pp. 600–603

IIDE Institute of Infectious Diseases and Epidemiology

Emergence 2010: NDM, KPC, OXA 48/181

Table 1 Characteristics of carbapenemase-producing *Enterobacteriaceae*

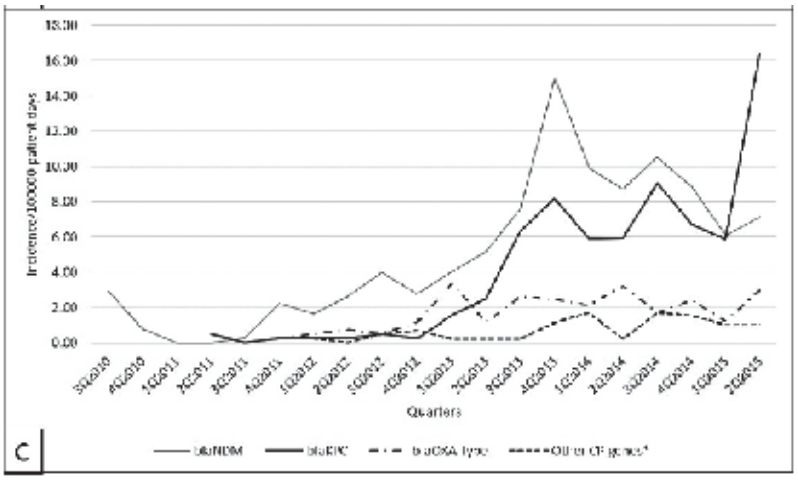
Species	Isolate	Site	Year	Nationality	Carbapenemase	MIC (mg L^{-1}) IMP	MEM	ETP	PFGE	ST	Plasmid Inc	Size (kb)	Type
K. pneumoniae	DB44384	Blood	1996	SIN	IMP-1	>32	>32	>32	dg	42	A/C	ca. 160	3
K. pneumoniae	DU32157	Urine	2011	SIN	IMP-1	4	4	16	KPN10	147	A/C	ca. 150	3
K. pneumoniae	DR37041	Resp	2010	SIN	IMP-1	>32	>32	>32	KPN4	885	A/C	ca. 160	3
C. freundii	DU10513	Urine	2012	SIN	IMP-1	4	8	16	nd	na	A/C	ca. 150	3
E. cloacae	DU31899	Urine	2011	SIN	IMP-1	1	1	4	ECL1	na	A/C	ca. 190	nt
E. cloacae	DM9800	Wound	2011	SIN	IMP-1	2	4	>32	ECL2	na	nt	ca. 270	nt
K. pneumoniae	DM23092	Wound	2004	BAN	IMP-1	3	3	16	KPN1	11	nt	nt	nt
K. pneumoniae	DS6941	Stool	2010	SIN	IMP-4	>32	>32	>32	KPN6	568	nt	ca. 150	nt
E. cloacae	DM8861	CVP tip	2012	SIN	KPC-2	8	4	8	ECL7	na	Neg	ca. 50	2
E. coli	DM6277	Wound	2012	SIN	KPC-2	2	2	8	ECO7	3054	Neg	ca. 50	2
K. pneumoniae	DR2160	Resp	2012	SIN	KPC-2	16	32	16	KPN14	841	Neg	ca. 50	2
K. pneumoniae	DU51131	Urine	2011	SIN	KPC-2	>32	8	>32	KPN12	11	Neg	ca. 50	2
K. pneumoniae	DB2244	Blood	2012	SIN	KPC-2	>32	>32	>32	KPN13	11	FIIK	ca. 100	nd
K. pneumoniae	DU1301	Urine	2010	SIN	NDM-1	>32	>32	>32	KPN2	11	Neg	ca. 80	10
K. pneumoniae	DU52392	Urine	2011	SIN	NDM-1	8	8	>32	KPN11	11	Neg	ca. 80	11
C. sedlakii	DM5680-1	Tissue	2012	SIN	NDM-1	32	32	32	nd	na	Neg	ca. 90	12
E. cloacae	DM5887-3	Wound	2012	SIN	NDM-1	>32	>32	>32	ECL6	na	R	ca. 110	13
K. pneumoniae	DU1883	Urine	2011	SIN	NDM-1	>32	>32	>32	KPN8	147	Neg	ca. 120	14
K. pneumoniae	DM3906	Abd fluid	2012	SIN	NDM-1	>32	>32	>32	KPN8-1	147	FIIK	ca. 160	nd
E. coli	DS8293	Stool	2010	SIN	NDM-1	>32	>32	>32	ECO1	2083	FII	ca. 110	15
E. coli	DU48916	Urine	2011	IND	NDM-1	>32	>32	>32	dg	405	A/C	ca. 150	16
E. cloacae	DB6217	Blood	2012	RIN	NDM-1	16	>32	>32	ECL5	na	A/C	ca. 150	16
E. cloacae	DM16303	Wound	2011	SIN	NDM-1	>32	32	>32	ECL4	na	Neg	ca. 40	4
K. pneumoniae	DU43320	Urine	2010	SIN	NDM-1	>32	8	>32	KPN5	273	Neg	ca. 40	4
K. pneumoniae	DR2834	Resp	2011	MAL	NDM-1	>32	>32	>32	KPN9	273	Neg	ca. 40	4
K. pneumoniae	DS1731	Stool	2011	SIN	NDM-1	>32	>32	>32	KPN9-1	273	Neg	ca. 40	4
E. coli	DS205	Stool	2011	BAN	NDM-1	>32	>32	>32	ECO2	648	Neg	ca. 40	5
E. cloacae	DM15118	Wound	2011	VIE	NDM-1	>32	>32	>32	ECL3	na	Neg	ca. 60	8
E. coli	DS474	Stool	2011	SIN	NDM-1	>32	>32	>32	ECO3	101	FII	ca. 60	9
E. coli	DS1878	Stool	2011	SIN	NDM-1	2	4	>32	ECO4	2451	A/C	ca. 370	nd
K. pneumoniae	DS159	Stool	2011	RIN	NDM-1	>32	>32	>32	KPN8	nd	nd	nd	nd
K. pneumoniae	DU44951	Urine	2010	VIE	NDM-1	>32	>32	>32	KPN7	1	nt	ca. 40	nt
E. coli	DM20217*	Abd fluid	2011	SIN	NDM-7	>32	>32	>32	ECO5	205	Neg	ca. 40	6
K. pneumoniae	DU7433	Urine	2010	BAN	NDM-1	>32	>32	>32	KPN3	14	A/C	ca. 60	7
K. pneumoniae	DR40294	Resp	2011	SIN	NDM-1	>32	>32	>32	KPN3-1	14	nt	ca. 280	nt
K. pneumoniae	DX1083*	Resp	2011	BAN	OXA-181	>32	>32	>32	KPN3-1	14	nt	ca. 150	nt
K. pneumoniae	DB53879	Blood	2011	BAN	OXA-181	32	>32	>32	KPN3-1	nd	nt	ca. 150	nt
K. pneumoniae	DU54621	Urine	2011	BAN	OXA-181	>32	>32	>32	KPN3-1	nd	nt	ca. 150	nt
K. pneumoniae	R16-09*	Resp	2012	SIN	OXA-181	>32	>32	>32	KPN3-1	nd	nt	ca. 150	nt
E. coli	DB4758	Blood	2012	SIN	OXA-48	>32	32	>32	ECO6	2003	Neg	ca. 50	1
K. pneumoniae	DU20470-1	Urine	2012	SIN	OXA-48	4	1	8	KPN15	29	Neg	ca. 50	1

Clinical and Molecular Epidemiology of Carbapenem-Resistant Enterobacteriaceae Among Adult Inpatients in Singapore

IIDE Institute of Infectious Diseases and Epidemiology

Kalisvar Marimuthu,[1,2,a] Indumathi Venkatachalam,[2,a] Wei Xin Khong,[1,a] Tse Hsien Koh,[4] Benjamin Pei Zhi Cherng,[3] My Van La,[5] Partha Pratim De,[6,19] Prabha Unny Krishnan,[5,6,19] Thean Yen Tan,[7] Raymond Fong Kok Choon,[8] Surinder Kaur Pada,[9] Choong Weng Lam,[10] Say Tat Ooi,[11] Rama Narayana Deepak,[12] Nares Smitasin,[13] Eng Lee Tan,[14] Jia Jun Lee,[1] Asok Kurup,[15] Barnaby Young,[1] Nancy Tee Wen Sim,[16] Koh Cheng Thoon,[2,17] Dale Fisher,[2,13] Moi Lin Ling,[18] Brenda Ang Sze Peng,[1,19] Yik-Ying Teo,[20,21,22,23,24] Li Yang Hsu,[1,25] Raymond Tzer Pin Lin,[5,26] Rick Twee-Hee Ong,[20] Jeanette Teo,[26,b] and Oon Tek Ng[1,19,b], for the Carbapenemase-Producing Enterobacteriaceae in Singapore (CaPES) Study Group

Clinical Infectious Diseases® 2017;64(S2):S68–75



Comparative Analysis Between CPE and NCPE

In the multivariate analysis, significantly greater carbapenem exposure (OR: 3.23; 95% CI: 1.67–6.25) and hematological malignancies (OR: 2.85; 95% CI: 1.10–7.41) were associated with the NCPE group while chronic pulmonary disease was associated with the CPE group (OR: 0.35; 95% CI: 0.14–0.92) (Table 1). The average length of stay for all CRE patients was 38 days (IQR, 17–65), with 17.8% of CRE patients readmitted within 30 days of discharge. In-hospital and 30-days post-discharge mortality of CRE patients were 19.7% and 3.7%, respectively. There was no difference in length of stay, readmission, or mortality between CPE and NCPE.

Tracking inter-institutional spread of NDM and identification of a novel NDM-positive plasmid, pSg1-NDM, using next-generation sequencing approaches

Wei Xin Khong[1]†, Kalisvar Marimuthu[1,2]†, Jeanette Teo[3], Yichen Ding[4], Eryu Xia[5], Jia Jun Lee[1], Rick Twee-Hee Ong[6], Indumathi Venkatachalam[3], Benjamin Cherng[7], Surinder Kaur Pada[8], Weng Lam Choong[8], Nares Smitasin[3], Say Tat Ooi[9], Rama Narayana Deepak[9], Asok Kurup[10], Raymond Fong[11], My Van La[12], Thean Yen Tan[11], Tse Hsien Koh[7], Raymond Tzer Pin Lin[3,12], Eng Lee Tan[13], Prabha Unny Krishnan[14], Siddharth Singh[15], Johann D. Pitout[16–18], Yik-Ying Teo[5,6,19–21], Liang Yang[4] and Oon Tek Ng[1]* on behalf of the Carbapenemase-Producing Enterobacteriaceae in Singapore (CaPES) Study Group‡

J Antimicrob Chemother 2016; **71**: 3081–3089

Table 1. Clinical and microbiological characteristics of study isolates

Sample ID	Travel history	Collection date	DOA	DOD	Sample site	Hospital	Plasmid (coverage, %)	Organism	ST
16	—	06/09/2010	01/09/2010	17/09/2010	urine	B	pNDM-ECS01 (100)	Ec	NA
11	—	09/09/2010	08/09/2010	11/09/2010	urine	B	unknown	KP	437
1	—	22/09/2010	21/09/2010	28/09/2010	urine	B	pNDM-ECS01 (100)	EC	410
21[a]	Australia	14/10/2010	13/10/2010	15/10/2010	urine	B	pNDM-ECS01 (100)	KP	48
26[a]	Australia	14/10/2010	13/10/2010	15/10/2010	RS	B	pNDM-ECS01 (100)	KP	48
36[a]	Australia	14/10/2010	13/10/2010	15/10/2010	RS	B	pNDM-ECS01 (100)	EC	69
41	Malaysia	26/11/2010	15/09/2010	10/12/2010	urine	B	pNDM-ECS01 (100)	EC	131
46	—	03/12/2010	17/10/2010	14/12/2010	RS	B	pNDM-ECS01 (100)	EC	131
51	—	22/09/2011	21/09/2011	13/10/2011	bile	B	pNDM_MGR194 (100)	EC	205
53	—	19/10/2011	19/05/2011	20/01/2012	urine	B	pNDM-ECS01 (100)	EC	131
S9	Thailand	09/12/2013	08/12/2013	07/01/2014	RS	C	pNDM-ECS01 (100)	KP	14
S7[b]	—	10/12/2013	22/10/2013	14/12/2013	RS	C	pNDM-ECS01 (100)	KP	14
S2[b]	—	10/12/2013	22/10/2013	14/12/2013	RS	C	pNDM-ECS01 (100)	EC	101
S8	Vietnam	14/01/2014	02/01/2014	12/02/2014	WS	A	unknown	KP	16
S10	India	28/01/2014	09/01/2014	07/04/2014	WS	A	pSg1-NDM (100)	KP	147
KP2	—	03/02/2014	06/01/2014	08/02/2014	RS	A	pSg1-NDM (100)	KP	147
KP1	—	04/02/2014	29/01/2014	13/02/2014	urine	A	pNDM-ECS01 (100)	KP	11
S5	Malaysia	05/02/2014	30/01/2014	14/02/2014	RS	C	pNDM-ECS01 (99)	KP	34
S6	—	06/02/2014	05/02/2014	07/03/2014	RS	C	pNDM-ECS01 (100)	KP	34
S4	Malaysia	07/02/2014	29/01/2014	15/03/2014	RS	C	pNDM-ECS01 (100)	KP	34
KP4	Bangladesh, India	12/02/2014	11/02/2014	23/03/2014	RS	A	pittNDM01_plasmid1 (94)	KP	14
KP3	India, Malaysia	13/02/2014	11/02/2014	19/04/2014	RS	C	pHC105-NDM (100)	KP	147
S3	—	20/02/2014	04/02/2014	27/02/2014	WS	C	pNDM-ECS01 (99)	EC	novel ST[d]
S1	—	11/03/2014	28/02/2014	18/03/2014	RS	C	pNDM-ECS01 (100)	EC	69
KP5	—	17/03/2014	24/01/2014	23/03/2014	WS	A	pSg1-NDM (100)	KP	147
KP6	Malaysia	04/05/2014	04/05/2014	15/05/2014	RS	C	unknown	KP	147
KP7	—	29/05/2014	29/05/2014	23/06/2014	RS	C	pNDM-ECS01 (99)	KP	399
KP9[c]	—	07/06/2014	02/06/2014	05/07/2014	RS	C	pSg1-NDM (100)	KP	147
KP8[c]	—	19/06/2014	02/06/2014	05/07/2014	urine	C	pSg1-NDM (100)	KP	147
KP10	—	23/07/2014	20/06/2014	08/08/2014	RS	C	blaNDM_plasmid2 (100)	KP	133
KP11	—	02/08/2014	02/08/2014	03/08/2014	RS	D	pNDM-ECS01 (100)	KP	496
KP12	—	14/08/2014	14/08/2014	30/08/2014	urine	D	pNDM-ECS01 (100)	KP	496
KP13	—	06/09/2014	03/07/2014	28/09/2014	urine	A	pSg1-NDM (100)	KP	147

pNDM-ECS01
Thailand

pNDM_MGR194
Chennai, India

pittNDM01
India → Pittsburgh

pHC105-NDM
Spain

blaNDM-1 plasmid
plasmid2
Ohio

pSg1-NDM
Novel

National strategic action plan antimicrobial resistance

1 November 2017

https://www.moh.gov.sg/action-plan-AMR

Overview

- One health approach
  - Led by Ministry of Health
  - Agri-food and Veterinary Authority
  - National Environment Agency
  - Public Utilities Board

- Education, surveillance, research, prevention and control of infection, optimising antibiotic use

- International collaboration e.g. WHO GLASS, OIE, ASEAN Livestock, Global Water Research Coalition

Education

Current

- Public education on vaccination and social hygiene, not AMR
- WAAW activities in public hospitals and 2 public libraries
- Education for veterinarians and farmers
- Food safety and hygiene messages

Priorities for action

- Public education from 2018
- Collaborating with Ministry of Education on curriculum development
- Enhance postgraduate education to doctors, pharmacists and veterinarians
- Engage animal feed manufacturers and distributors of veterinary drugs

Knowledge, attitudes and practices towards antibiotic use in upper respiratory tract infections among patients seeking primary health care in Singapore

Darius Shaw Teng Pan[1†], Joyce Huixin Huang[1†], Magdalene Hui Min Lee[1], Yue Yu[1], Mark I-Cheng Chen[2,3*], Ee Hui Goh[2], Lili Jiang[2], Joash Wen Chen Chong[2], Yee Sin Leo[1,2,3,4], Tau Hong Lee[3], Chia Siong Wong[3], Victor Weng Keong Loh[5], Adrian Zhongxian Poh[6], Tat Yean Tham[1,5,6], Wei Mon Wong[5,7,8] and Fong Seng Lim[1,5]

BMC Family Practice (2016) 17:148

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- 914 patients in 24 private primary care clinics:
  - 34% expected antibiotic for cough and cold, of which 40% would ask doctors for antibiotics, 10% would go to another doctor if they did not get antibiotic
- Knowledge level could be better:
  - 78% thought antibiotics were effective against viruses, and 65% felt antibiotics cured cough and cold faster
  - 12% kept antibiotic at home, 14% took left-over antibiotic, 7% gave antibiotic to family members

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Surveillance

Current

- National Antimicrobial Resistance and Control Committee reports on MDRO and antibiotic usage in public hospitals
- Reference National Public Health Laboratory
- Antibiotic sales to farmers and veterinarians
- Antibiotic residues in food products and animal feed
- MRSA, ESBL E coli and MDR Salmonella testing in imported food
- Environmental testing for antibiotic levels, drug-resistant bacteria and AMR genes

Priorities for action

- Extend surveillance to private hospitals and community
- Harmonise laboratory methods
- Extend to all animal production sectors (poultry, ruminants, aquaculture)
- AMR testing in imported and retail food
- Systematic One Health surveillance report by 2019
- Risk assessment

Research

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Current

- Human AMR research funded via National Research Foundation, NRMC, Communicable Disease Public Health Research Grant, Industry Alignment Fund
- Some research in AMR in imported and retail food, and environment

Priorities for action

- AMR is one of 3 infectious disease focus areas in Research, Innovation and Enterprise 2020 plan
  - National AMR research agenda with One Health focus
  - Inter-sectoral transmission pathways
  - Genomic surveillance of AMR
  - Sociobehavioural research
  - Socioeconomic impact
- Baseline AMR data in indicator bacteria in local poultry, dairy and fish farms
- Applied research in alternative to antibiotics: vaccines, animal management systems, husbandry practices

Prevention and control of infections

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Current

- National childhood and adult immunisation schedules
- National Infection Prevention Committee
- Biosecurity requirement and animal husbandry practice → licensing
- Animal vaccination
- Food hygiene
- Water and waste management

Priorities for action

- Enhance infection control for CPE
- Enhance adult vaccination
- ASEAN Sectoral Working Group for Livestock and Fisheries recommendations
- Improve animal management and promote animal vaccine use
- Pathogen surveillance in food and environment

Optimising antibiotic use

Current

- Antibiotics prescription only
- National ASP in public hospitals since 2011
- Antibiotics not used for growth promotion
- Nitrofurantoin, chloramphenicol and avoparcin banned in animal feed, and livestock and aquaculture farms
- Farmers allowed to give antibiotics

Priorities for action

- Extend ASP to private hospitals
- Guidelines for antibiotic use in primary care
- Veterinary drug registration and prescription of antibiotics in livestock and aquaculture
- Veterinary national antibiotic guideline and ASP

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Antimicrobial stewardship in Singapore

Reducing antimicrobial resistance through appropriate antibiotic usage in Singapore

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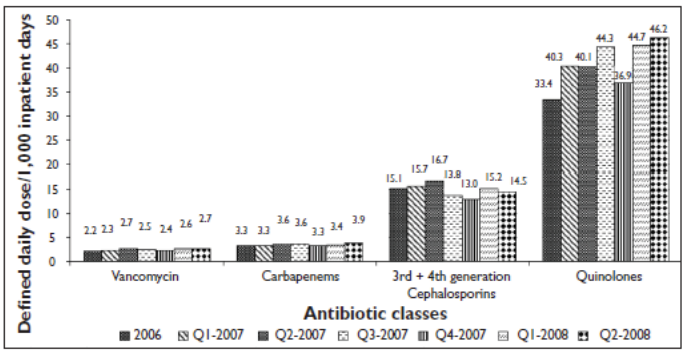
Hsu L Y, Kwa A L, Lye D C, Chlebicki M P, Tan T Y, Ling M L, Wong S Y, Goh L G

Singapore Med J 2008; 49 (10) : 749



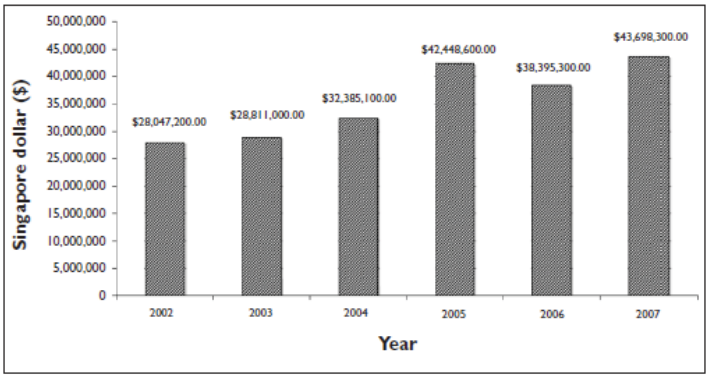


Fig. 1 Bar chart shows combined usage data of key antibiotic classes in local public hospitals according to defined daily dose per 1,000 patient-days.

Surveillance of Broad-Spectrum Antibiotic Prescription in Singaporean Hospitals: A 5-Year Longitudinal Study

IIDE Institute of Infectious Diseases and Epidemiology

Yi-Xin Liew[1], Prabha Krishnan[2], Chay-Leng Yeo[3], Thean-Yen Tan[4], Siok-Ying Lee[5], Wan-Peng Lim[6], Winnie Lee[1], Li-Yang Hsu[7]*, Network for Antimicrobial Resistance Surveillance (Singapore)

PLoS ONE December 2011 | Volume 6 | Issue 12 | e28751

Stable fluoroquinolone
Increasing carbapenems and gram positive agents
Decreasing 3rd and 4th generation cephalosporins

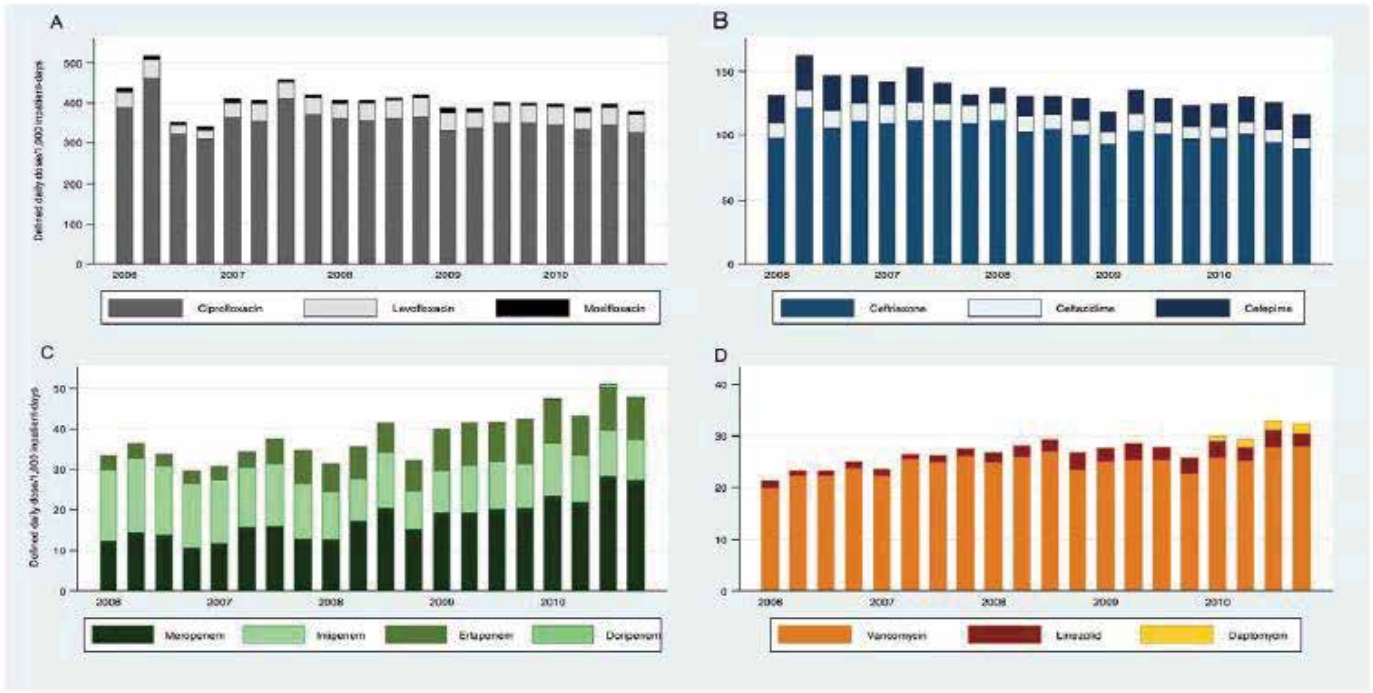


Figure 2. Prescription trends for individual antibiotics within major classes of broad-spectrum antibiotics in Singaporean hospitals, 2006–2010. (A) Fluoroquinolones. (B) Third and fourth generation cephalosporins. (C) Carbapenems. (D) Gram-positive agents.

ASP Singapore 2011

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- Funding ASP in all public hospitals
- Pharmacists and ID doctors
- Formula for manpower calculation
- CDSS for ASP
- Practice guidelines for selected antibiotics, common infections and surgical prophylaxis
- Antibiotic usage, DDD/1000 patient-days
  - Augmentin, tazocin
  - Vancomycin, daptomycin, linezolid
  - Ceftriaxone, ceftazidime, cefepime
  - Ciprfloxacin, levofloxacin, moxifloxacin
  - Carbapenems
  - Triazoles, echinocandins, amphotericin

ASP Singapore 2011

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- Formulary restriction
  - Echinocandins, new triazoles, liposomal amphotericin B, linezolid, daptomycin, tigecycline, doripenem
  - Topical mupirocin and fusidic acid
- Prospective audit on carbapenems, piperacillin-tazobactam and cefepime
  - Compliance with feedback
- Safety indicators
  - Length of hospital stay
  - 30-day mortality
  - 30-day re-admission

ASP Singapore 2011

- 6 adult hospitals and 1 paediatric → multidisciplinary, hospital-wide approach
- Prospective review and feedback on carbapenems and piperacillin-tazobactam
- CDSS in place in all hospitals (ARUSC in 2, SCM in 5, EPIC in 1)
- ASP pharmacists → ASP ID doctors

ASP manpower funding

Table A2: Number of Beds to ASP Manpower Ratio

	Tier 1 Hospitals - Tertiary care or hospitals with complex immunocompromised patients **(SGH, NUH)**	**Tier 2 Hospitals –** Intermediate RHs **(KKH,TTSH,CGH)**	**Tier 3 Hospitals –** General Patients **(All others)**
Beds:FTE ratio for ID Physician			
Without IT support	2,000:1	2,000:1	2,000:1
With IT support	2,000:1	2,000:1	2,000:1
Beds:FTE ratio for ASP pharmacists			
Without IT support	200:1	300:1	400:1
With IT support	300:1	400:1	500:1

Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey

Lancet Glob Health 2018
Published Online
April 19, 2018
http://dx.doi.org/10.1016/S2214-109X(18)30186-4

*Ann Versporten, Peter Zarb, Isabelle Caniaux, Marie-Françoise Gros, Nico Drapier, Mark Miller, Vincent Jarlier, Dilip Nathwani, Herman Goossens, on behalf of the Global-PPS network**

	Countries (n)	Hospitals (n)	Medical wards		Surgical wards		Intensive-care units		Haematology oncology wards		Pneumology wards		Transplant (bone marrow or solid transplants)		Total	
			Admitted (n)	Anti-microbial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Antimicrobial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Antimicrobial use (%, country range)
Eastern Europe	2	8	778	11·6%	1381	33·2%	107	67·3%	11	9·1%	105	30·5%	..	..	2382	27·4% (23·7–27·8)
Northern Europe	5	36	4959	29·8%	2371	37·7%	370	55·9%	242	49·6%	101	53·5%	51	60·8%	8094	34·4% (29·0–37·8)
Southern Europe	13	53	6443	32·6%	5475	40·0%	1010	64·1%	646	33·6%	561	60·2%	52	76·9%	14187	39·0% (27·2–62·0)
Western Europe	5	118	17483	23·4%	8851	28·0%	1467	56·0%	1048	43·1%	1111	49·7%	89	80·9%	30049	28·1% (25·1–37·1)
Africa	5	12	619	49·9%	1101	49·0%	64	64·1%	..	..	..	..	..	..	1798	50·0% (27·8–74·7)
East and south Asia*	6	29	6644	33·0%	5663	34·2%	702	65·5%	847	54·0%	409	46·2%	146	86·3%	14411	37·2% (29·6–78·5)
West and central Asia	9	27	1873	42·0%	1249	44·7%	396	47·7%	156	48·1%	..	..	..	..	3677	43·8% (22·4–85·7)
Oceania	2	9	1781	29·8%	604	52·5%	76	69·7%	46	54·3%	..	..	..	..	2516	37·0% (33·3–38·5)
Latin America	4	19	1942	31·8%	1571	37·3%	468	55·1%	92	28·3%	..	..	41	65·9%	4122	36·8% (32·5–43·4)
North America	2	24	3605	32·4%	1136	44·2%	524	59·4%	202	55·4%	34	58·8	39	66·7%	5540	38·6% (30·9–44·8)

A version of this table containing numerical data for all percentages is in the appendix. Empty cells mean that no cases or too few cases (ie, fewer than 10 admitted or treated inpatients) were recorded (these cases are included in the totals). *Includes south, east, and southeast Asia.

Table 1: **Antimicrobial use in adult hospital inpatients, by UN region, 2015**

Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey

Lancet Glob Health 2018
Published Online
April 19, 2018
http://dx.doi.org/10.1016/S2214-109X(18)30186-4

*Ann Versporten, Peter Zarb, Isabelle Caniaux, Marie-Françoise Gros, Nico Drapier, Mark Miller, Vincent Jarlier, Dilip Nathwani, Herman Goossens, on behalf of the Global-PPS network**

	Antimicrobial prescriptions	Antibiotic prescriptions	Targeted treatment*	Targeted treatment (resistant organisms)*	Reason recorded†	Stop or review date recorded†	Parenteral administration‡	Guidelines available§	Compliant to local guidelines¶	No guidelines available‖
Eastern Europe (n=653)	747	708	51 (7·8%)	42 (6·4%)	64·3%	50·5%	87·6%	79·8%	85·7%	19·2%
Northern Europe (n=2783)	3880	3536	396 (14·2%)	80 (2·9%)	81·4%	51·6%	62·2%	90·0%	83·4%	6·5%
Southern Europe (n=5534)	7674	6837	838 (15·1%)	292 (5·3%)	69·5%	29·1%	80·0%	60·5%	70·8%	29·6%
Western Europe (n=8458)	10612	9485	2204 (26·1%)	469 (5·5%)	80·5%	40·3%	64·0%	81·0%	78·7%	10·1%
Africa (n=899)	1502	1213	131 (14·6%)	25 (2·8%)	70·4%	36·6%	62·7%	49·5%	67·9%	26·7%
East and south Asia** (n=5363)	7607	6781	938 (17·5%)	287 (5·4%)	74·6%	43·5%	71·8%	76·4%	81·5%	21·4%
West and central Asia (n=1612)	2252	2084	236 (14·6%)	153 (9·5%)	72·8%	19·8%	85·2%	53·4%	66·3%	40·5%
Oceania (n=932)	1411	1226	218 (23·4%)	63 (6·8%)	85·1%	27·0%	60·5%	87·4%	73·2%	11·7%
Latin America (n=1518)	2403	2170	403 (26·5%)	231 (15·2%)	81·4%	40·3%	84·4%	76·5%	64·1%	19·9%
North America (n=2139)	3125	2752	511 (23·9%)	127 (5·9%)	84·9%	39·6%	73·1%	77·3%	85·8%	18·5%
Total (n=29 891)	41213	36792	5926 (19·8%)	1769 (5·9%)	76·9%	38·3%	71·4%	74·3%	77·4%	19·2%

Data are n or %. A version of this table containing numerical data for all percentages is in the appendix. *Patients receiving at least one antibiotic for systemic therapeutic use only (ie, health-care-associated or community-acquired infection). †Includes all antimicrobials; the total number of antimicrobial prescriptions was used to calculate percentages. ‡Patients who received at least one parenteral antibiotic for systemic use. §Antibiotic prescriptions for which guidelines were available to guide antibiotic choice (not route, dose, or duration), which was calculated as all antibiotic prescription for which a local guideline was available/all antibiotic prescription. ¶The number of antibiotic prescriptions for which guidelines were available was used as the denominator to calculate percentages. ‖The total number of antibiotic prescriptions was used as the denominator to calculate percentages. **Includes south, east, and southeast Asia.

Table 4: **Overview of antimicrobial and antibiotic quality indicators for adult inpatients by region, year 2015**

Broadspectrum cephalosporin and beta-lactamase inhibitor usage

Figure 3.3: Cephalosporins (cefepime, ceftazidime and ceftriaxone), Defined Daily Dose (DDD) per 1,000 inpatient days, 2011 – 2016

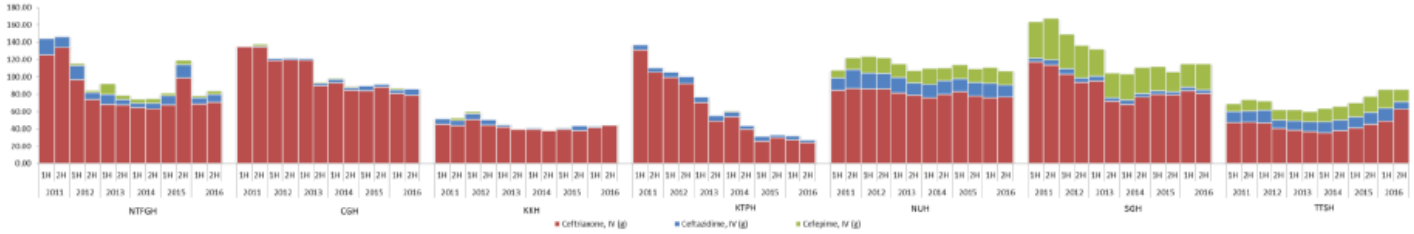
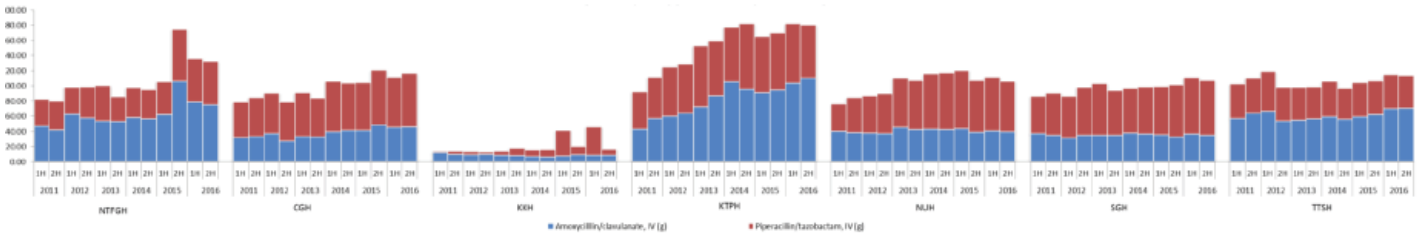


Figure 3.1: Amoxycillin/clavulanate and piperacillin/tazobactam, Defined Daily Dose (DDD) per 1,000 inpatient days, 2011 – 2016



Carbapenem and PO ciprofloxacin usage

Figure 3.6: Carbapenems, Defined Daily Dose (DDD) per 1,000 inpatient days, 2011 – 2016

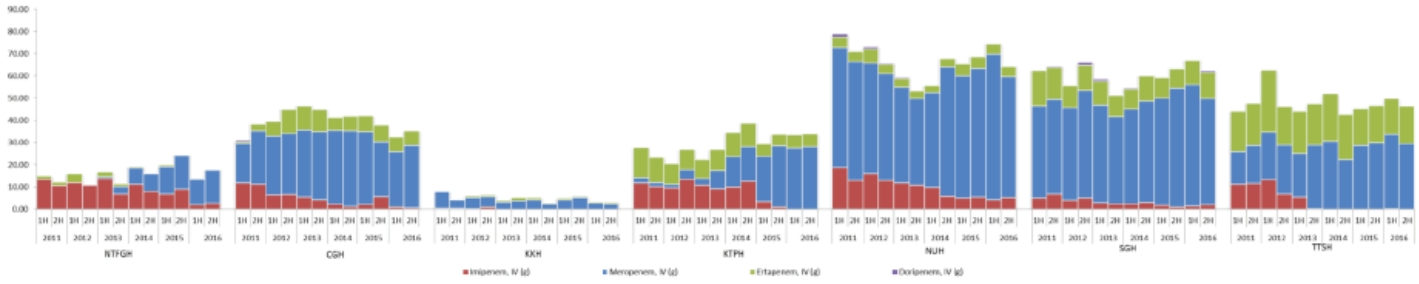
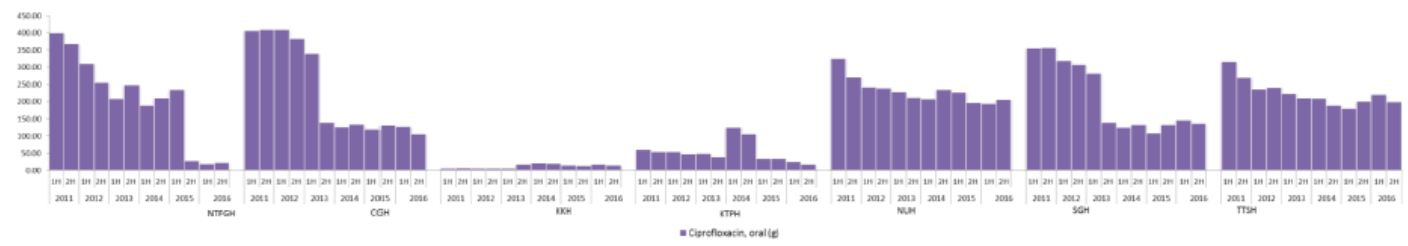


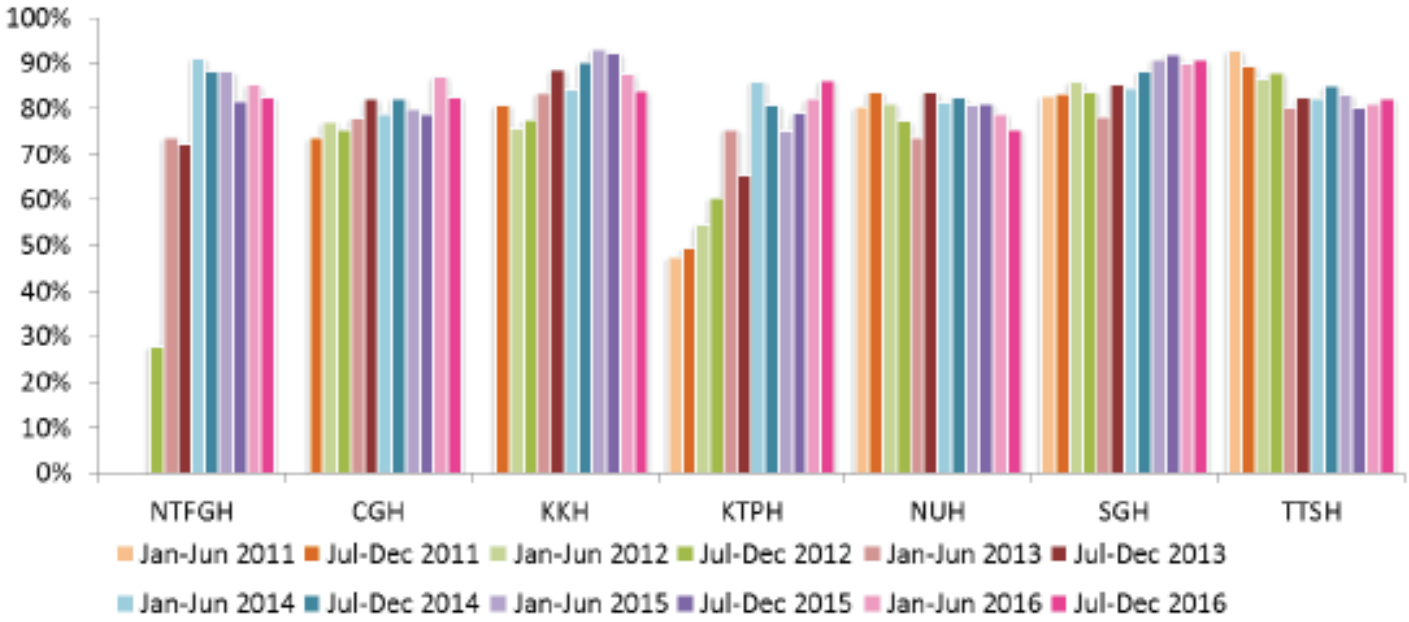
Figure 3.5: Fluoroquinolones (Oral Ciprofloxacin), Defined Daily Dose (DDD) per 1,000 inpatient days, 2011 – 2016

The sudden drops in use of oral ciprofloxacin in H2 2013 in SGH and CGH, and H1 2015 - H2 2016 in NTFGH, are due to the introduction of data collection IT software that do not account for outpatient use of ciprofloxacin.



National comparison

Figure 3.9: Initial appropriateness of carbapenems, 2011 - 2016



National comparison

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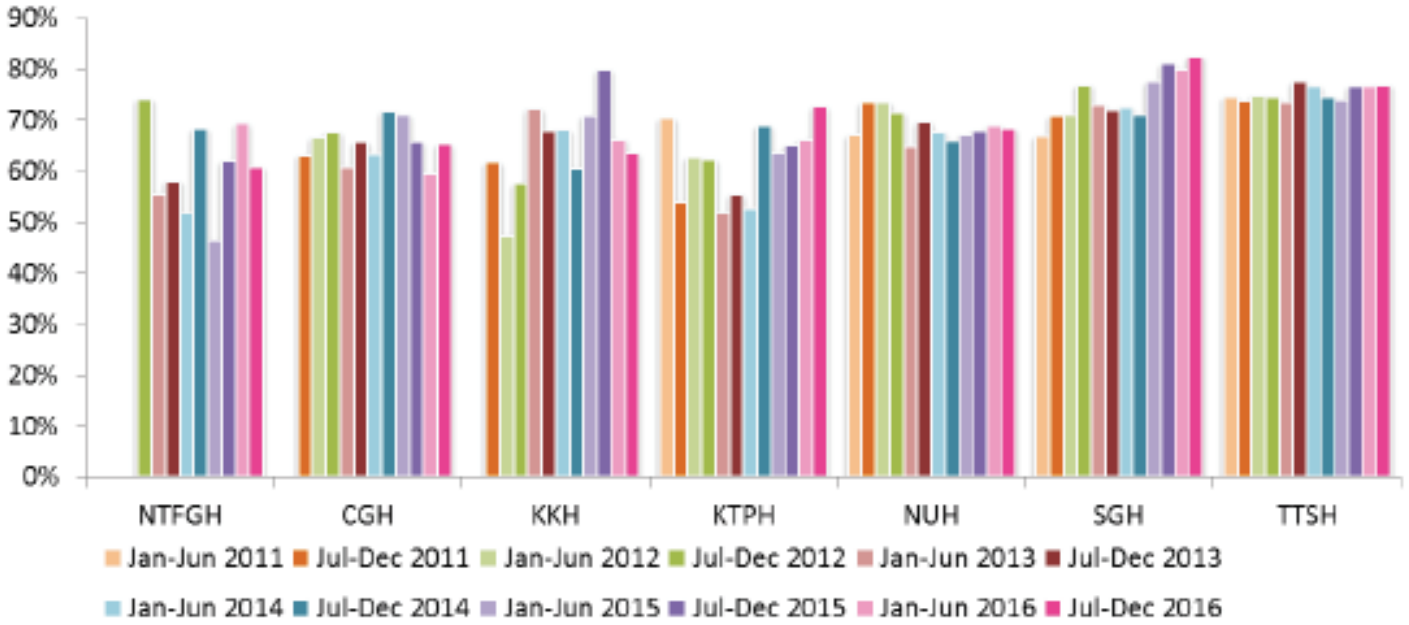
Figure 3.10: Acceptance of ASP interventions, 2011-2016

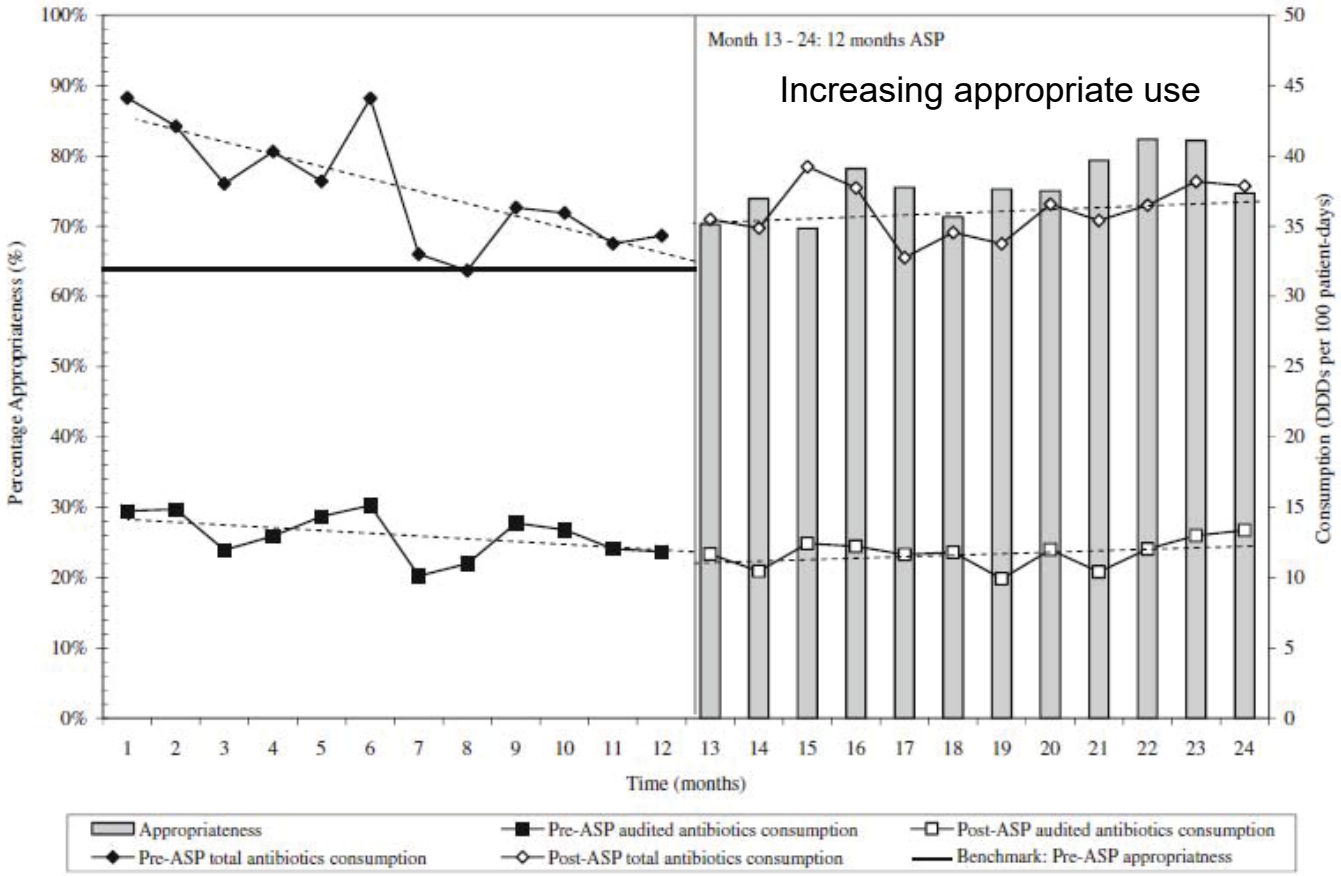


The effect of a whole-system approach in an antimicrobial stewardship programme at the Singapore General Hospital

J. Teo · A. L. H. Kwa · J. Loh · M. P. Chlebicki · W. Lee

Eur J Clin Microbiol Infect Dis (2012) 31:947–955

IIDE Institute of Infectious Diseases and Epidemiology



Impact of an antimicrobial stewardship programme on patient safety in Singapore General Hospital

Yi Xin Liew[a,*], Winnie Lee[a], Joan Chain Zhu Loh[b], Yiying Cai[a], Sarah Si Lin Tang[a], Cheryl Li Ling Lim[a], Jocelyn Teo[a], Rachel Wen Qin Ong[a], Andrea Lay-Hoon Kwa[a,*], Maciej Piotr Chlebicki[b]

International Journal of Antimicrobial Agents 40 (2012) 55–60

IIDE Institute of Infectious Diseases and Epidemiology

Types of intervention recommended by the antimicrobial stewardship programme that may have an impact on morbidity and mortality ($N = 743$).

Intervention	Accepted [n (%)][a]		Rejected [n (%)][a]		P-value
	Total	Patients who died	Total	Patients who died	
De-escalation based on culture results	97 (16.8)	13 (2.2)	27 (16.4)	5 (3.0)	0.555
Discontinue antibiotic	270 (46.7)	32 (5.5)	86 (52.1)	11 (6.7)	0.851
Narrowing of empirical coverage	49 (8.5)	6 (1.0)	38 (23.0)	1 (0.6)	0.239
Intravenous-to-oral switch	162 (28.0)	4 (0.6)	14 (8.5)	1 (0.6)	0.346
Total	578/743 (77.8)	55 (9.5)	165/743 (22.2)	18 (10.9)	0.557

No safety signals of concern for culture-guided de-escalation, stopping antibiotic, narrowing empiric coverage, and IV → PO switch

Cost-effectiveness

Liew YX, et al. IJAA 2015;46:594-5.

- Comparison between accepted and rejected groups offered ASP interventions
- Acceptance of ASP interventions associated with cost saving:
  - Antibiotic cost, SGD$107
  - Shortened length of stay (6.4 days), SGD$6683
  - Reduced re-admission, SGD$8416

Safety and clinical outcomes of carbapenem de-escalation as part of an antimicrobial stewardship programme in an ESBL-endemic setting

Kaung Yuan Lew[1], Tat Ming Ng[2], Michelle Tan[2], Sock Hoon Tan[2], Ee Ling Lew[2], Li Min Ling[3], Brenda Ang[3], David Lye[3,4] and Christine B. Teng[1,2*]

J Antimicrob Chemother 2015; **70**: 1219–1225

Table 2. Primary and secondary outcomes

Outcomes	De-escalated (n=204)	Not de-escalated (n=96)	P	Absolute risk difference (95% CI)
Clinical success, *n* (%)	183 (89.7)	85 (88.5)	0.84	1.2 (−5.8 to 9.8)
Survival at discharge, *n* (%)	173 (84.8)	79 (82.3)	0.58	2.5 (−5.9 to 12.3)
30 day mortality from start of carbapenem, *n* (%)	25 (12.3)	14 (14.6)	0.58	−2.3 (−11.6 to 5.4)
30 day readmission due to infection, *n* (%)	15 (7.4)	8 (8.3)	0.81	−0.9 (−8.8 to 5.0)
Duration of carbapenem use (days), median (IQR)	6 (4–8)	8 (7–11)	<0.001	−2 (−3 to −2)
Total duration of antimicrobial therapy (days), median (IQR)	9 (7–14)	9 (7–12)	0.70	0 (0)
Length of hospitalization from start of carbapenem use (days), median (IQR)	18 (9–35)	20 (9–40)	0.62	−2.0 (−6 to 3)
Adverse drug reaction[a], *n* (%)				
antibiotic-associated diarrhoea	9 (4.4)	12 (12.5)	0.015	−8.1 (−16.4 to −1.7)
rash	1 (0.5)	1 (1.0)	0.54	−0.6 (−5.2 to 1.8)
neurotoxicity (altered mental status)	1 (0.5)	0	>0.99	0.5 (−3.4 to 2.7)
number of patients with adverse drug reaction	11 (5.4)	12 (12.5)	0.037	−7.1 (−15.5 to −0.5)
Incidence of MDR organisms at 30 days, *n* (%)				
carbapenem-resistant *A. baumannii*	4 (2.0)	7 (7.3)	0.042	−5.3 (−12.4 to −0.6)
other carbapenem-resistant Gram-negative bacteria[b]	6 (2.9)	1 (1.0)	0.44	1.9 (−3.0 to 5.3)
CDAD	2 (1.0)	4 (4.2)	0.081	−3.2 (−9.3 to 0.4)
Candida sp. in sterile sites	1 (0.5)	0	>0.99	0.5 (−3.4 to 2.7)

Implementation hurdles of an interactive, integrated, point-of-care computerised decision support system for hospital antibiotic prescription

A.L. Chow[a,b,1], A. Ang[c,1], C.Z. Chow[a], T.M. Ng[d], C. Teng[d,e], L.M. Ling[f], B.S. Ang[b,f], D.C. Lye[c,f,*]

International Journal of Antimicrobial Agents 47 (2016) 132–139

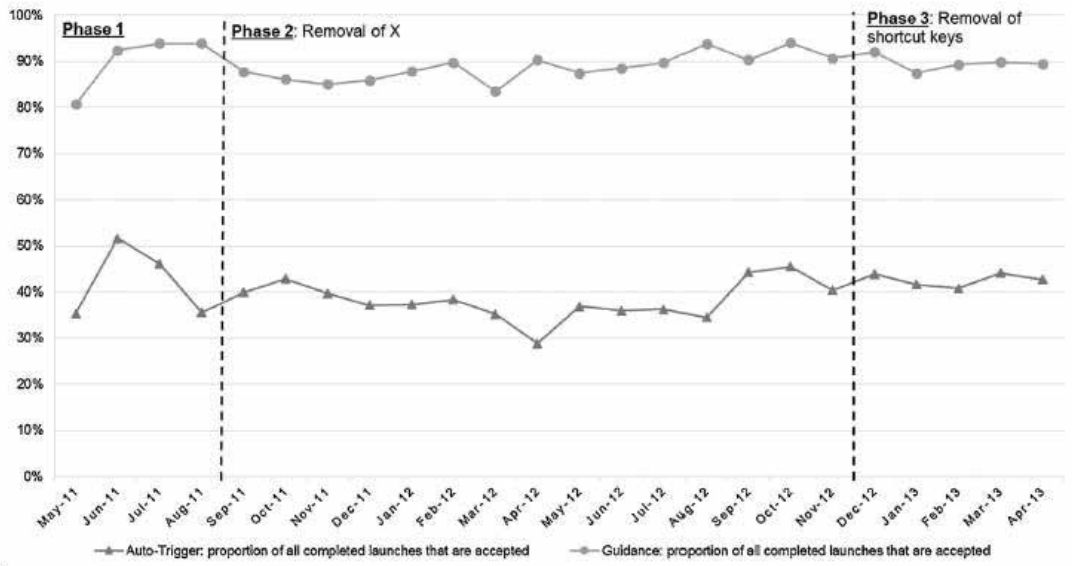


Fig. 4. Trend of proportion of accepted ARUSC recommendations per month. ARUSC, Antibiotic Resistance Utilisation and Surveillance-Control.

auto-trigger. Amongst ARUSC launches for guidance, being from a medical department [adjusted odds ratio (aOR) = 1.20, 95% confidence interval (CI) 1.04–1.37] and ARUSC launch during on-call (aOR = 1.81, 95% CI 1.61–2.05) were independently associated with acceptance of ARUSC recommendations. Junior

Mortality Benefits of Antibiotic Computerised Decision Support System: Modifying Effects of Age

Angela L. P. Chow[1,2], David C. Lye[3,4] & Onyebuchi A. Arah[2,5]

SCIENTIFIC REPORTS | 5:17346 |

Antibiotic computerised decision support systems (CDSSs) are shown to improve antibiotic prescribing, but evidence of beneficial patient outcomes is limited. We conducted a prospective cohort study in a 1500-bed tertiary-care hospital in Singapore, to evaluate the effectiveness of the hospital's antibiotic CDSS on patients' clinical outcomes, and the modification of these effects by patient factors. To account for clustering, we used multilevel logistic regression models. One-quarter of 1886 eligible inpatients received CDSS-recommended antibiotics. Receipt of antibiotics according to CDSS's recommendations seemed to halve mortality risk of patients (OR 0.54, 95% CI 0.26–1.10, $P = 0.09$). Patients aged ≤65 years had greater mortality benefit (OR 0.45, 95% CI 0.20–1.00, $P = 0.05$) than patients that were older than 65 (OR 1.28, 95% CI 0.91–1.82, $P = 0.16$). No effect was observed on incidence of *Clostridium difficile* (OR 1.02, 95% CI 0.34–3.01), and multidrug-resistant organism (OR 1.06, 95% CI 0.42–2.71) infections. No increase in infection-related readmission (OR 1.16, 95% CI 0.48–2.79) was found in survivors. Receipt of CDSS-recommended antibiotics reduced mortality risk in patients aged 65 years or younger and did not increase the risk in older patients. Physicians should be informed of the benefits to increase their acceptance of CDSS recommendations.

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Thank you for your attention

David_lye@ttsh.com.sg

NUS National University of Singapore | Yong Loo Lin School of Medicine

LEE KONG CHIAN SCHOOL OF MEDICINE

Prof. Victor Lim

Position: Pro Vice-Chancellor

Department/organization: International Medical University

Economy: Malaysia

Educational Background

- 1974 MBBS, the University of Malaya
- 1978 MSc, Medical Microbiology from the University of London
- 1981 passed the Royal College of Pathologists examinations (MRCPath)

Professional Career

- 2004-2008 President of the Western Pacific Society of Chemotherapy
- 2008-2011 Master of the Academy of Medicine of Malaysia
- 1999-2003 President of the Malaysian Society for Infectious Diseases and Chemotherapy

Publications

- Lim V Enhancing microbiology diagnostics in the Asia Pacific – a perspective from Malaysia. Malaysian J Pathol 2014; 36 (Suppl A) : 11.
- McNeil HC, Lean S, Lim V, Clarke SC. The state of ESKAPE in Malaysia. International Journal of Antimicrobial Agents 2016; 48:578-9.
- Tricarico, Serena, McNeil, Hannah C., Cleary, David W., Head, Michael G., Lim , Victor, Kok Seng Yap, Ivan, Chun Wie, Chong, Siang Tan, Cheng, Norazmi, Mohd Nor, Ismail, Aziah, Seong Guan Cheah, Eddy, Faust, Saul N., Jefferies, Johanna MC, Roderick, Paul J., Moore, Michael, Yuen, Ho Ming, Newell, Marie-Louise, Mcgrath, Nuala, Webb, Jeremy, Doncaster, C. Patrick, Kraaijeveld, Alex R., Webb, Jeremy S. and Clarke, Stuart C. Pneumococcal conjugate vaccine implementation in middle-income countries. Pneumonia 2017; 9 : 6.
- Lim V. The role of behavioural science in antibiotic stewardship. International Journal of Antimicrobial Agents 2017; 50 (Suppl 1) : S71.
- Lim VKE. Changing behavior to improve antibiotic stewardship. International Journal of Antimicrobial Agents 2017; 50 (Suppl 2) : S16.

Speech Abstract

The Antibiotic Stewardship Programme in Malaysia

Malaysia is a developing economy in South East Asia with a population of 31 million. The per capita GDP is USD 28,900 in 2017 and its annual total expenditure on health is 4.5% of GDP.

In 2003 the Ministry of Health established a fairly well defined national strategy for the purpose of antibiotic stewardship. This is a multifaceted strategy and a governance structure was set up for its implementation. The National Infection and Antibiotic Control Committee is chaired by the Director General of Health and similar committees are also established at state and institutional levels.

A National Antibiotic Resistance Surveillance System was established earlier in 1990. In 2017 the 42 participating laboratories contributed data on more than 800,000 isolates. Biannual prevalence surveys of hospital associated infection are conducted in Ministry of Health hospitals while the Malaysian Registry for Intensive Care monitors the incidence of ventilator associated pneumonia (VAP) and central venous catheter associated blood stream infection (CVC-BSI). The monitoring of antibiotic utilization nationwide is undertaken annually through the National Medicines Use surveys. Monitoring of antibiotic utilisation in the Ministry of Health and selected private hospitals is focused on 4 major groups of compounds namely cephalosporins, carbapenems, quinolones and glycopeptides.

At the institutional level all government hospitals have antibiotic formularies and guidelines. However the effectiveness of antibiotic stewardship at an institution depends very much on the presence of “champions”. In the private sector doctors can use any product so long as it is registered by the Drug Control Authority and consultants operate as independent contractors in private hospitals. Professional societies also issue practice guidelines from time to time but the effectiveness of these guidelines is questionable.

In 2017 Malaysia launched its 5-year Action Plan on Antimicrobial Resistance in response to WHO’s Global Action Plan. The objectives are aligned to the Global Plan and under each Objective, the strategies, actions, implementation dates, target groups and units responsible are defined as are evaluation indices. The Plan will intensify current activities and establish new initiatives. Most importantly the health and agricultural ministries will work together in implementing the plan.

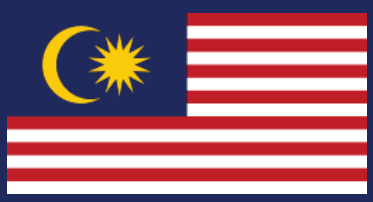
Other measures in antibiotic stewardship include the legislative control of prescription and sales of antibiotics for medicinal use as well as non-medicinal use and the regulation of marketing and promotional activities by pharmaceutical companies. Generally Malaysia seems to be on the right track but we still have some way to go to ensure the participation of all the major stakeholders.

The Antibiotic Stewardship Programme in Malaysia

Victor Lim
International Medical University,
Kuala Lumpur, Malaysia

Malaysia

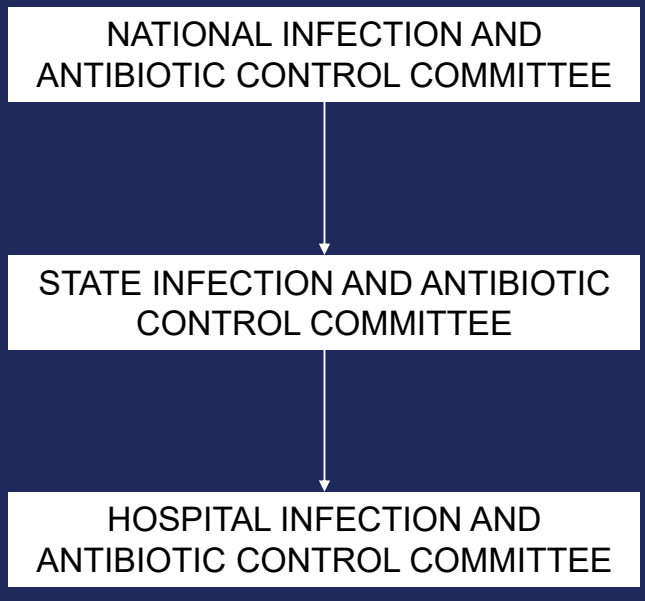
- Developing economy in South East Asia
- Population : 31 million (2017)
- Per capita GDP : USD 28,900 (2017)
- Infant mortality rate : 6.7/1000 births (2016)
- Maternal mortality ratio : 29.1/100,000 live births
- Total expenditure on health : 4.5% of GDP



Establishment of a National Strategy

- In 2003 the Ministry of Health with the assistance of WHO prepared a national strategy for the containment of antimicrobial resistance
- Measures included
  - Infection And Antibiotic Control Committees (IACC) at hospital, state and national levels
  - Strengthening the antibiotic resistance surveillance system
  - Developing and implementing antibiotic guidelines for primary care practitioners
  - Improving access to and upgrading the quality of microbiological diagnostic facilities
  - Increasing public awareness of antibiotic resistance
  - Controlling and regulating the use of antibiotics in agriculture

Governance and Management

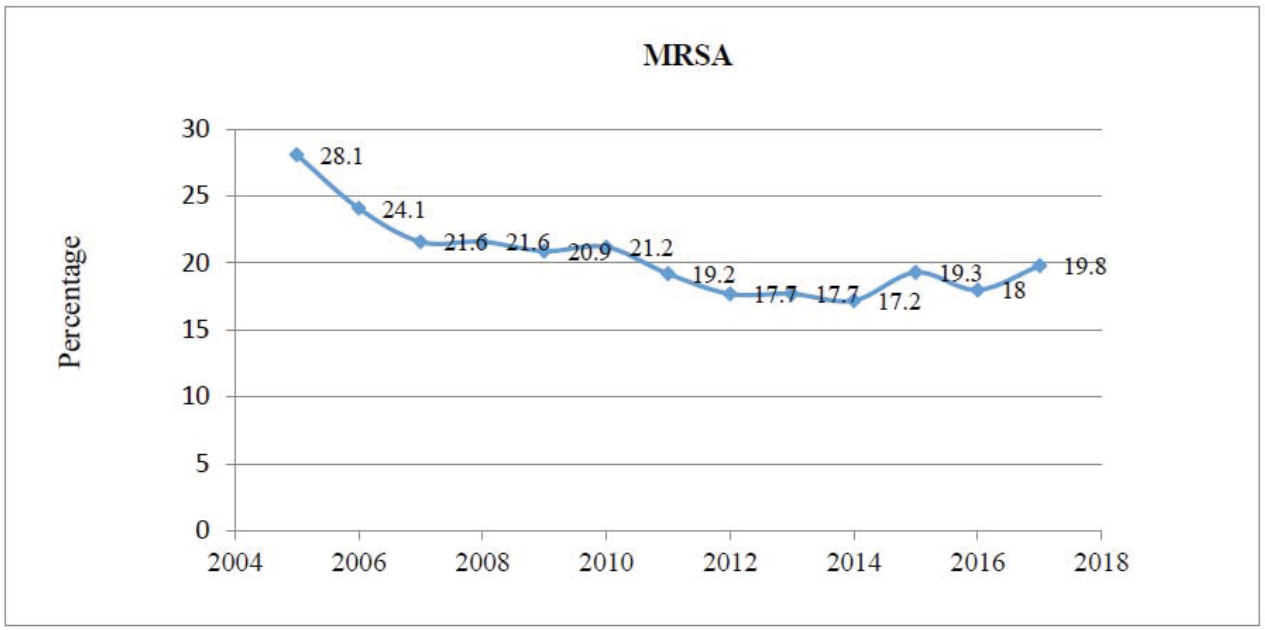


National Committee

- Meets twice a year
- Chaired by the Director General of Health
- Attended by all state representatives and selected technical experts
- Reviews reports including
  - Antibiotic resistance surveillance
  - Nosocomial infection prevalence rates
  - Antibiotic utilisation rates
- Makes policies and recommendations based on the data collected

Resistance surveillance programme

- National Surveillance of Antibiotic Resistance
  - Established in 1990
  - 42 participating laboratories; over 800,000 isolates in 2017
  - Standard methodology : CLSI and standard antibiotic panels
  - WHO Net software
  - Quality assurance



National Surveillance for Antimicrobial Resistance 2018. http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html

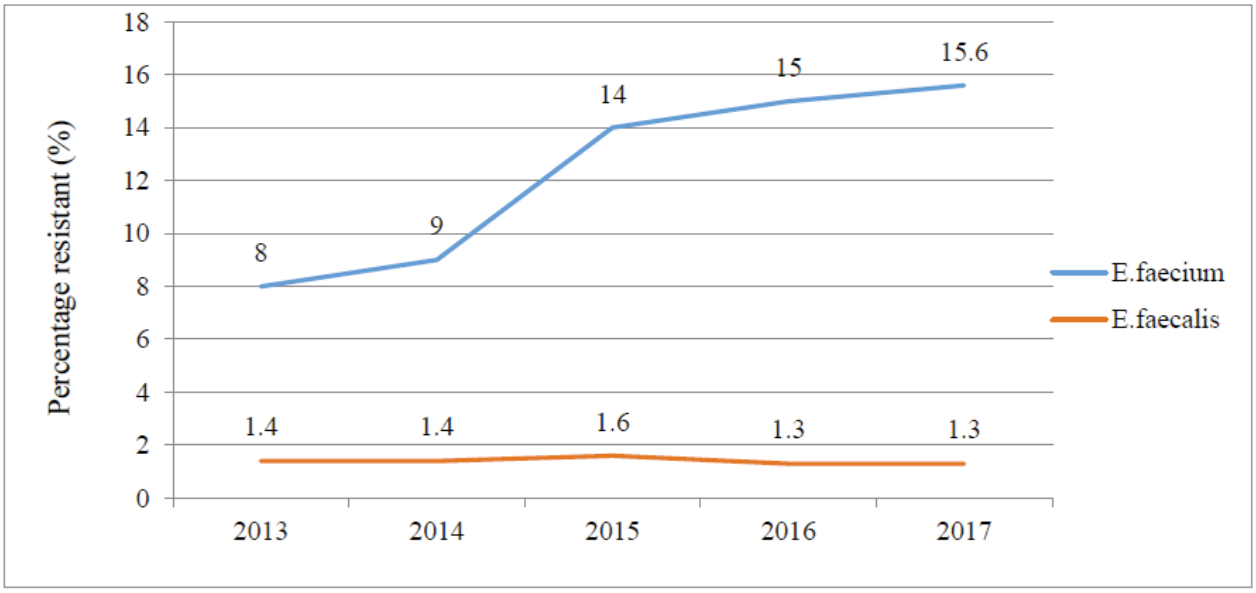


Figure 13: Trend of vancomycin resistance in *Enterococcus faecium* and *Enterococcus faecalis* from all clinical samples, 2013-2017.

National Surveillance for Antimicrobial Resistance 2018. http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html

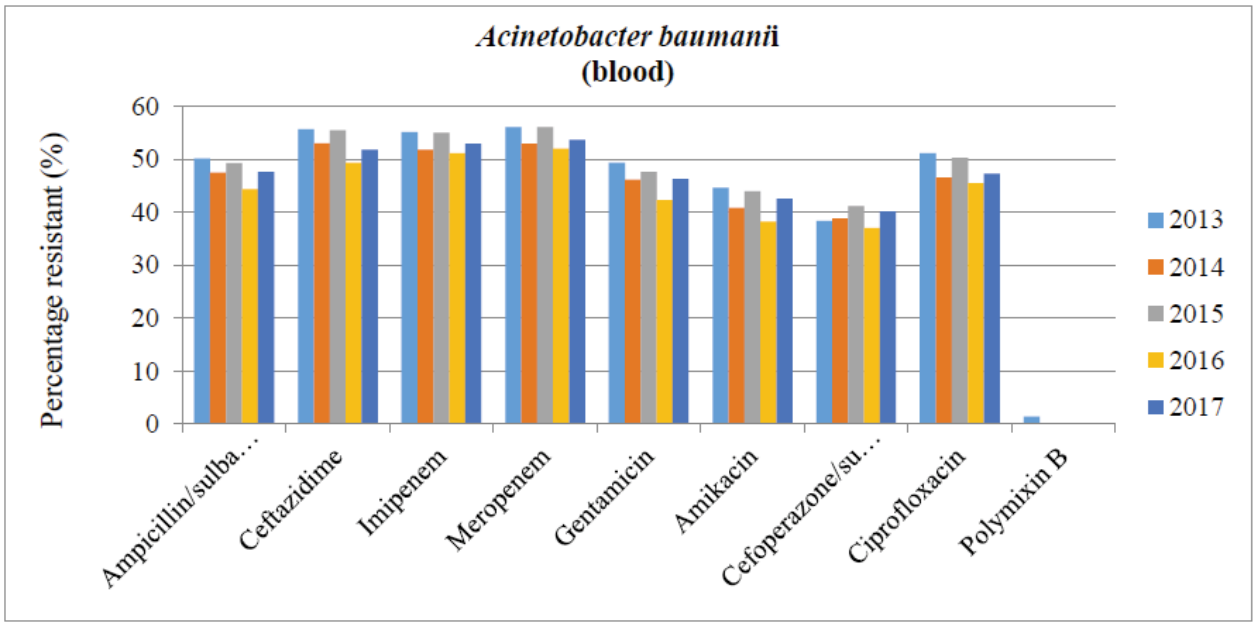


Figure 18: Antibiotic resistance trend for *Acinetobacter baumanii* isolated from blood, 2013-2017.

National Surveillance for Antimicrobial Resistance 2018. http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html

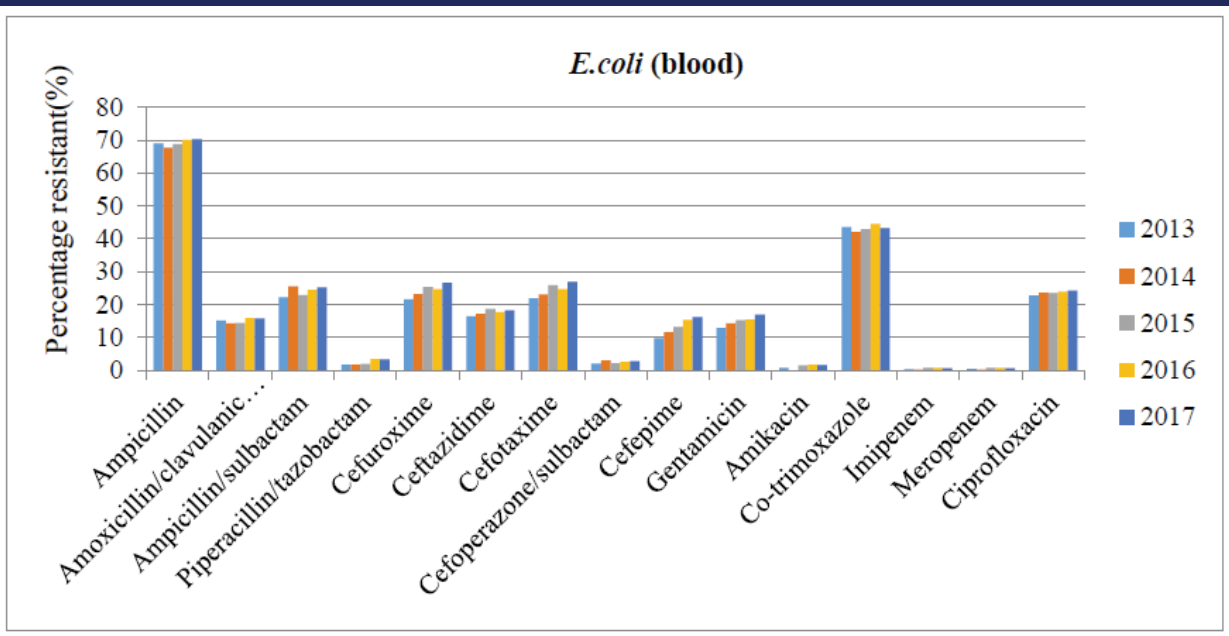


Figure 21: Antibiotic resistant trend for *E. coli* isolated from blood, 2013-2017.

National Surveillance for Antimicrobial Resistance 2018. http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html

Carbapenem-resistant Enterobacteriaceae

E. coli

Antibiotic	2013 (%R) (no. tested)	2014 (%R) (no. tested)	2015 (%R) (no. tested)	2016 (%R) (no. tested)	2017 (%R) (no. tested)
Imipenem	0.2 (12206)	0.3 (13654)	0.4 (13360)	0.9 (10871)	0.6 (12289)
Meropenem	0.2 (11838)	0.2 (13386)	0.5 (13167)	0.8 (10645)	0.7 (12439)

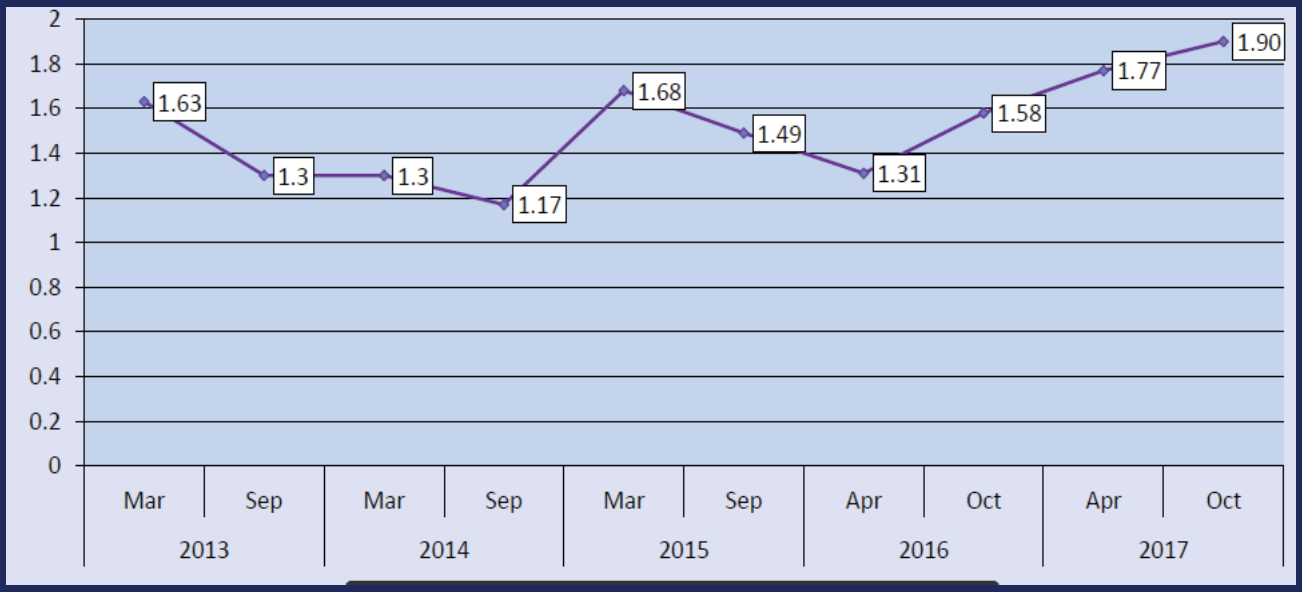
Klebsiella

Antibiotic	2013 (%R) (no. tested)	2014 (%R) (no. tested)	2015 (%R) (no. tested)	2016 (%R) (no. tested)	2017 (%R) (no. tested)
Imipenem	1.5 (24477)	1.3 (28787)	2.4 (31025)	2.3 (29339)	2.7 (30319)
Meropenem	1.7 (23303)	1.6 (27911)	2.8 (30253)	2.6 (28254)	2.9 (31151)

National Surveillance for Antimicrobial Resistance 2018.
http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html

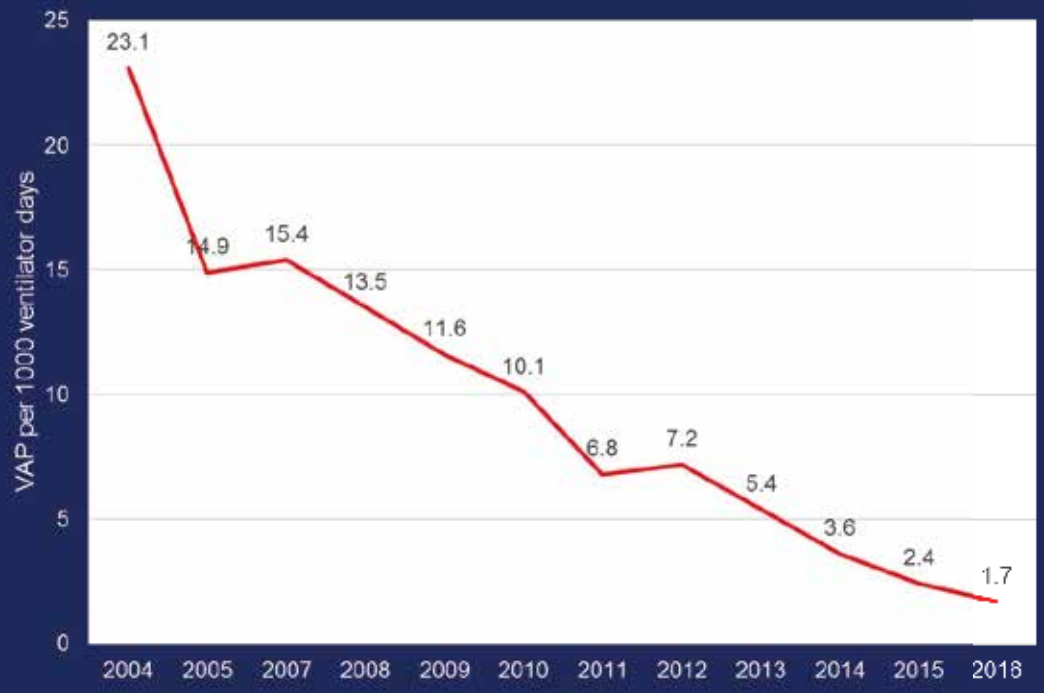
National Hospital Associated Infection Surveillance Programme

- Prevalence studies conducted twice a year
  - CDC definitions of infections
  - Universal surveillance on a defined day
  - Data collected, analysed and published by the Quality Division of the Ministry of Health
- Malaysian Registry for Intensive Care
  - ventilator-associated pneumonia
  - CVC – BSI
  - 50 ICUs and 37,759 admissions in 2016



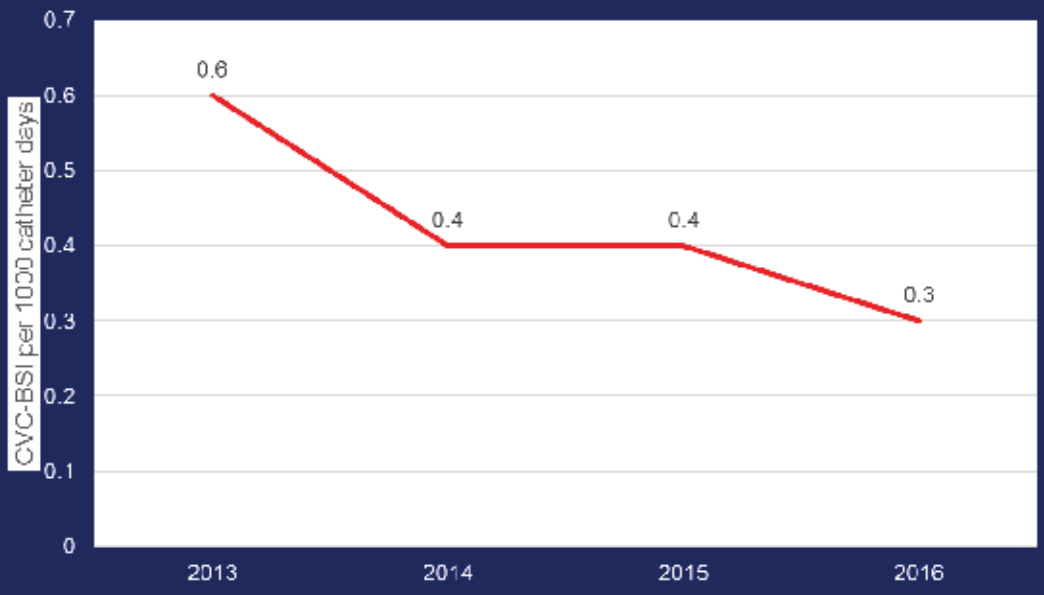
Medical Development Division, Ministry of Health of Malaysia, 2018

Ventilator-associated Pneumonia



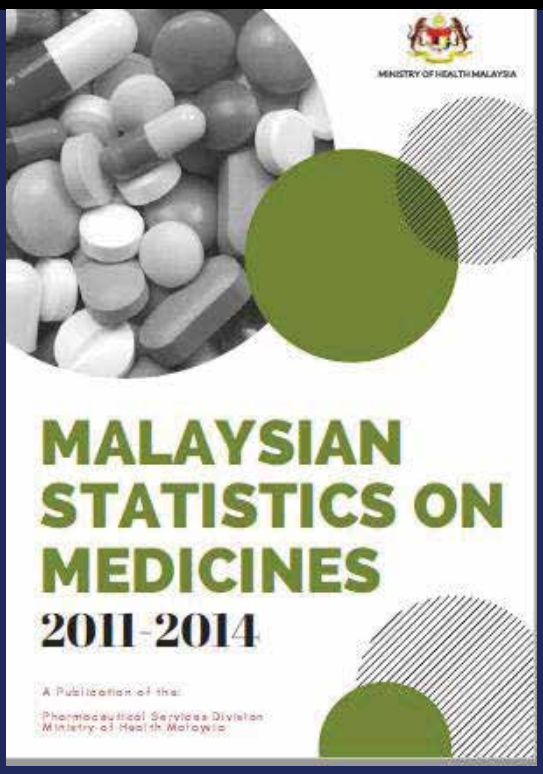
Malaysian Registry of Intensive Care 2016
https://www.crc.gov.my/wp-content/uploads/documents/report/mric_report_2016.pdf

CVC-BSI



Malaysian Registry of Intensive Care 2016
https://www.crc.gov.my/wp-content/uploads/documents/report/mric_report_2016.pdf

Antibiotic Utilisation Monitoring



- National drug utilization studies started in 2004 and conducted on an annual basis
- Data collected from both public and private sectors; primary to tertiary care facilities
- Uses the ATC classification system and unit of measurement expressed as daily defined doses according to WHO recommendations
- In 2014 the overall antibacterial (JO1) use : 10.87 DDD/1000 population/day

https://www.pharmacy.gov.my/v2/en/documents/malaysian-statistics-medicines.html

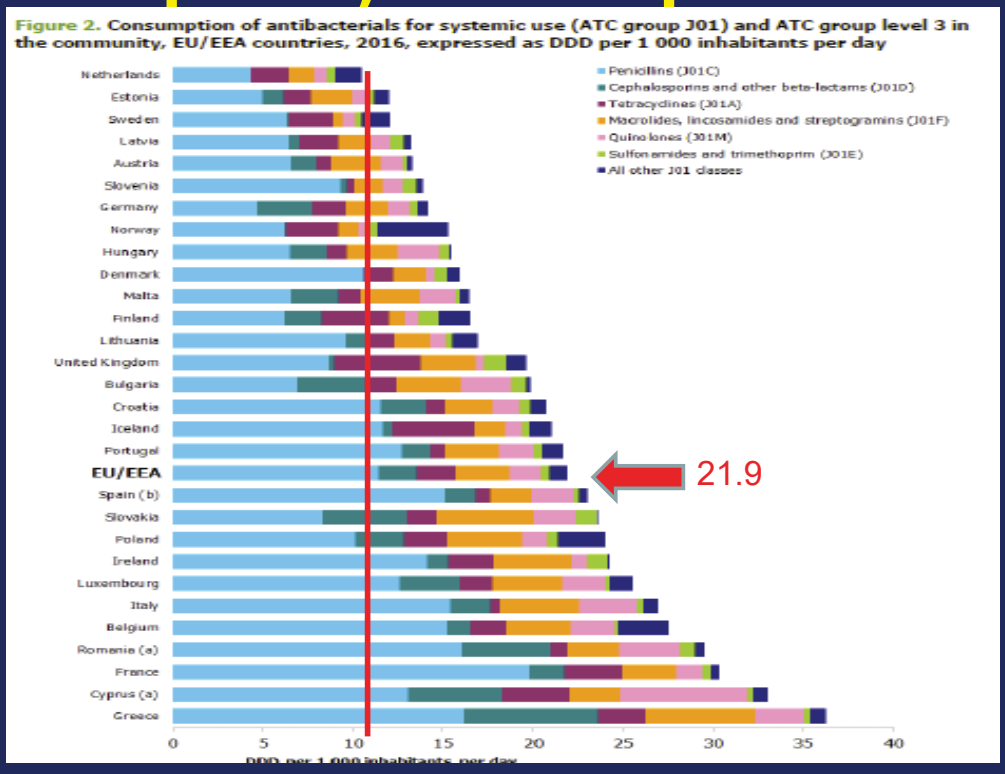
Use of anti-bacterials 2011-2014

Table 15.1: Use of antimicrobial agents, by therapeutic group from 2011 to 2014.

ATC	Therapeutic Group	Sector	Utilisation (DDD/1,000 inhabitants/day)			
			2011	2012	2013	2014
J01	Antibacterials for systemic use	Public	3.4935	3.6324	3.7084	3.8052
		Private	6.0941	7.1103	7.1820	7.0650
		Total	**9.5876**	**10.7427**	**10.8904**	**10.8702**

- Significant increases in the use of
  - Cefepime (164%)
  - Piperacillin-tazobactam (66%)
  - Carbapenems (30%)

Antibiotic Consumption (ATC Group J01) in Europe 2016



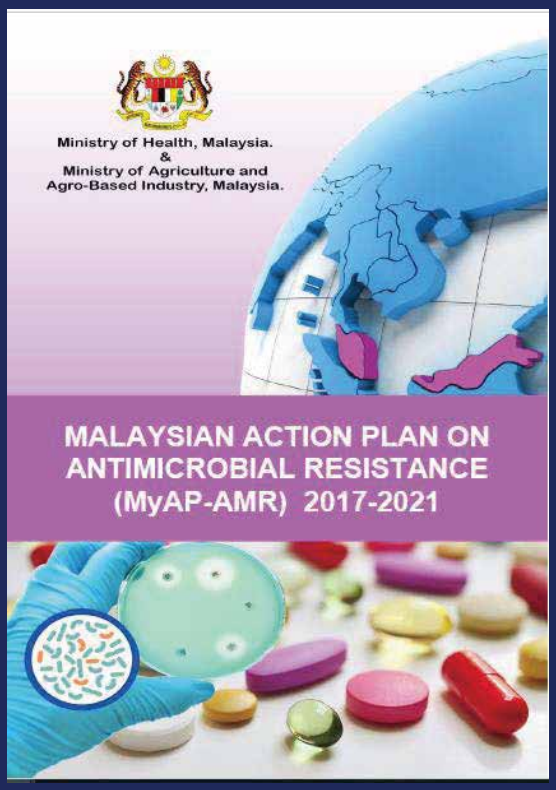
Antibiotic use monitoring in government hospitals

- Monitoring of antibiotic utilisation in MOH hospitals and 1 private chain of hospitals
- Ongoing activity for certain classes of antibacterials
  - Cephalosporins
  - Quinolones
  - Carbapenems
  - Glycopeptides
- Data expressed as DDD/100 admissions
- Submission of data to National Infection and Antibiotic Control Committee
- Identification of outliers and discussion of remedial measures

Formularies and guidelines

- Governmental sector
  - National antibiotic guidelines and national formulary
  - All hospitals can modify these guidelines to suit their needs
- Private sector
  - Doctors can use any product so long as it is registered by the Drug Control Authority
  - Independent contractors in private hospitals
  - Out-of-pocket payment
- Professional society practice guidelines
- Effectiveness of guidelines questionable

MyAP-AMR 2017 - 2021

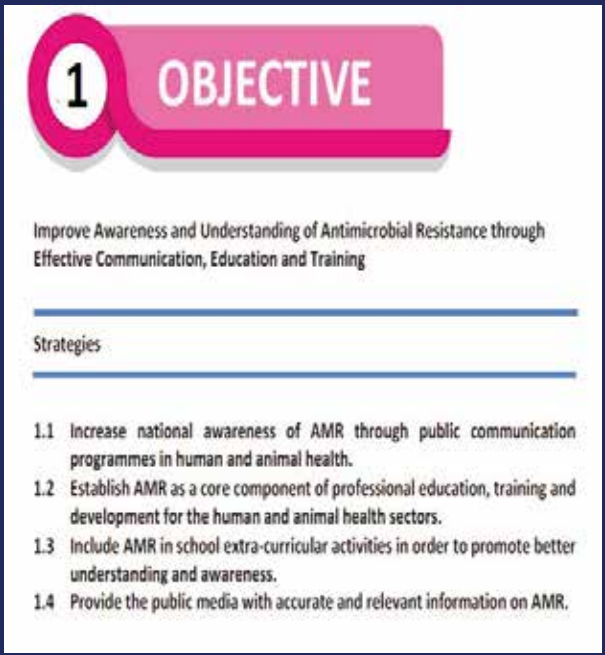


- Launched in 2017
- Joint programme by Ministries of Health and Agriculture
- In response to adoption of the Global Action of AMR by the World Health Assembly in 2015
- One Health approach

Framework

Key Priority Areas	Objectives
1. Public Awareness and Education	Improve awareness and understanding of AMR through effective communication, education and training
2. Surveillance and Research	Strengthen the knowledge and evidence base through surveillance and research
3. Infection Prevention and Control	Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
4. Appropriate Use of Antimicrobials	Optimize the use of antimicrobial medicines in human and animal health

National Action Plan



1 OBJECTIVE

Improve Awareness and Understanding of Antimicrobial Resistance through Effective Communication, Education and Training

Strategies

1.1 Increase national awareness of AMR through public communication programmes in human and animal health.
1.2 Establish AMR as a core component of professional education, training and development for the human and animal health sectors.
1.3 Include AMR in school extra-curricular activities in order to promote better understanding and awareness.
1.4 Provide the public media with accurate and relevant information on AMR.

- Under each objective
  - Strategies
    - Actions
    - Dates
    - Target groups
    - Responsible Units
    - Evaluation indices
  - Intensification of current activities as well as new initiatives
  - Working together

Conclusions

- Efforts in antibiotic stewardship has been on-going for nearly 3 decades
- There has been some successes but major challenges still remain
  - Largely a top-down approach
  - High prevalence of antimicrobial resistance
  - Limited participation outside the Ministry of Health
  - Until recently little involvement of the agricultural sector

Prof. Wing Hong Seto

Position: Co-Director

Department/organization: WHO Collaborating Centre for Infectious Disease Epidemiology and Control, The University of Hong Kong

Economy: Hong Kong, China

Educational Background

- 1972 MB,BS
- 1981 MRCP (UK)
- 1981 MRCPI
- 1984 MRCpath
- 1992 FHKCPath - Founding Fellow.
- 1994 FHKAM (Pathology) - Founding Fellow.
- 1996 American Board Certified in Healthcare Quality [CPHQ]
- 1997 FRCPath

Professional Career

- Co-Director, WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, HKU, Hong Kong
- Clinical Professor (hon) School of Public Health, HKU
- Consultant Advisor (Hon), for Quality and Safety, HKU Shenzhen Hospital
- Consultant Microbiologist, Hong Kong Baptist Hospital, Hong Kong.

Publications

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- Nancy H. L. Leung, Jie Zhou, Daniel K. W. Chu, Han Yu, William G. Lindsley, Donald H. Beezhold, Hui-Ling Yen, Yuguo Li, Wing-Hong Seto, Joseph S. M. Peiris, Benjamin J. Cowling: Quantification of Influenza
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Speech Abstract

Effective Antimicrobial Stewardship Program in Hong Kong

The WHO has stated that "antimicrobial resistance is clearly a global issue" [1]. Resistance to first-line drugs for most of the key pathogens causing infections disease ranges from zero to almost 100%. The WHO has identified antimicrobial use as the key driver of resistance. It is thus critically important to control antibiotics abuse which is the very essence of the Antibiotic Stewardship Program (ASP). It should also be appreciated that the ASP should be developed together with an effective Infection Control program and Surveillance activities[1]. This is logical because Infection Control will prevent the spread of resistant bacteria and only with proper surveillance, can evaluation be made on the efficacy of implemented measures. These three are linked up like a "three legged stool."

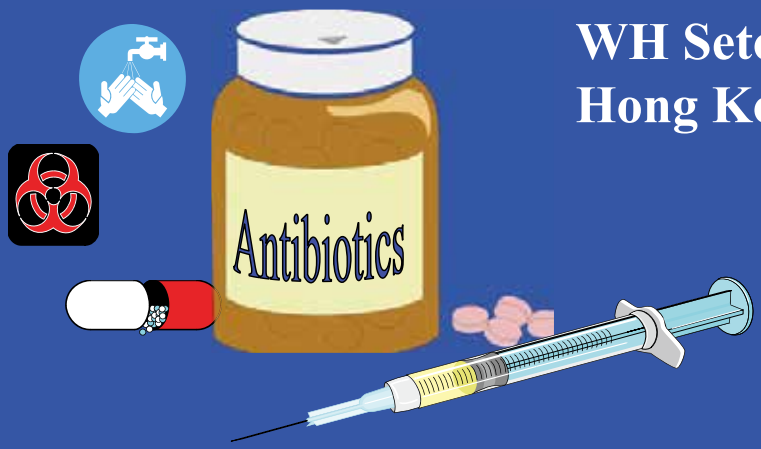
In an effective ASP, multiple strategies should be incorporated. There is ample room for local innovations although two core strategies are recommended by the Infectious Disease Society of America[2]. The first is prospective audit with intervention feedback. To be successful a guideline must first be promulgated and feedback should be given to any variance from the guideline. In Hong Kong, the feedback is given on the same day of the audit, a scheme known as Immediate Concurrent Feedback (ICF) with the effective reduction of >10% of the expensive antibiotics prescribed[3]. A summary of the various interventions used in Hong Kong will be provided which resulted in a savings of millions of dollars[3]. The program is carried out by Infection Control nurses with the more difficult cases reserved for physicians. Finally ASP should also be conducted in the outpatient setting. A summary of programs reported by the CDC and one conducted in Hong Kong will be briefly summarized.

References:

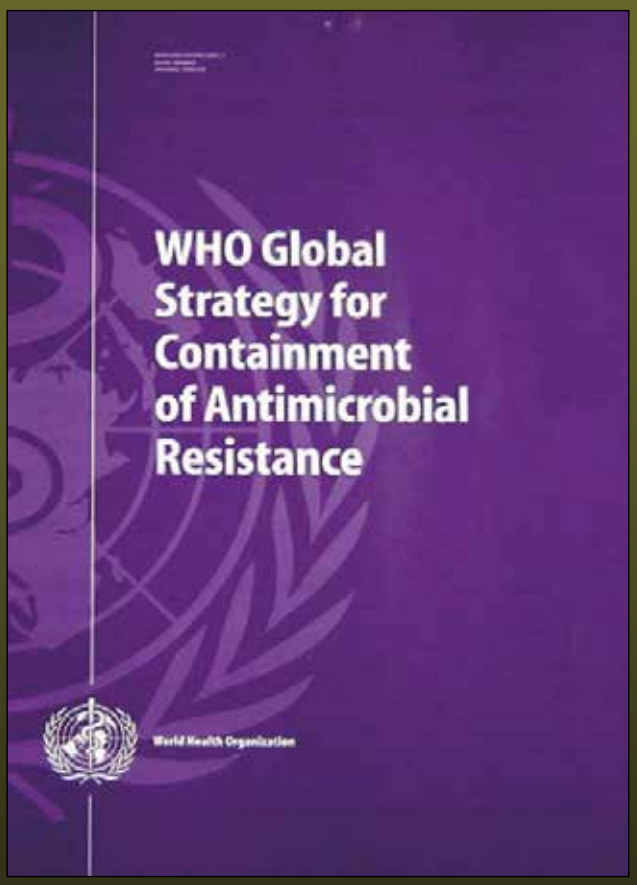
1. WHO Global Strategy for Containment of Antimicrobial Resistance. WHO 2001.
2. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America 2007:44: 159-177

Cheng V, To K, Li L, Tang B, Chan J, Kwan S, Mak R, Tai J, Ching P, Ho P, Seto W: Antimicrobial stewardship program directed at broad-spectrum intravenous antibiotics prescription

The Antibiotics Stewardship in Hong Kong



WH Seto,
Hong Kong, China



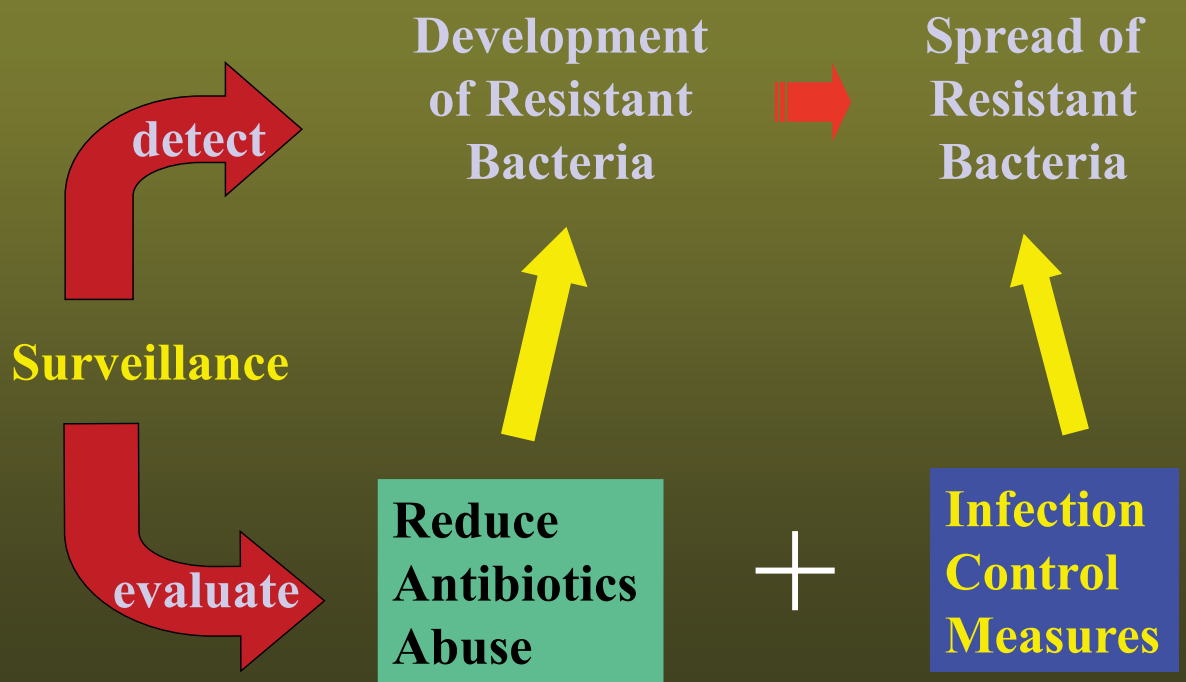
September 2001

"Antimicrobial resistance poses a global challenge"

"likely to result in the absence of effective therapies for some pathogens within the next ten years"

"Antimicrobial use is the key driver of resistance"

Control of Antimicrobial Resistance



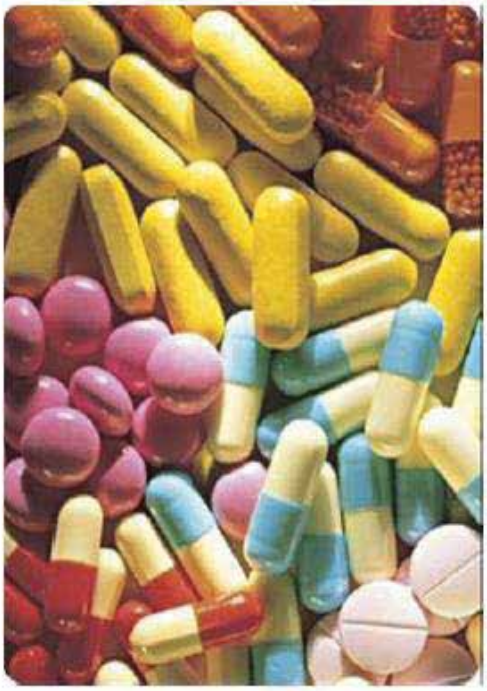
Antibiotic resistance – the three keys to control

- Infection Control
- Antibiotic stewardship
- Surveillance
  - Antibiotic-resistant bacteria
  - Antibiotic usage

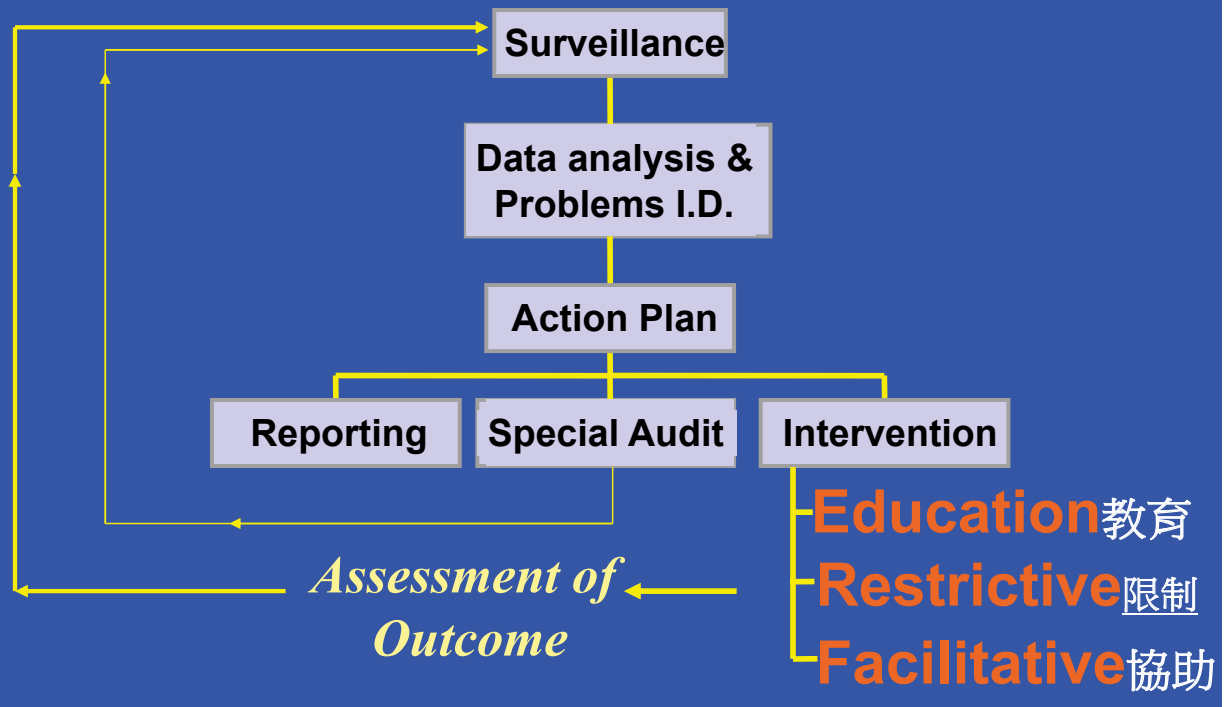
Control of antibiotic resistance is like a three-legged stool – if you take away one of the legs – the whole thing falls over!

Antibiotic Stewardship - Definition

- The appropriate use of antibiotics and the limitation of unnecessary antibiotic administration/exposure
  - Optimising diagnosis
  - Selecting appropriate antibiotics
  - Optimal dosing



Antibiotics Utility Review Programme



Implementing antibiotics guidelines
Education Intervention:

- Lectures and Teaching Programme
- Written manuals, newsletters and susceptibility patterns

Education alone does not necessary work

- The failure of Physician Education as a Cost Containment Strategy.

  -Schroeder et al, JAMA

- The Short and Long Term Effects of a Handbook on Antimicrobial Prescribing Patterns of antimicrobial therapy.

  -D'Eramo et al, Infection Control

Effect was only sustained for 3 months

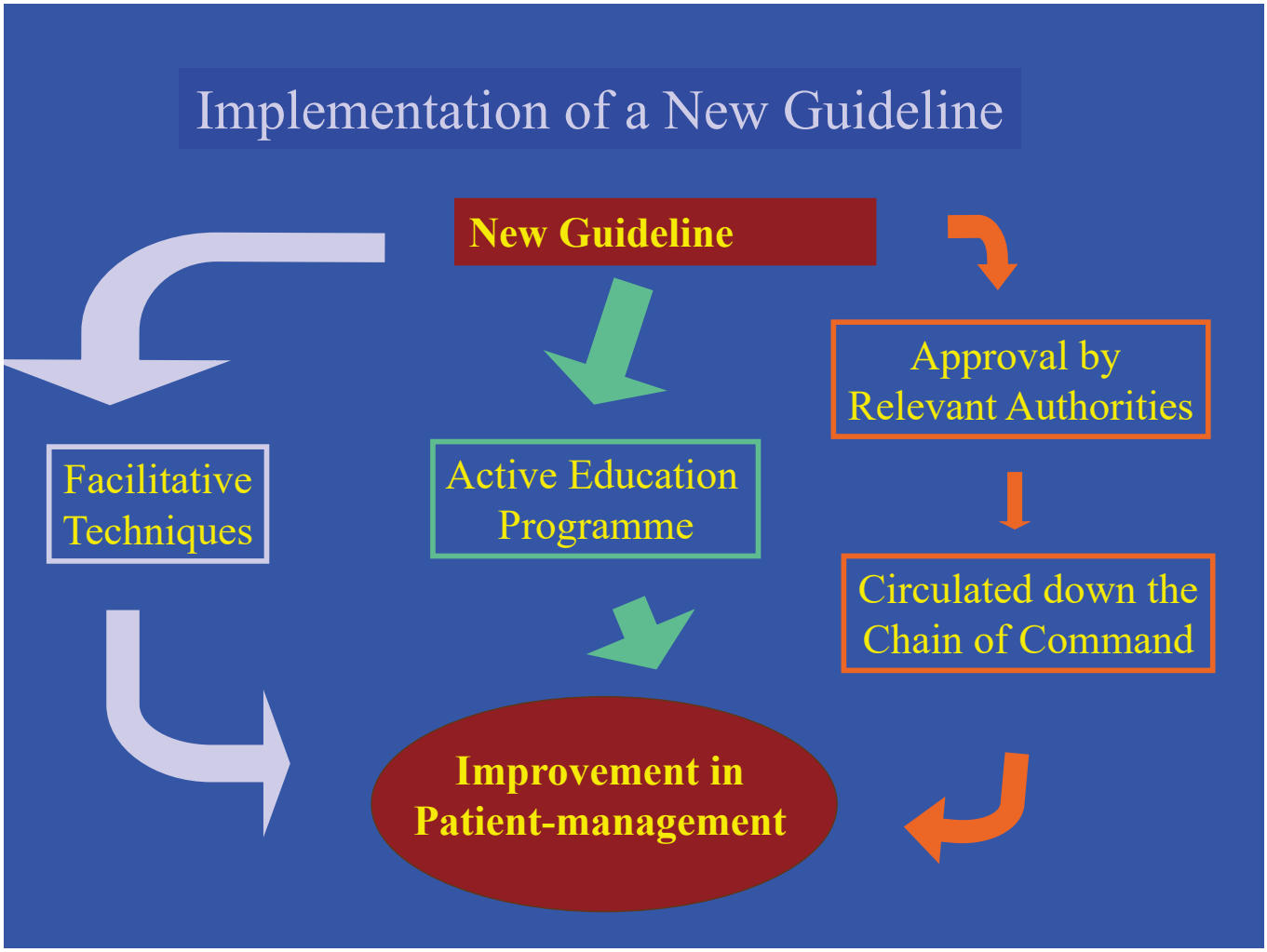
Restrictive Intervention

- **Formulary Restrictions**
- **Pharmacy justification**
  - Automatic stop policies
  - Antibiotic order form
- **Required Consultation and endorsement**
- **Therapeutic Interchange Programme**
- **Selective reporting of susceptibility tests**
- **Restriction of Interactions with Pharmaceutical Representatives**

On restrictive policies:

"These strategies are probably the most onerous to prescribing physicians ……"

John & Fishman, CID'97;24:471



Facilitative Interventions

1. Feedback non-generic and non-formulary drugs (Feely et al BMJ 1990).
2. Retrospective audits with feedback **(Am J Med '89;86:442).**
3. Interaction & feedback by professional team **(John et al CID '97;24:471).**
4. Computerized decision support **(Brent James, IMC).**
5. Interactive workshop **(Dwiprahasto, ICIUM 2004; O'Brien T, Cochrane Database of Systemic Reviews, Issue 4, 2002).**
6. Use of opinion leaders **(Everitt et al ICHE 1999, O'Brien T, Cochrane Database of Systemic Reviews, Issue 4, 2002).**
7. Concurrent feedback **(Anasari et al, JAC 2003:52:842)**

I.C.F.

Immediate - feedback occurs on day of audit

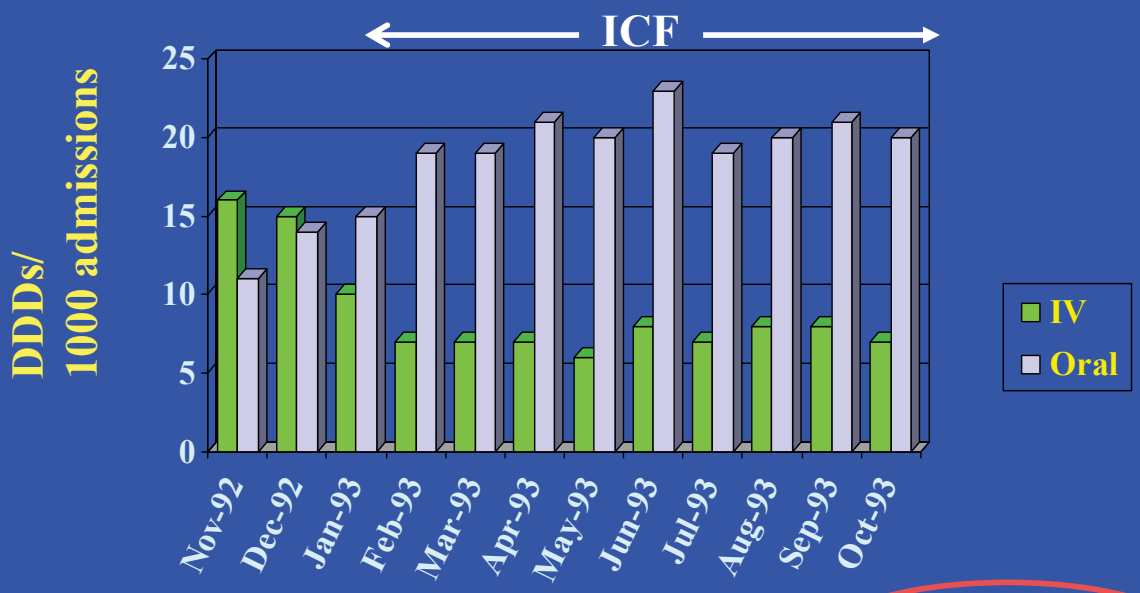
Concurrent - patient still in hospital

Feedback - specific for doctor & prescription

Help of an ICN & Pharmacy

I. C. F.

Usage of Co-amoxiclav/Sultamicillin in QMH



Save $360,000

Seto et al, BJ Clin Pharmacol 96;41:229

"Of interest in the Seto Study, feedback could be produced relatively inexpensively by a part-time nurse"

Hemeryck et al, BJ Clin Pharmacol 97:43:449

Patient admitted to the hospital are usually started on IV antibiotics therapy, then switched to equivalent oral therapy after clinical improvement (usually within 72 hours).

Advantages of early IV-to-PO switch programs include reduced cost, early hospital discharge, less need for home IV therapy and virtual elimination of IV line infections

There is no difference in clinical outcome using equivalent IV or PO antibiotics

C

CUNHA, 2012
New York

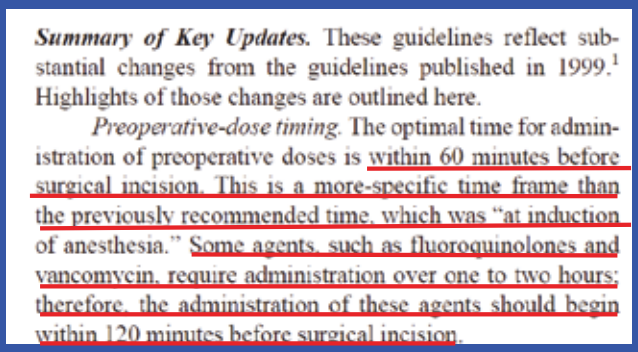
Principles in Surgical Antibiotics Prophylaxis

1. Not for clean operations except :
   - Prosthesis
   - Drastic outcomes if infected (eg.CNS)
   - High risk (eg. age or prolonged duration)
2. Whenever possible use first generation cephalosporin
3. Avoid antibiotics that are used for treatment
4. Given on induction
6. Post-operative coverage are generally unwarranted

What about at induction?

WHO
The panel recommends the administration of SAP within 120 minutes before incision,

ASHP



Summary of Key Updates. These guidelines reflect substantial changes from the guidelines published in 1999.[1] Highlights of those changes are outlined here.

Preoperative-dose timing. The optimal time for administration of preoperative doses is within 60 minutes before surgical incision. This is a more-specific time frame than the previously recommended time, which was "at induction of anesthesia." Some agents, such as fluoroquinolones and vancomycin, require administration over one to two hours; therefore, the administration of these agents should begin within 120 minutes before surgical incision.

Impact – HK guideline
Timing: For many prophylactic antimicrobial agents, the administration of an initial dose should be given within 30 minutes before incision…..
facilitated by having the anaesthesiologist administer the drug in the operating room at induction.

Result of education and ICF in the surgical unit

	>3 does post-op	use 3rd gen. Cephalosporin
July - Sept/92	65%	17%
---------- Education Programme ----------		
Oct - Dec/92	61%	26%
---------- Start ICF ----------		
January/93	30%	30%
February	26%	21%
March	18%	16%
April	14%	6%
May	12%	4%

Prophylactic use of antibiotics in QMH.

Estimation for 1991.

Total patients on surgical prophylaxis: 6188 patients

Assuming 40% usage is inappropriate: 2475 patients

Estimated cost of inappropriate use: $2.5 million.

Estimated savings if appropriate use: $2.1 million.

Guideline for Vancomycin usage

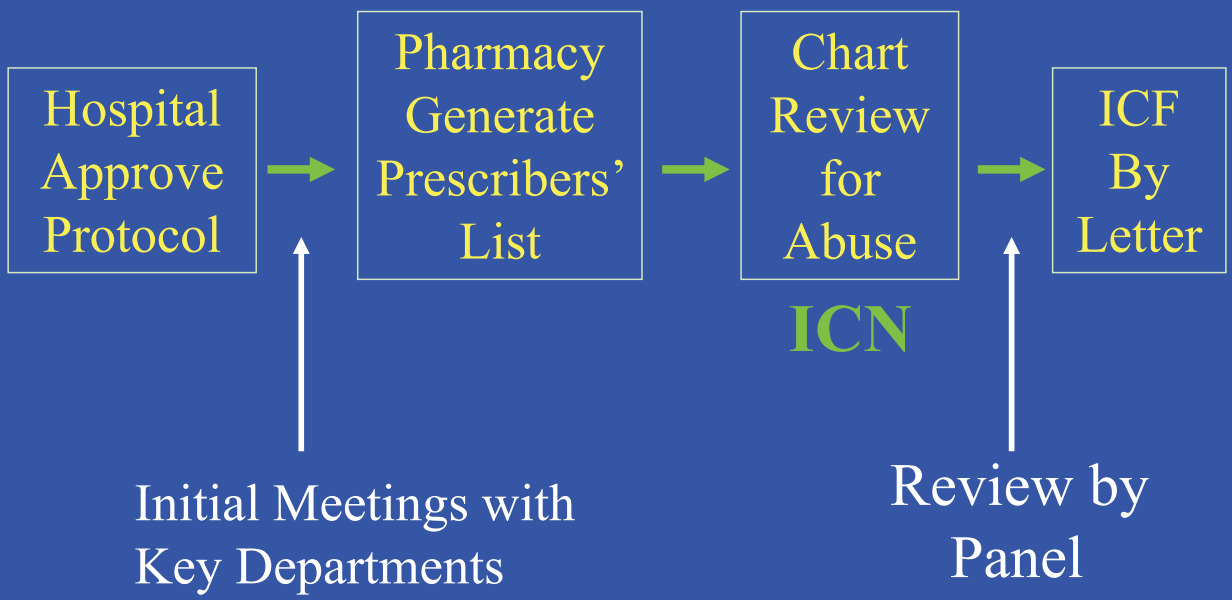
YES

1. Infections by β-lactam resistant gram+ve
2. Empirical Rx only for special patients at risk
3. β-lactam allergy with serious infections
4. AAC not responding to metronedazole
5. Surgical prophylaxis with prosthesis
6. Presumed pneumococcal meningitis

No

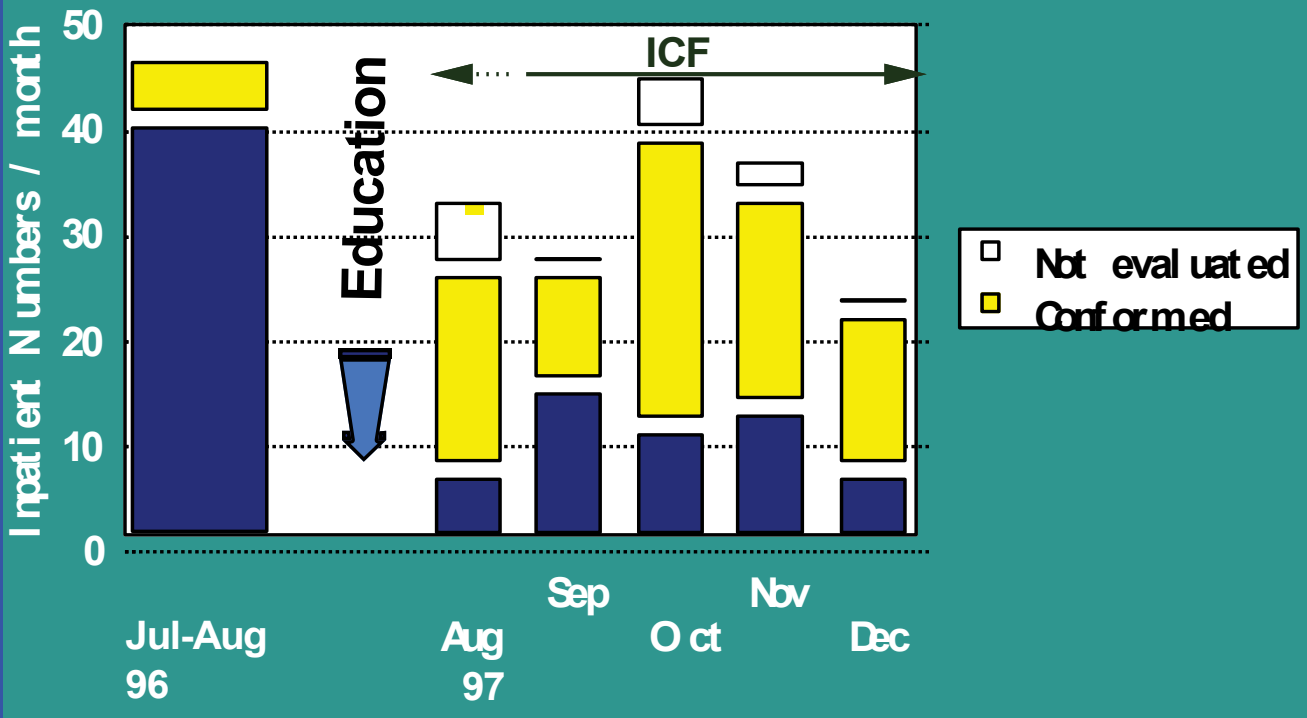
1. Most initial empirical Rx of neutropenic
2. 1 bld culture of CNS, Bacillus & Diptheroids
3. Rx of β-lactam sensitive organisms
4. Routine prophylaxis
5. Irrigation or topical application
6. Primary Rx of AAC

I. C. F.



VANCOMYCIN OR TEICOPLANIN PRESCRIPTIONS

Depts' of Medicine (ex BMT Centre) + Orthopaedics & Trauma



The Five Big Guns

Meropenam
Imipenam
Tazocin
Cefepime
Ceftzidime

Later: + Sulfperazone

5 Situations in which "Big Guns" Antibiotic Prescribing is NOT ADVISABLE

- No evidence of infection eg colonization
- For chemoprophylaxsis
- For infection by pathogen that is susceptible to "Lesser Guns"
- In combination with other β-lactam "Big Guns" antibiotics

- Empirical treatment of community acquired infections (in non-neutropenic patients) except:

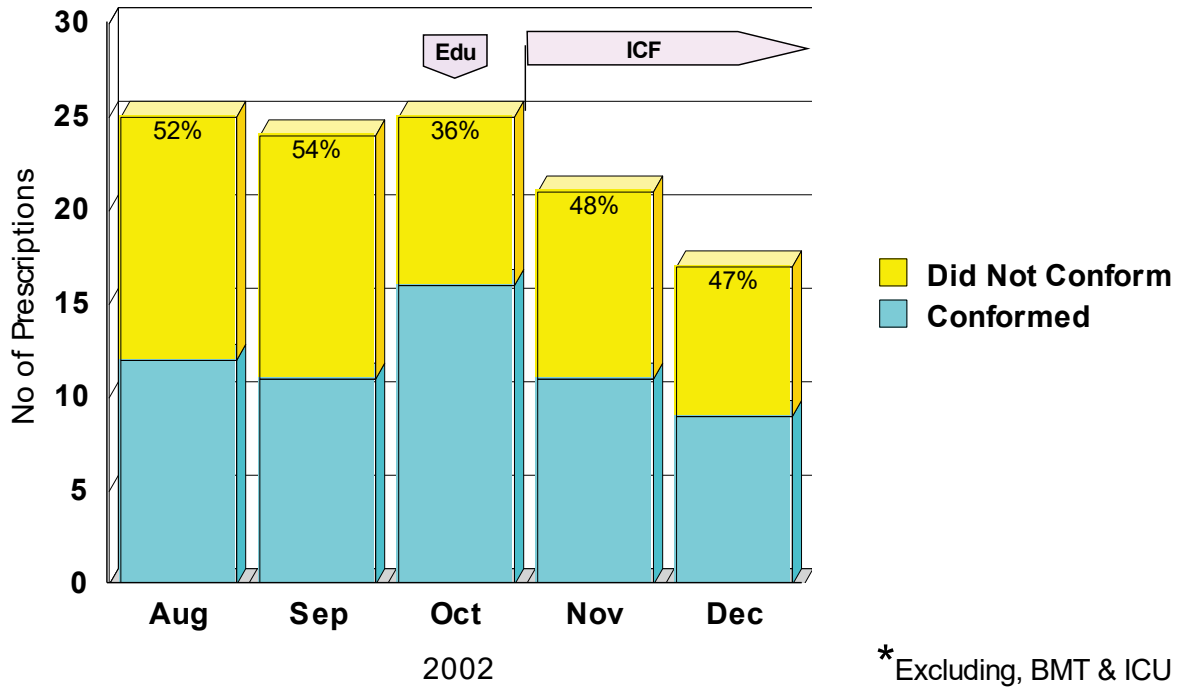
❖ Organ transplant recipients on high level immuno-suppression (ie prednisolone >30mg/day for 3 weeks or 10mg/day long term)

❖ Definite deterioration or persistent fever despite 72hr 1st line treatment

❖ Evidence of severe clinical sepsis (eg seriously ill CAP, haemodynamically unstable, meningitis, infective endocarditis)

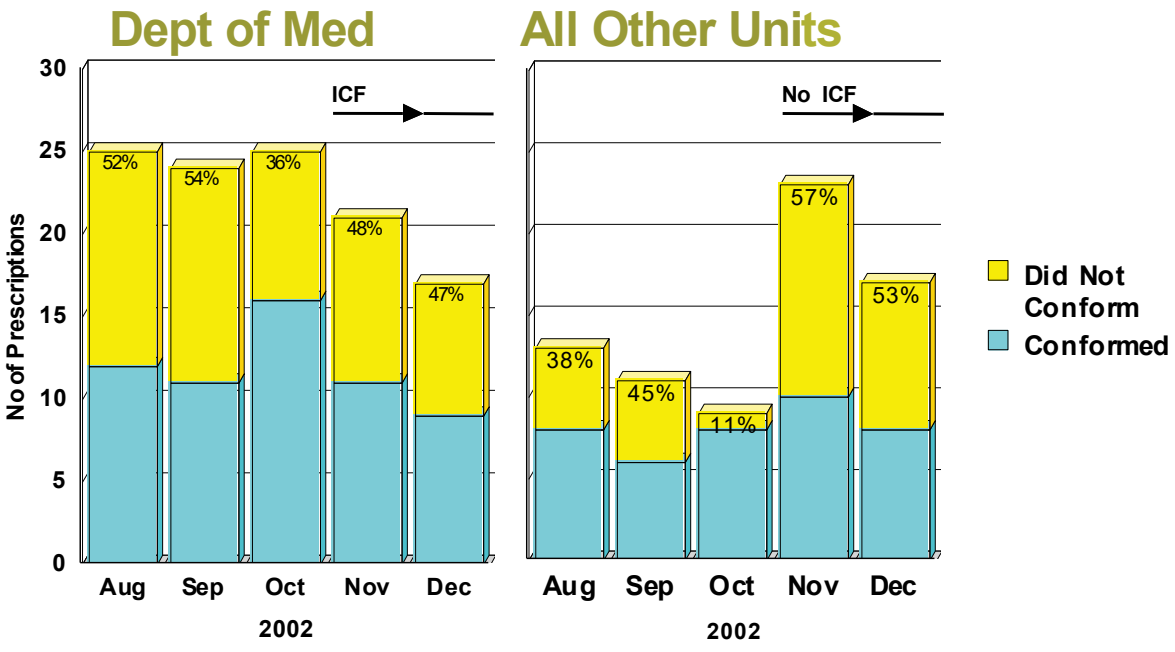
Audit of IV "Gig Gun" Antibiotic Prescribing

Preliminary Results: Dept of Med Wards* QM Hospital



*Excluding, BMT & ICU

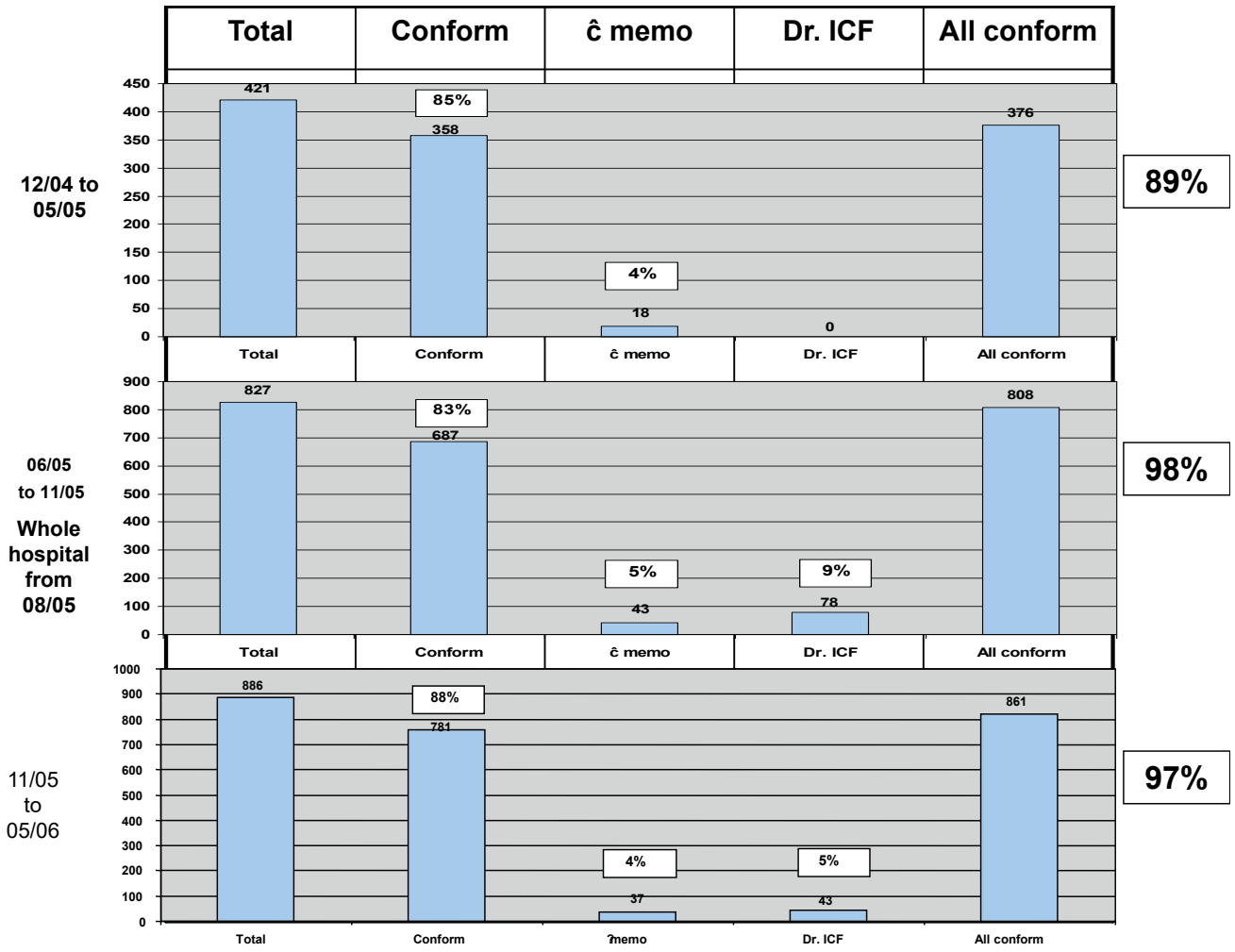
"Big Gun" Prescribing in Dept of Medicine Wards & All Other Depts of QM Hospital



Physician ICF – after initial ICN review

1. Non-severe nosocomial infections eg. nosocomial pneumonia < 5 days in Hospital + no previous admission.
2. Treatment duration eg. Nosocomial pneumonia ≥ 7 days **(unless Ps A or non-fermenters)**
3. Acute Pancreatitis – dealing with Imipenem (benefits found: Slavin et al Ar Sug 2001:386:155; Bassi et al JHP Surg 2001:8:211; Ratschko et al Gasto Clin Nam 1999:28:641; Sharma et al Pancreas2001:22:28)
4. Antibiotics for neutropenia/solid organ transplant
5. CAPD peritonitis – follow international protocol
6. PTBD – percutaneous transhepatic biliary drainage
7. Evaluation of critical vital signs and severe CAI
8. Patients on DNR.

Eur J Clin Microbiol Infect Dis
DOI 10.1007/s10096-009-0803-8


Total
Conform
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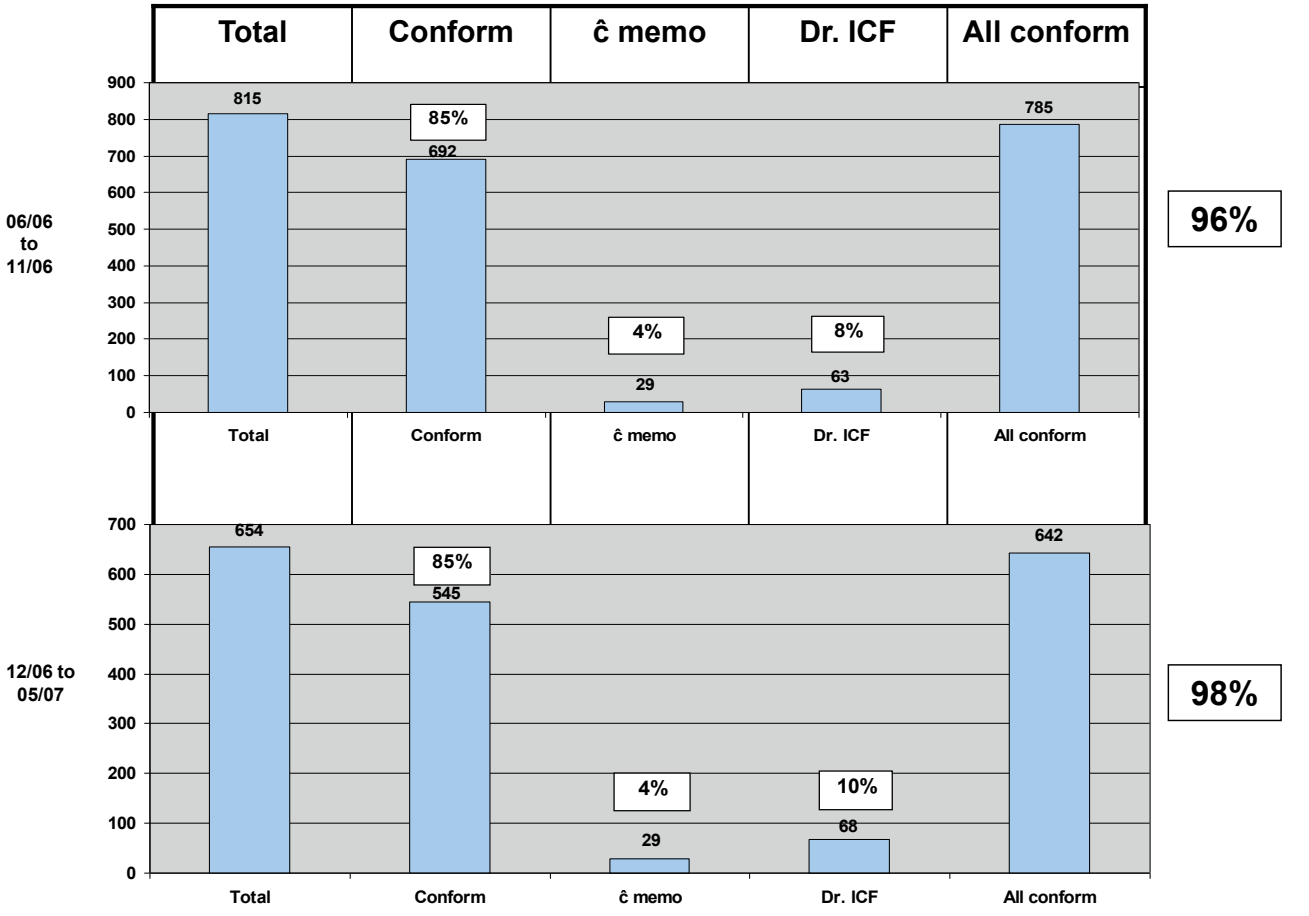
Dr. ICF
All conform
12/04 to 05/05
421
85%
358
4%
18
0
376
89%
06/05 to 11/05
Whole hospital from 08/05
827
83%
687
5%
43
9%
78
808
98%
11/05 to 05/06
886
88%
781
4%
37
5%
43
861
97%


Total
Conform
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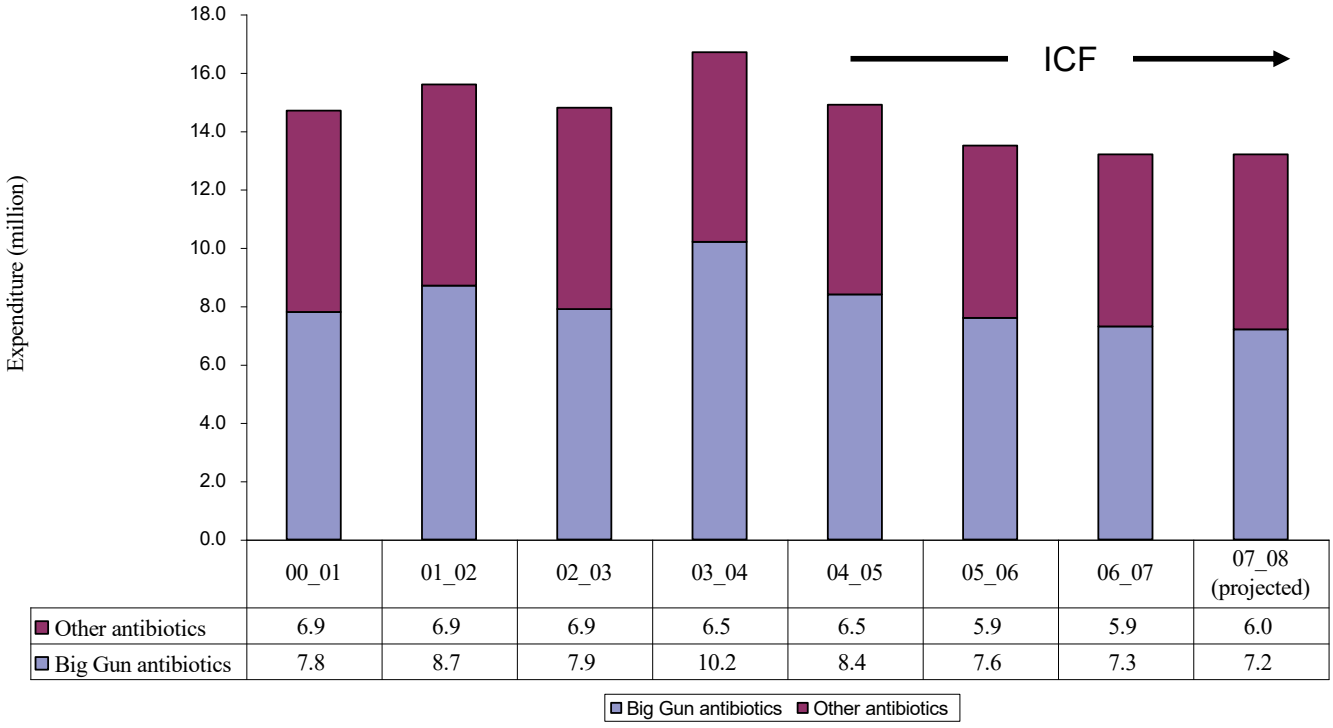
All conform
06/06 to 11/06
815
85%
692
4%
29
8%
63
785
96%
12/06 to 05/07
654
85%
545
4%
29
10%
68
642
98%

Antibiotic expenditure in QMH



	00_01	01_02	02_03	03_04	04_05	05_06	06_07	07_08 (projected)
Other antibiotics	6.9	6.9	6.9	6.5	6.5	5.9	5.9	6.0
Big Gun antibiotics	7.8	8.7	7.9	10.2	8.4	7.6	7.3	7.2

Data from Pharmacy, QMH

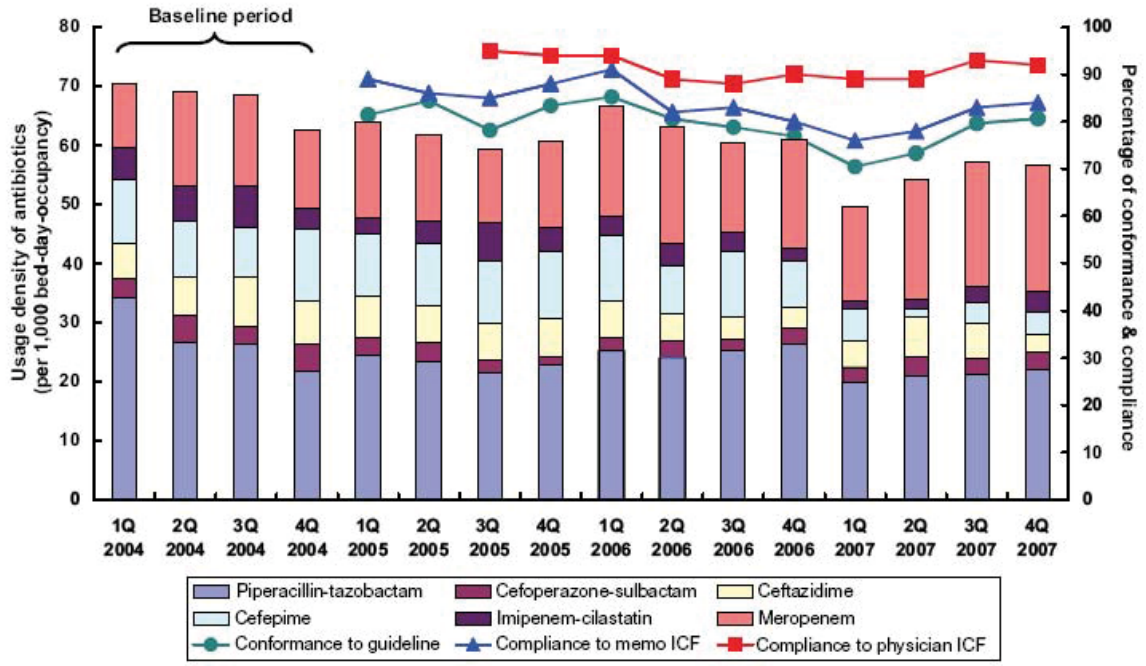


Fig. 1 Usage density of antibiotic, conformance to antibiotic prescription guideline, and compliance to the antibiotic stewardship program. Abbreviations: *1Q* first quarter, *2Q* second quarter, *3Q* third quarter, *4Q* fourth quarter, *ICF* immediate concurrent feedback

Eur J Clin Microbiol Infect Dis, 2009;28:1447

Just don't smile at the wrong time……..

Prof. Yee-Chun Chen

Position: Professor

Department/organization: Department of Internal Medicine, National Taiwan University Hospital and College of Medicine

Economy: Chinese Taipei

Educational Background

- M.D.,Taipei Medical College (now Taipei Medical University)
- Residency (Internal Medicine), National Taiwan University Hospital
- Fellowship (Infectious diseases), National Taiwan University Hospital
- PhD, Prof. Lee FJ Scott's laboratory, Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine

Professional Career

- Attending physician, Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital
- Professor of Medicine, National Taiwan University College of Medicine
- Director of Center for Infection Control, National Taiwan University Hospital
- Chief, Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital
- Deputy Director/Acting Director, National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes

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Speech Abstract

Healthcare-associated Infections in Intensive Care Units in Asia: Recent Trends Based on Healthcare-associated Infections Surveillance Network over an 8-year period

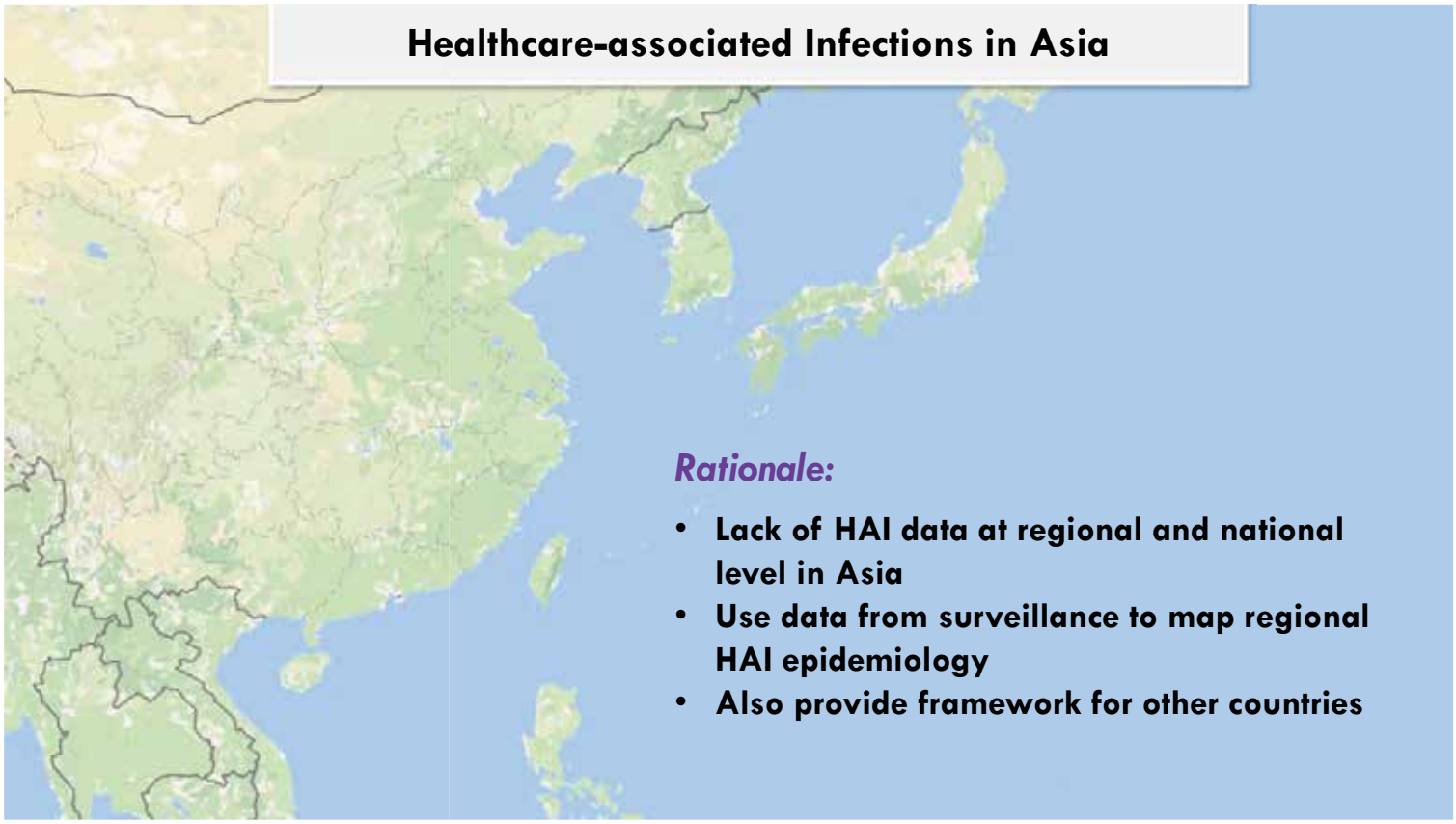
Background: Data from surveillance of healthcare-associated infections (HAI) provides feedback for implementation of infection prevention and control (IPC) programs. To address the paucity of such data in Asia, we searched for national HAI surveillance and IPC programs in this region.
Methods: Data were analysed from open access national surveillance reports of Chinese Taipei, South Korea and Japan from 2008 to 2015. IPC programs implemented were identified.
Results: There was a 53.0% reduction in overall HAI over the 8-year period. This consisted of a decrease from 9.34 to 5.03 infections per 1,000 patient-days in Chinese Taipei, from 7.56 to 2.76 in Korea, and from 4.41 to 2.74 in Japan (Poisson regression, all $p<0.05$). Across the three countries, *Escherichia coli* and *Candida albicans* were the major causative pathogens for urinary tract infection. *Staphylococcus aureus, Acinetobacter baumannii* and *Enterococcus faecium* were common bloodstream pathogens. For pneumonia, *S. aureus*, *A. baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* were the predominant pathogens, with considerable country differences. Although the number of participating ICUs has expanded, there was a 64.6% decrease in the number of isolates of methicillin-resistant *S. aureus*, a 38.4% decrease in carbapenem-resistant *P. aeruginosa* and a 49.2% decrease in carbapenem-resistant *A. baumannii* (CRAB) in Chinese Taipei (all $p<0.05$), and similarly in Korea with the exception of CRAB (30.5% and 50.4% reduction, respectively, both $p<0.05$**)**.
Conclusion: We found a significant decrease of HAI across the three countries in association with sequential multifaceted interventions. Further regional collaboration could be forged to develop joint strategies to prevent HAI.

Healthcare-associated Infections in Intensive Care Units in Asia: Recent Trends Based on Healthcare-associated Infections Surveillance Network over an 8-year period

Yee-Chun Chen, M.D., PhD.

Center for Infection Control, National Taiwan University Hospital; Department of Medicine, National Taiwan University College of Medicine; National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes

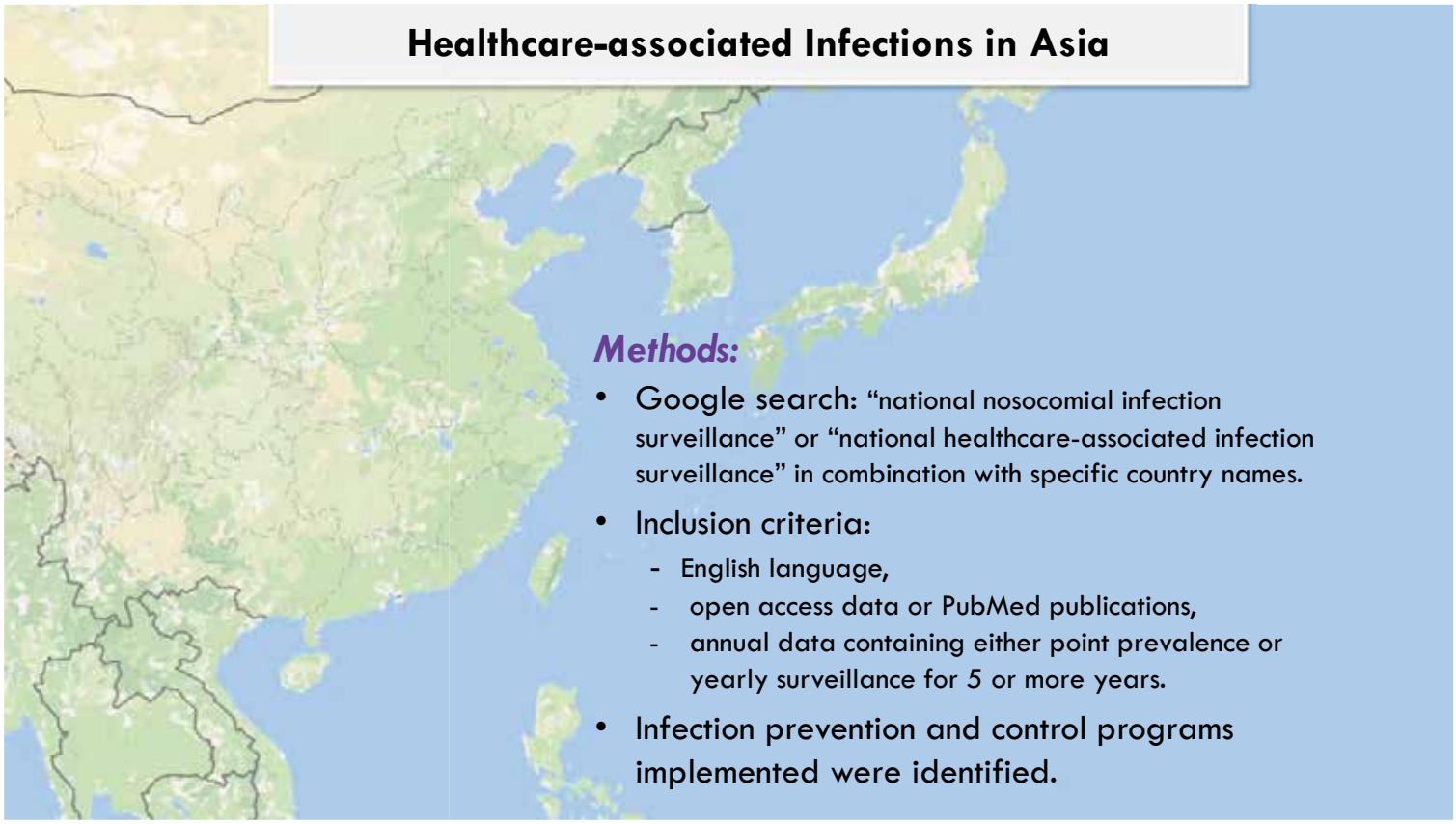
Healthcare-associated Infections in Asia



Rationale:

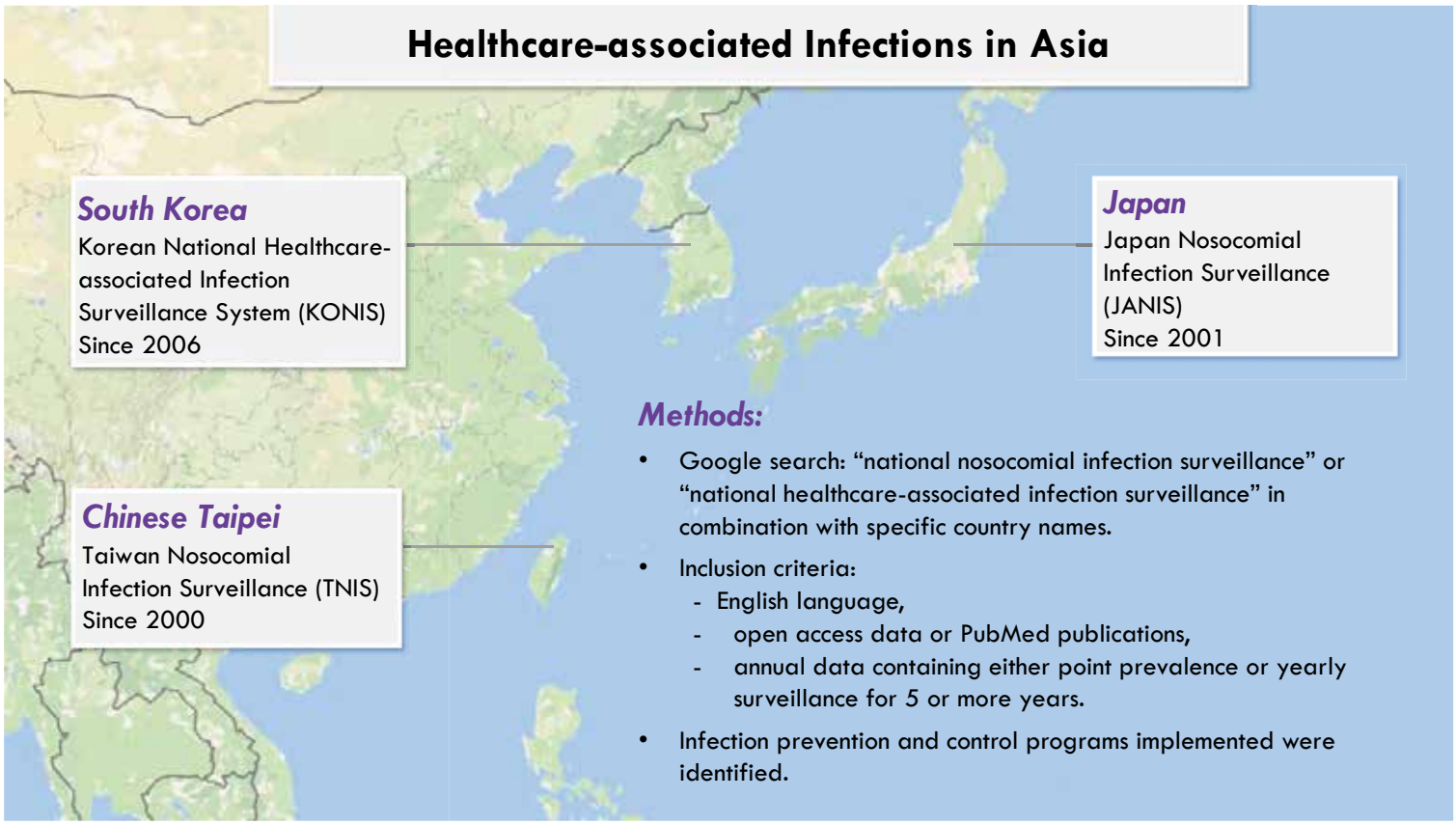
- **Lack of HAI data at regional and national level in Asia**
- **Use data from surveillance to map regional HAI epidemiology**
- **Also provide framework for other countries**

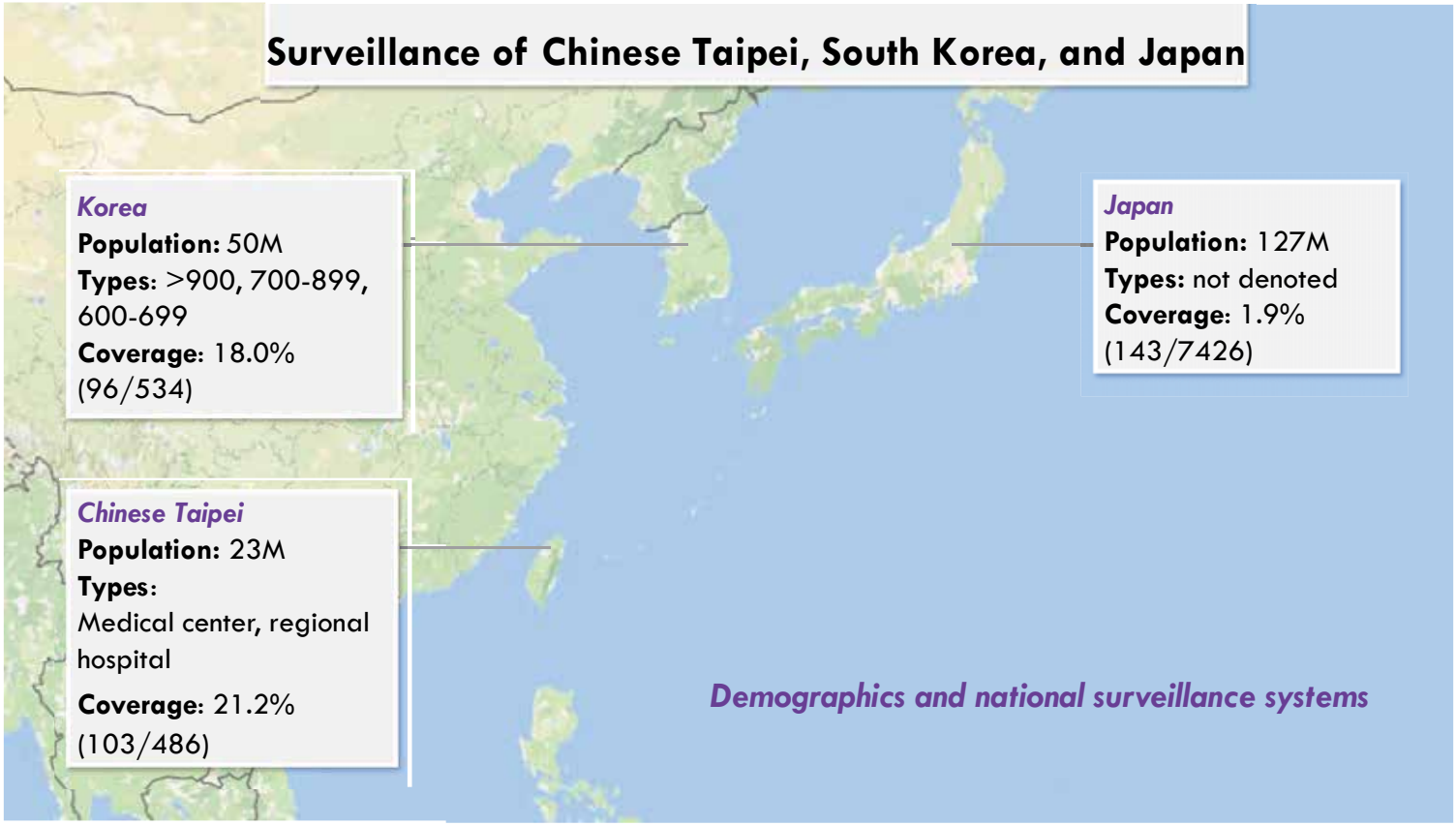
Healthcare-associated Infections in Asia



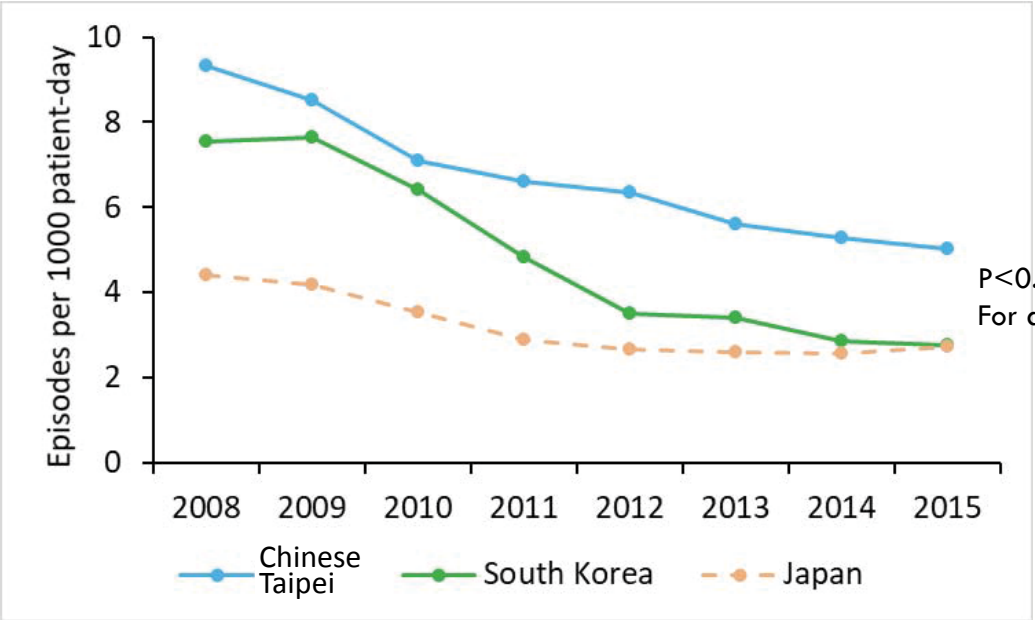
Methods:

- Google search: "national nosocomial infection surveillance" or "national healthcare-associated infection surveillance" in combination with specific country names.
- Inclusion criteria:
  - English language,
  - open access data or PubMed publications,
  - annual data containing either point prevalence or yearly surveillance for 5 or more years.
- Infection prevention and control programs implemented were identified.

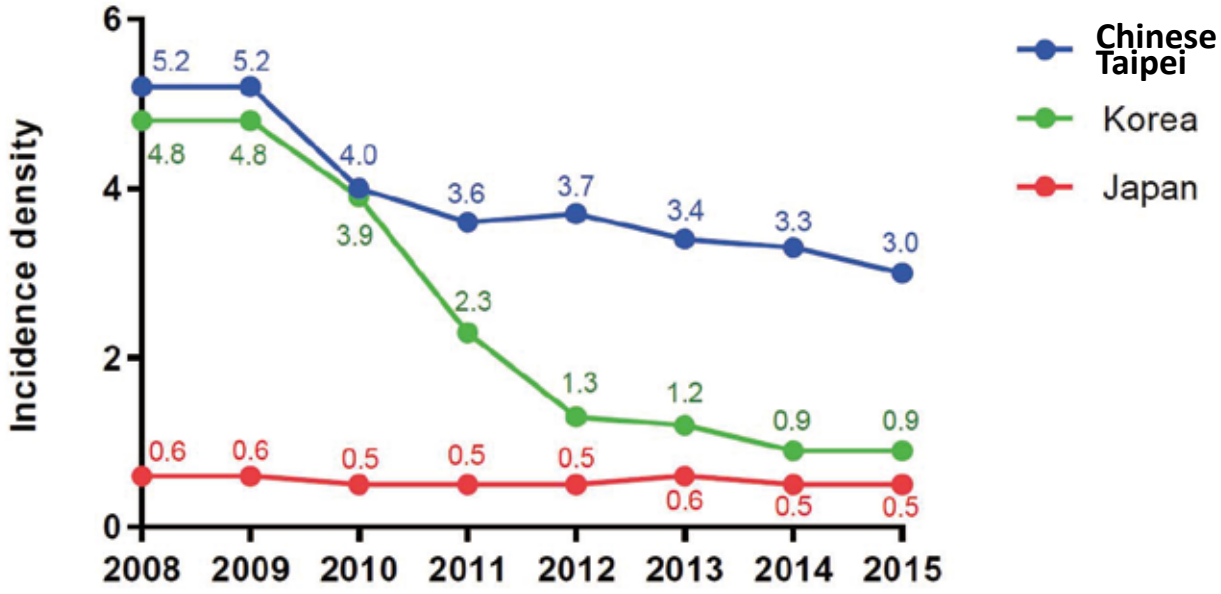

Healthcare-associated Infections in Asia
South Korea
Korean National Healthcare-associated Infection Surveillance System (KONIS)
Since 2006
Japan
Japan Nosocomial Infection Surveillance (JANIS)
Since 2001
Chinese Taipei
Taiwan Nosocomial Infection Surveillance (TNIS)
Since 2000
Methods:
• Google search: "national nosocomial infection surveillance" or "national healthcare-associated infection surveillance" in combination with specific country names.
• Inclusion criteria:
- English language,
- open access data or PubMed publications,
- annual data containing either point prevalence or yearly surveillance for 5 or more years.
• Infection prevention and control programs implemented were identified.


Surveillance of Chinese Taipei, South Korea, and Japan
Korea
Population: 50M
Types: >900, 700-899, 600-699
Coverage: 18.0% (96/534)
Japan
Population: 127M
Types: not denoted
Coverage: 1.9% (143/7426)
Chinese Taipei
Population: 23M
Types:
Medical center, regional hospital
Coverage: 21.2% (103/486)
Demographics and national surveillance systems

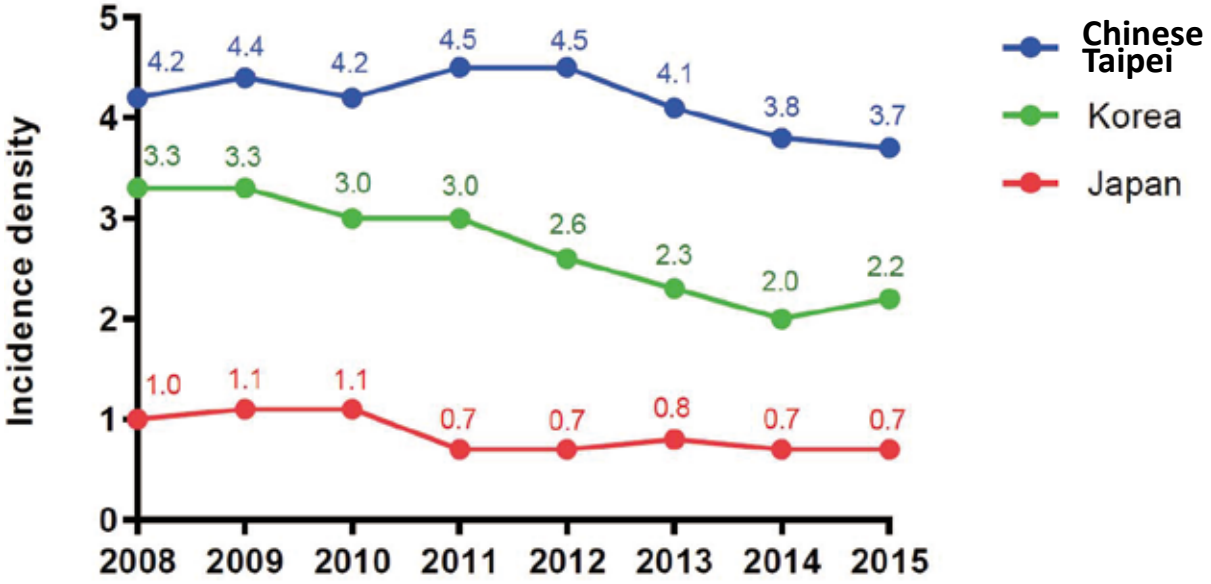
There was a 53.0% reduction in overall HAI over the 8-year period.



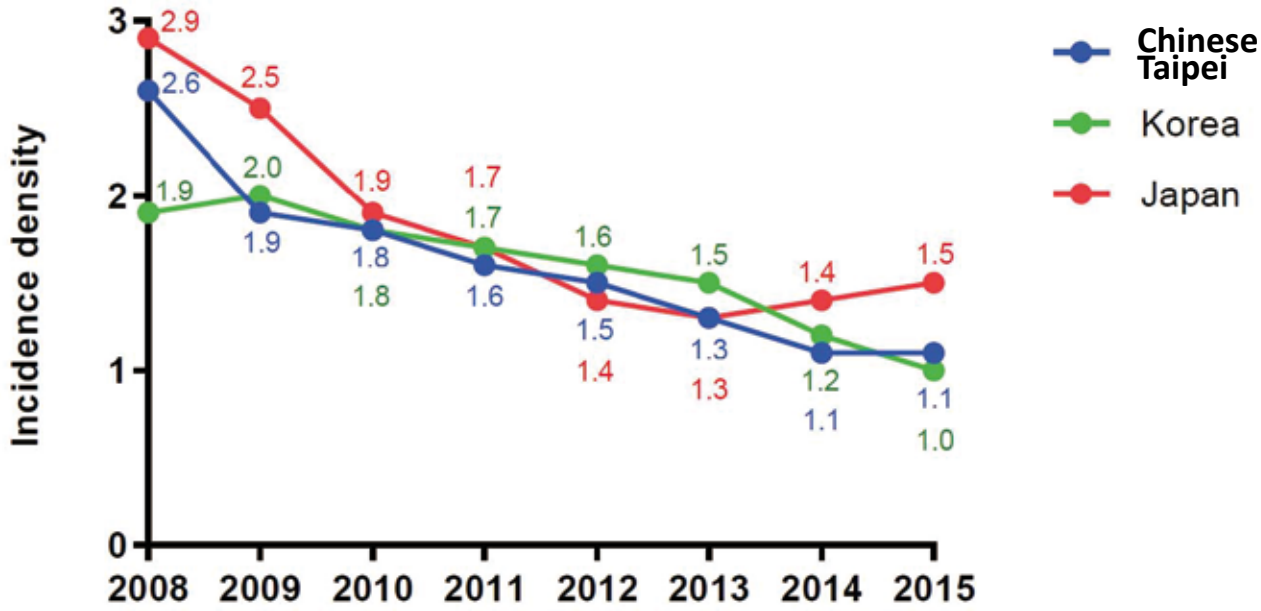
Catheter-associated urinary tract infection



Central line-associated bloodstream infections

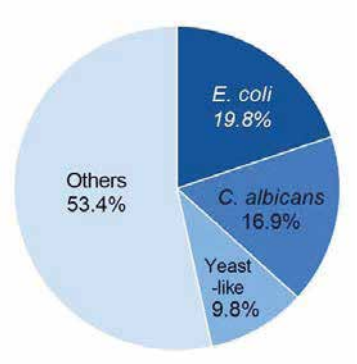


Ventilator-associated pneumonia

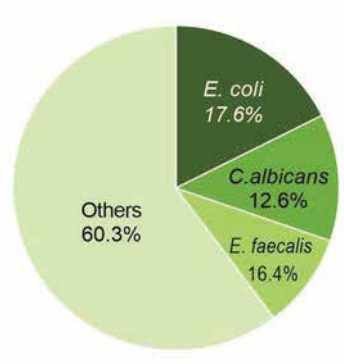


UTI causative pathogens

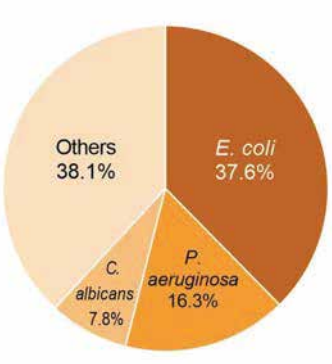
Chinese Taipei



South Korea



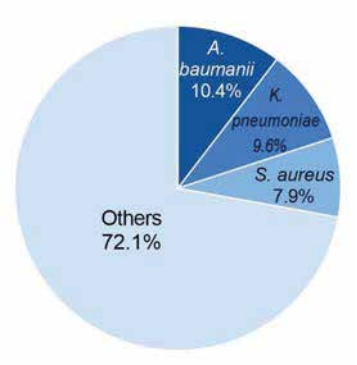
Japan



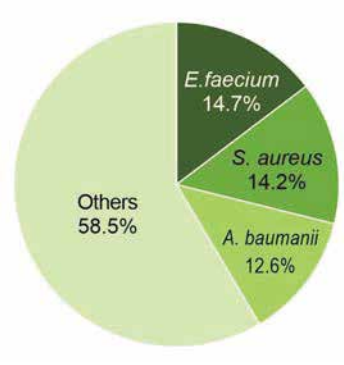
E. *coli* and C. *albicans* are common across all three countries

BSI causative pathogens

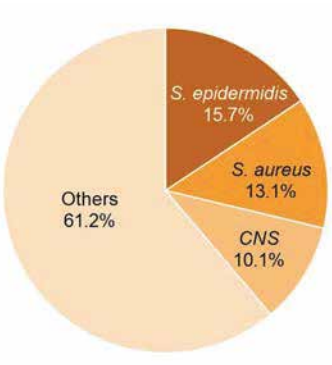
Chinese Taipei



South Korea



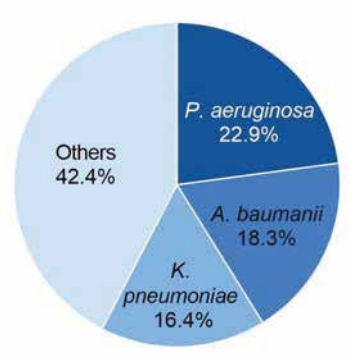
Japan



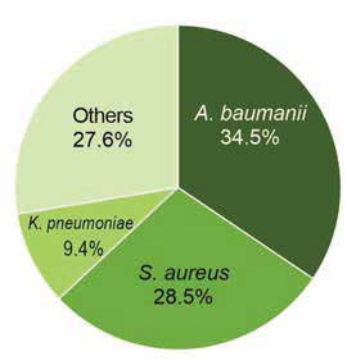
S. *aureus* is common across all three countries A. *baumanii* is important in Chinese Taipei and Korea

Pneumonia causative pathogens

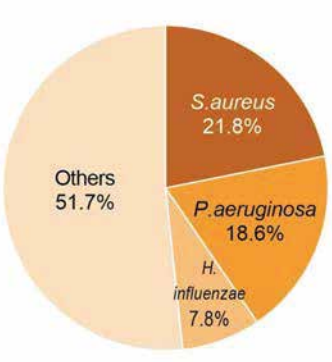
Chinese Taipei



South Korea

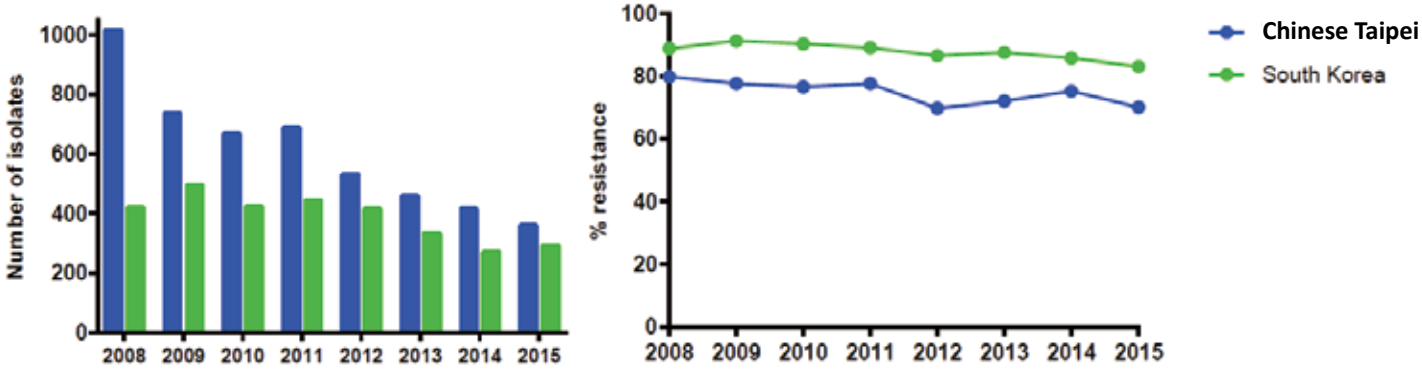


Japan

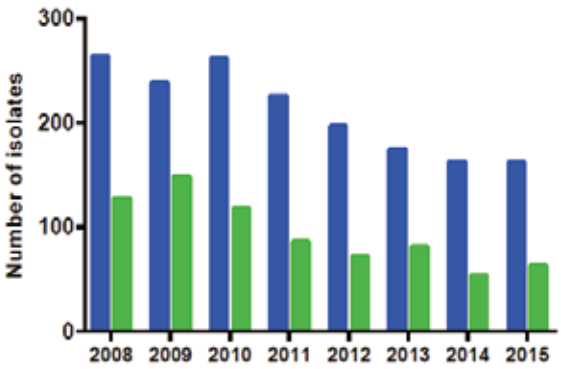


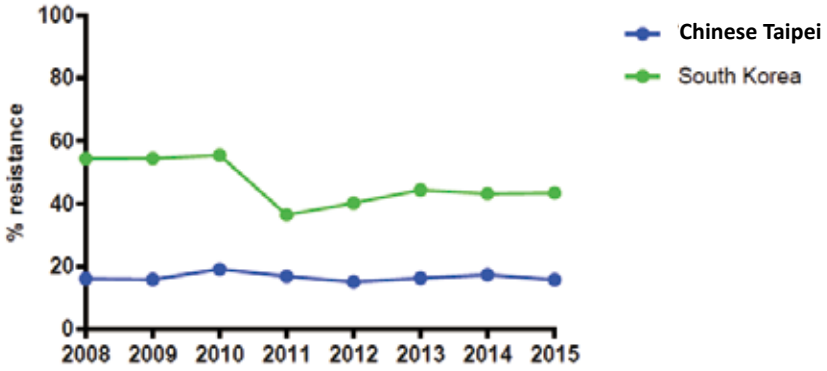
A. *baumanii* is important in Chinese Taipei and Korea
P. *aeruginosa*, K. *pneumonia*, S. *aureus* are important across the three countries

Methicillin-resistant *Staphylococcus aureus*



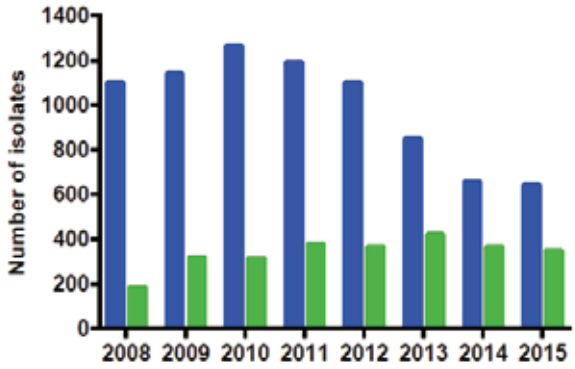
Carbapenem-resistant *Pseudomonas aeruginosa*

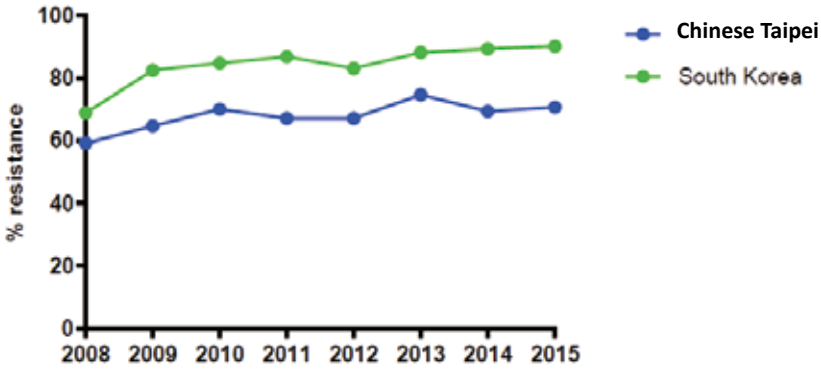




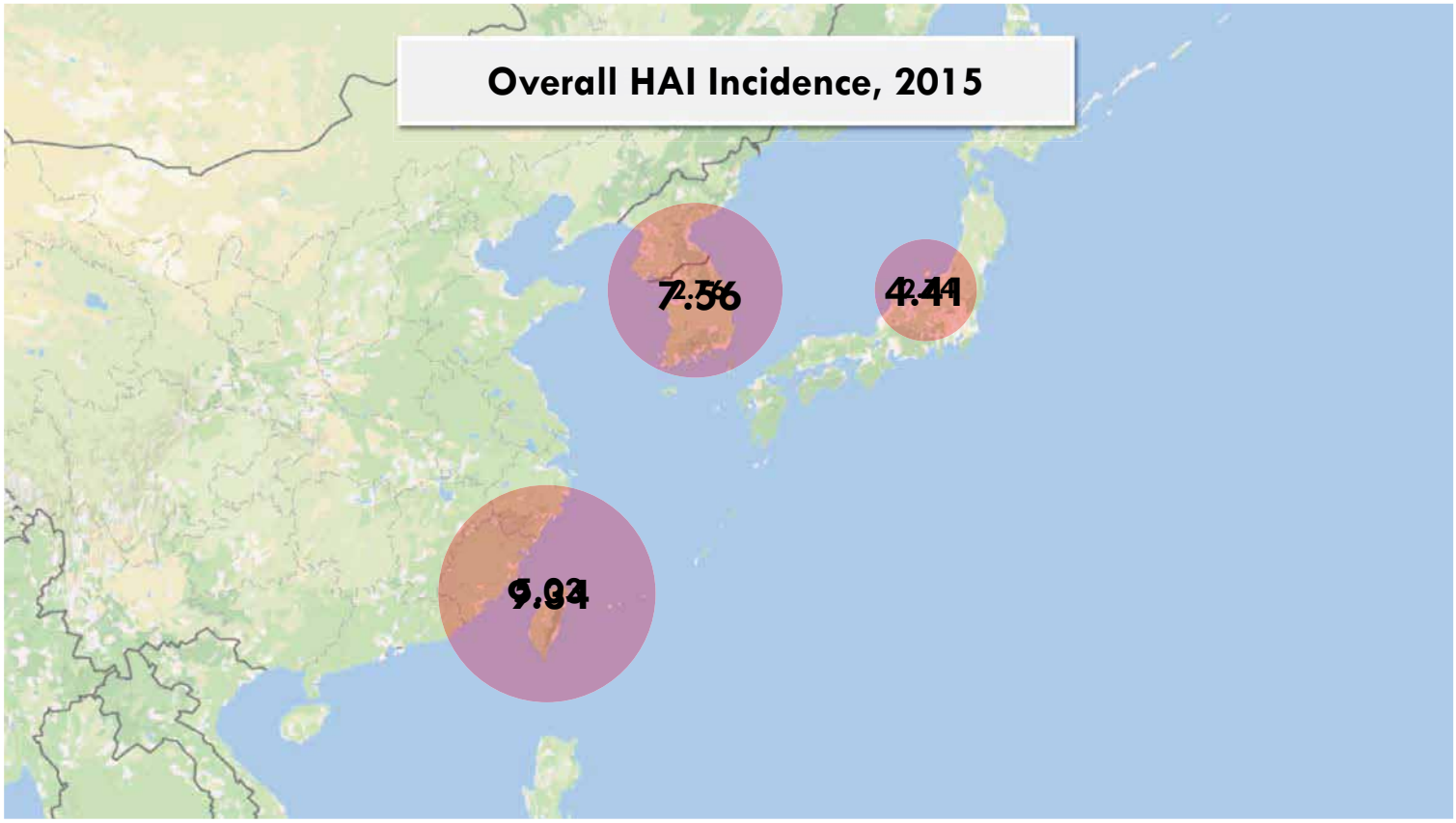
15

Carbapenem-resistant *Acinetobacter baumannii complex*

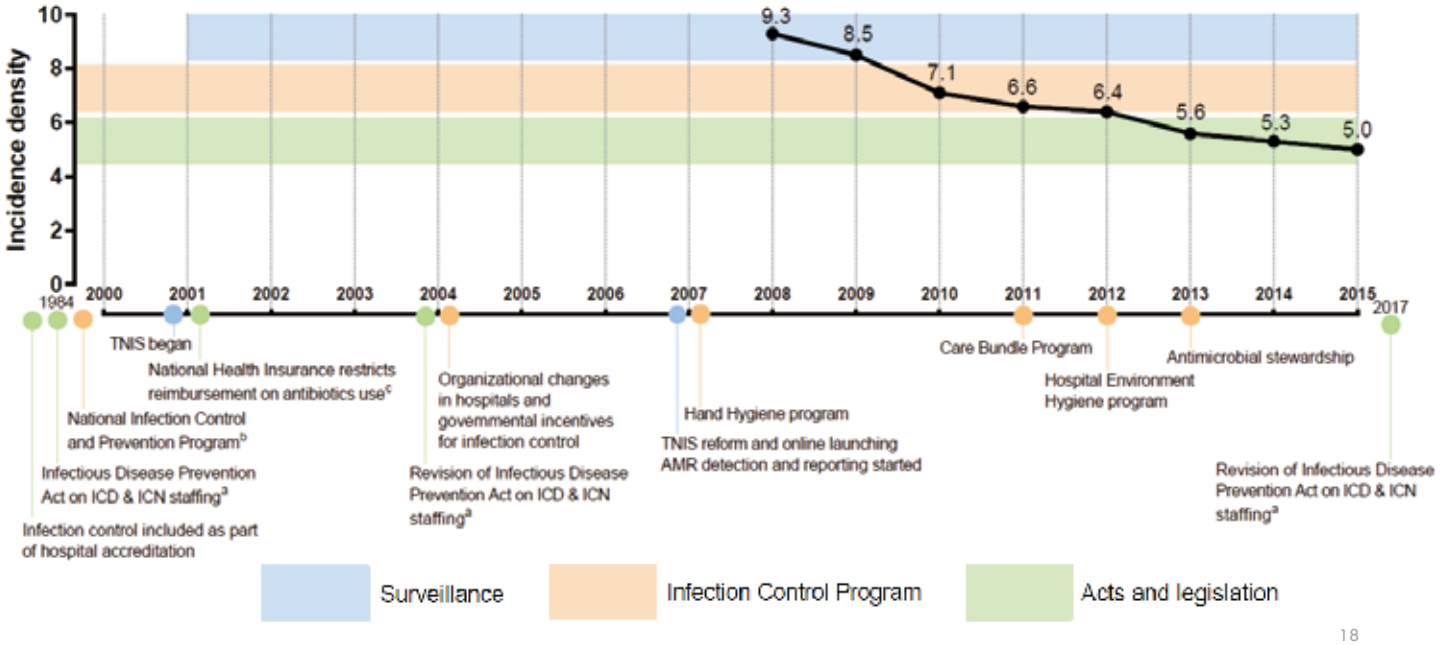




16

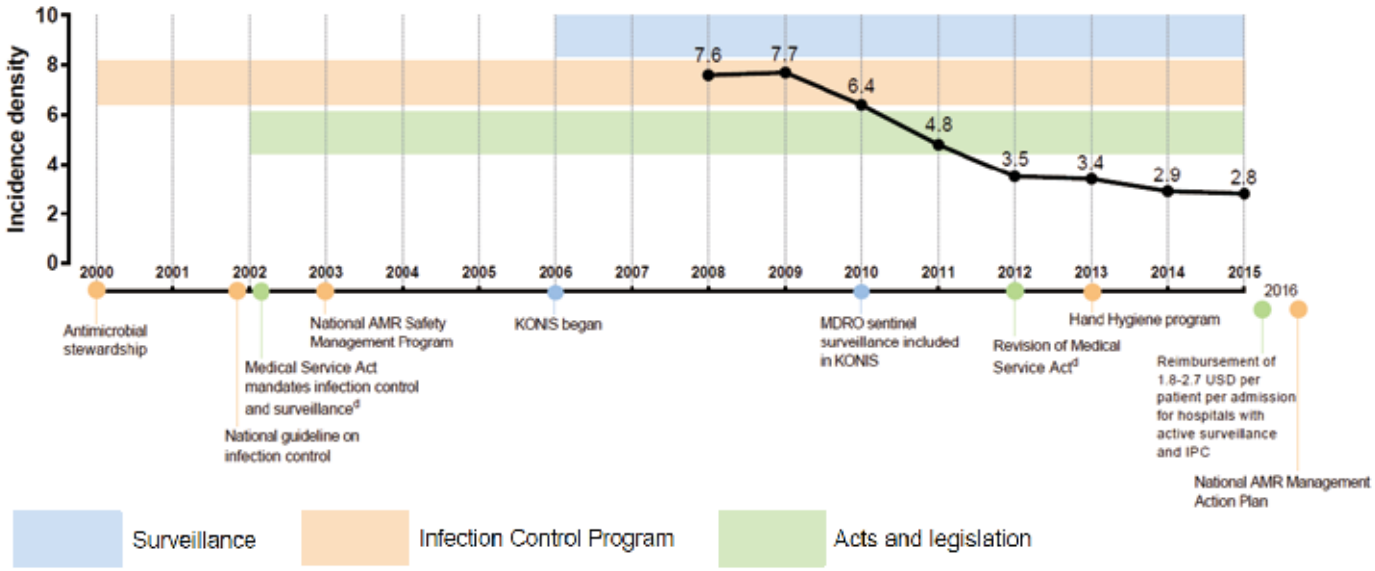


Chinese Taipei



18

Korea



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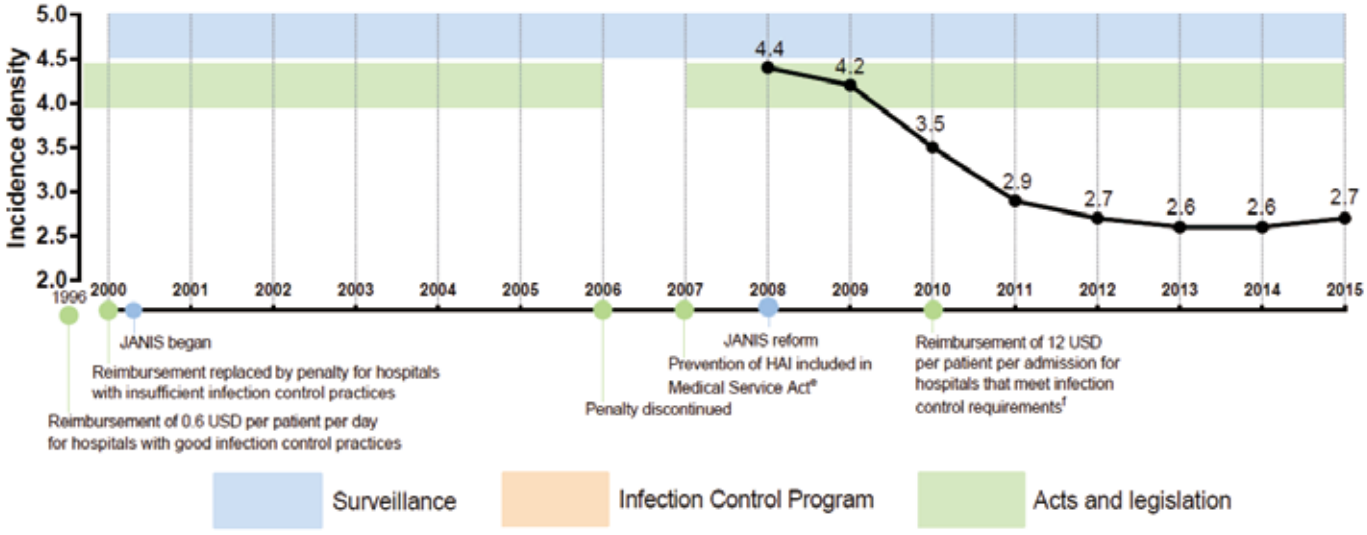
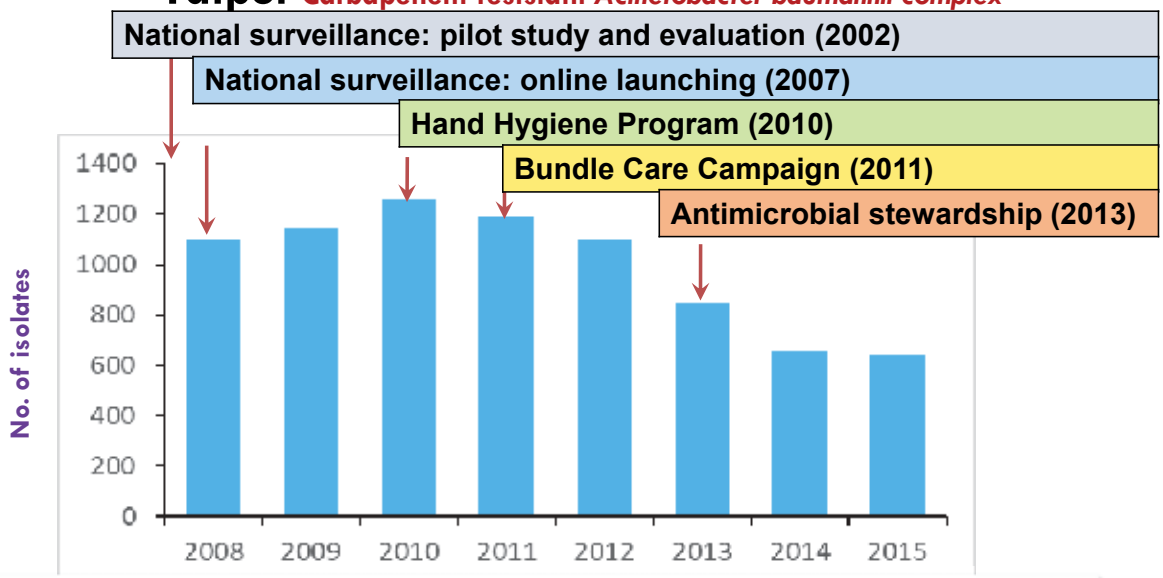
Japan



20

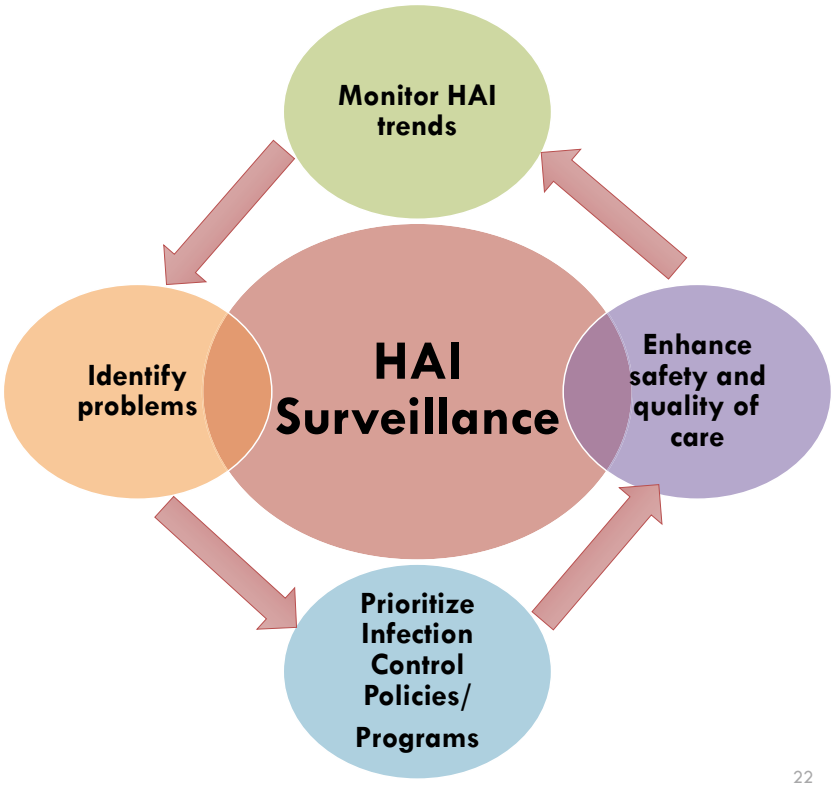
Integrated surveillance and intervention, Chinese Taipei *Carbapenem-resistant Acinetobacter baumannii complex*



Studies in South Korea found the reason for increased CRAB due to clonal outbreak, suggesting that infection control methods are important in reducing its incidence. J.Y. Choi et al., J Hosp Infect, 2015

Conclusion

- We found a significant decrease of HAI across the three countries in association with sequential multifaceted interventions.
- Further regional collaboration could be forged to develop joint strategies to prevent HAI.



22

Acknowledgements

Cho-Han Chiang[1], Sung-Ching Pan [2], Tyan-Shin Yang[1], Keisuke Matsuda[3], Hong Bin Kim[4,5], Young Hwa Choi[6], Satoshi Hori[7], Wang-Huei Sheng[1,2], Feng-Yee Chang,[8] Shan-Chwen Chang[1,2]

[1]College of Medicine, National Taiwan University

[2]Department of Internal Medicine, National Taiwan University Hospital

[3]Faculty of Medicine, Osaka University, Osaka, Japan

[4]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

[5]Division of Infectious Diseases, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

[6]Department of Infectious Diseases, Ajou University School of Medicine, Suwon, Republic of Korea

[7]Department of Infection Control Science, Juntendo University Faculty of Medicine, Tokyo, Japan

[8] Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center

CDC, : Ms. Lee-Jung Chien, Dr. Shu-Hui Tseng

Infection control personnel in Chinese Taipei, South Korea, and Japan who contributed to infection control and the surveillance efforts

Keynote Speech III
WHO Strategies to Fight Antimicrobial Resistance

Moderator

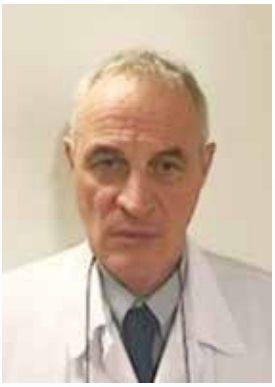
Prof. Shan-Chwen Chang

Dean, College of Medicine, National Taiwan University

Speaker

Prof. Didier Pittet

Chief Medical Officer, University hospitals of Geneva



Prof. Didier Pittet

Position: Chief Medical Officer

Department/organization: University hospitals of Geneva

Economy: Switzerland

Biography

Didier Pittet, MD, MS, born 20/03/1957, is Professor of Medicine, the Hospital Epidemiologist and Director of the Infection Control Programme and World Health Organization (WHO) Collaborating Centre on Patient Safety at the University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland. He holds Honorary Professorships at Imperial College London, UK, Hong Kong Polytechnic University School of Health Science, and the First Medical School of the Fu, Shanghai, China. Professor Pittet is Lead Adviser of the first WHO Global Patient Safety Challenge "Clean Care is Safe Care" and the African Partnerships for Patient Safety, Patient Safety, WHO Headquarter.

Prof Pittet is the recipient of several national and international honours including a CBE (Commander of the British Empire) awarded by Her Majesty Queen Elisabeth II for services to the prevention of healthcare-associated infection in the UK (2007), the Society for Healthcare Epidemiology of America Lectureship for his contribution to infection control and healthcare epidemiology (2008) and the European Society of Clinical Microbiology and Infectious Diseases' Award for Excellence (2009). The book "Clean Hands Save Lives" by the French writer Thierry Crouzet (Editions L'Âge d'Homme, 2014), translated in 11 languages as of December 2014, describes Didier Pittet medical odyssey to promote hand hygiene and patient safety worldwide. D Pittet is co-author of more than 500 publications in peer-reviewed journals and 50 textbook chapters (H-index 66; total citations 15960 as of 25/1/2015). He serves on the editorial boards of several journals and is an editorial consultant of the Lancet. Professor Pittet current research interests include the epidemiology and prevention of healthcare-associated infections, methods for improving compliance with barrier precautions and hand hygiene practices, as well as innovative methods for improving the patient care and safety. He is also involved in research on the epidemiology of infectious diseases, and public and global health issues.

In 2004, Pittet was approached by the WHO World Alliance of Patient Safety to lead the First Global Patient Safety Challenge under the banner "Clean Care is Safer Care" (http://www.who.int/gpsc/en/). The mandate was to galvanise global commitment to tackle health-care associated infection, which had been identified as a significant area of risk for patients in all United Nations Member States. Pittet proposed that WHO Guidelines for Hand Hygiene in Health Care be developed under his leadership in consultation with a large group of international experts. The final version of the Guidelines (http://whqlibdoc.who.int/publications/2009) was published in 2009 together with a multimodal improvement strategy, based on the successful model developed in Geneva and published in The Lancet in 2000. Concepts from the social sciences led to the creation of a multimodal strategy based on education, performance monitoring and feedback, and culture change in addition to the key component: introduction of alcohol-based handrub at the point of care to replace handwashing at the sink ("system change"). As of December 2014, "Clean Care is Safer Care" has been endorsed by ministers of health in over 130 countries worldwide representing a coverage of more than 95% of the world population. Save Lives: Clean Your Hands is the Challenge's annual campaign, that include the 5 May designated by WHO " World Hand Hygiene Day, with almost 18,000 hospitals registered from more than 179 countries at the end of December 2014. Alcohol-based hand rub is promoted actively as the new standard of care, including in resource-poor countries. Universal system change has been made possible worldwide and is today considered as the new standard of patient care.

Over 20 years of experience with culture change at the University of Geneva Hospitals constitute the solid scientific basis of the work of Didier Pittet and this experience and leadership has permitted him to lead international strategies at the healthcare setting and national levels in Australia, Belgium, Canada, France, Hong Kong, Iran, Italy, Spain, Switzerland, UK, USA, and various countries in Africa, Asia, the Middle and Far East, and Central and South America. The experience of his team in engaging nations and healthcare settings worldwide in a universal commitment to patient safety is unique.

Speech Abstract

WHO Strategies to Fight Antimicrobial Resistance

Prof. Didier Pittet, MD, MS, CBE

Director, Infection Control and WHO Collaborating Centre on Patient Safety, The University of Geneva Hospitals and Faculty of Medicine; Lead Adviser, *SAVE LIVES: Clean Your Hands*, Service Delivery, WHO Headquarter, Geneva, Switzerland.

The World Health Organization (WHO) is "*the directing and coordinating authority on international health within the United Nations system*". The objective of WHO is the attainment by all peoples of the highest possible level of health. Health, as defined in the WHO Constitution, is a "state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". WHO has a broad constitutional mandate and extensive law-making and convening power. The Constitution of WHO has a list of not less than 22 functions as providing technical guidance and harnessing scientific expertise, setting technical standards, helping countries to implement project, being a convening and negotiation forum for states and being an international norms setter. In other words, WHO cumulates technical, political and normative functions.

WHO has a strong antimicrobial resistance (AMR) mandate and has tackled AMR for a long time both regarding AMR in general but also regarding specific diseases such as HIV-AIDS, tuberculosis and Malaria. WHO is virtually active in all challenges (surveillance, infection prevention, conservation, containment, access and innovation) regarding AMR including in areas that are traditionally covered by other international organizations. In terms of knowledge, WHO has a strong network of experts that inform the activities of the organization. In terms of norms, WHO has adopted several resolutions on AMR and work on areas related to AMR. For example, WHO has been working on innovation in public health to evaluate diverse ways to incentive research and development of new antimicrobials. In terms of policies, WHO has formulated joint policies regarding AMR through the adoption of its 2015 WHO Global Action Plan and related plans for specific diseases. The broad normative functions of WHO makes WHO an essential forum in the area of "policy and regulations" considering however that international law has its advantage and benefits and it not per se a guarantee of effectiveness. In terms of institutions, recent innovation at WHO include the creation of mechanisms for surveillance (e.g. AGISAR, GLASS), stewardship (e.g. Global Framework for Development & Stewardship to Combat Antimicrobial Resistance, AMR awareness week) and research and development (e.g. GARDP in partnership with DNDi). Many activities conducted in partnerships with other actors. The main mechanisms for intersectoral collaboration regarding AMR include the tripartite collaboration with FAO and OIE, the Codex Alimentarius (WHO and FAO), the trilateral collaboration on public health, innovation and trade. Considered together the activities of the WHO include 1) synthesising scientific knowledge and producing technical guidance, 2) producing norms ranging from soft to hard law, 3) formulating global policies on AMR and 4) supporting project implementation. Given its wide range of activities and functions, WHO is the main player regarding AMR. The complexity of the challenges makes that WHO has to rely on the expertise of other international organizations. WHO should continue to orchestrate the global response on AMR based on strong collaboration within different departments at WHO and beyond through inter-organizational collaboration. Given the strong interdisciplinary nature of AMR, WHO might extend the range of WHO collaborative centres to better integrate social science research on AMR.

Keynote Speech IV
Antimicrobial Resistance Detection and Containment; A Current US Approach

Moderator

Dr. Yi-Chun Lo

Deputy Director-General, Centers for Disease Control

Speaker

Dr. Michael Bell

Deputy Director, Division of Healthcare Quality Promotion,
Centers for Disease Control and Prevention

Dr. Yi-Chun Lo

Position: Deputy Director-General

Department/organization: Centers for Disease Control

Economy: Chinese Taipei

Educational Background

- M.D., National Taiwan University College of Medicine

Professional Career

- 2003-2008 Internal Medicine Residency and Infectious Disease Fellowship, National Taiwan University Hospital
- 2009-2011 Epidemic Intelligence Service, US CDC
- 2012-2016 Medical Officer and FETP Director, CDC
- 2016- Deputy Director-General, CDC

Publication

- Cheng CY, Wu HH, Zou H, Lo YC. Epidemiological characteristics and associated factors of acute hepatitis A outbreak among HIV-coinfected men who have sex with men in Taiwan, June 2015–December 2016. J Viral Hepat 2018 [Epub ahead of print]
- Wu HH, Shen YT, Chiou CS, Fang CT, Lo YC. Shigellosis outbreak among MSM living with HIV: a case-control study in Taiwan, 2015−2016. Sex Transm Infect 2018 [Epub ahead of print]
- Lo YC. Implementation of the IHR Joint External Evaluation: Taiwan's Experiences. Health Secur 2017;15:132−6.
- Liao YS, Liu YY, Lo YC, Chiou CS. Azithromycin-nonsusceptible Shigella flexneri 3a in men who have sex with men, Taiwan, 2015−2016. Emerg Infect Dis 2017;23:345−6.
- 11. Chiou CS, Izumiya H, Kawamura M, Liao YS, Su YS, Wu HH, Chen WC, Lo YC. The worldwide spread of ciprofloxacin-resistant Shigella sonnei among HIV-infected men who have sex with men, Taiwan. Clin Microbiol Infect 2016;22:383.e11−6.

Dr. Michael Bell

Position: Deputy Director

Department/organization: Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention

Economy: the United States

Biography

Dr. Michael Bell is the Deputy Director of CDC's Division of Healthcare Quality Promotion. Prior to that he served as the Associate Director for Infection Control and was the Executive Secretary for the US Healthcare Infection Control Practices Advisory Committee. His career has focused on investigating and preventing transmission of healthcare-associated illness, development of evidence-based infection control guidelines, and optimizing systems of care. Prior to his current position at CDC, he was the Chief of the Epidemiology Unit at the Viral Special Pathogens Branch, addressing control of high-risk pathogens.

He received his medical degree from the University of Washington and trained in Infectious Diseases at the University of California San Francisco.

Speech Abstract

Antimicrobial Resistance Detection And Containment; a Current US Approach

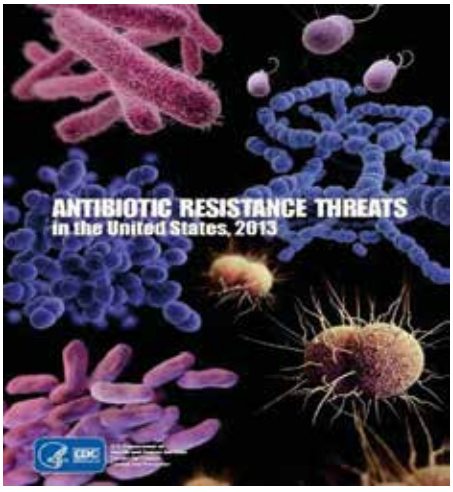
Antibiotics are a precious resource that we must not lose. Antimicrobial resistance (AMR) is a natural phenomenon that is continuous in the presence of antibiotics. Traditional approaches to AMR in the United States did not effectively contain this growing threat. Today, the US approach is focused on Prevention of Infections and Appropriate Antibiotic Use, Early Detection and Fast Response for Containment of AMR threats, along with Innovation to support better diagnosis, treatment, and control of AMR pathogens, and address the roles of the microbiome and environment in AMR. Implementation of these efforts has required significant investments in national and local capacities. The Centers for Disease Control and Prevention, in partnership with state and local public health systems, human and animal health sectors, industry and academia, international collaborators, and patient representatives is leveraging those investments to ensure that we continue to have effective antibiotics on which to rely in the coming decades.

Antimicrobial Resistance Detection and Containment; a current US approach

Michael Bell, MD
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
No conflicts of interest to declare

Antimicrobial Resistance: A Growing Threat

- Sickens **>2 million** people and kills at least **23,000** people each year
- **>$20 billion** each year in healthcare costs



Antimicrobial Resistance Threatens Every Person, Modern Medicine, and Industries

- Antibiotic resistant germs avoid the effects of the drugs designed to kill them
- AMR affects all communities and, without action, will continue to get worse
- AMR is not preventable, but it can be contained
- We still have time to make a difference

Resistant germs can be anywhere and can affect every aspect of human life

Resistance Threatens U.S. Healthcare and Undermines Our Ability to Heal and Cure

Life-saving treatments depend on antibiotics that work

1.6M+ NEW CANCER DIAGNOSES
650k receiving outpatient chemo

3.9M CHILDBIRTHS
One-third (1.3M) C-sections

16M SURGERIES

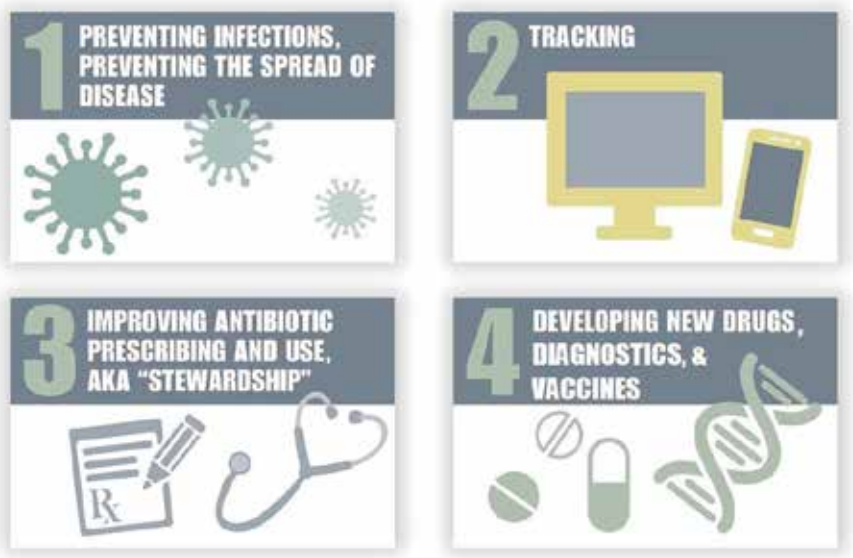
468k ON DIALYSIS
193k kidney transplants (total living)

34k ORGAN TRANSPLANTS/YEAR
Impossible without antibiotics

117M WITH A CHRONIC DISEASE
29.1M with diabetes
53M with arthritis

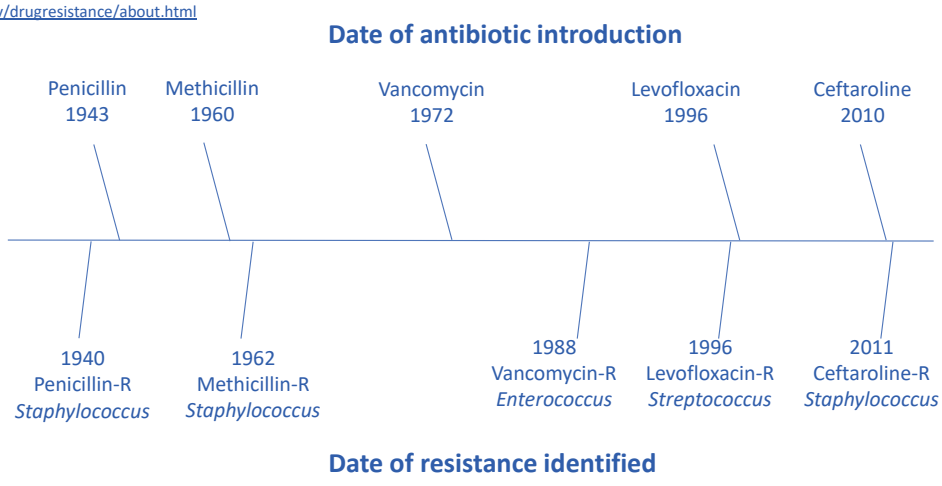
New Drugs Alone Are Not Enough…

Combating AR requires comprehensive, aggressive action across the U.S. gov't and around the globe



Antibiotic Use Drives Resistance

http://www.cdc.gov/drugresistance/about.html



National Momentum on AR: Post CDC Threat Report

2013

- CDC's *AR Threat Report*

2014

- Executive Order 13676
- *National Strategy on CARB*
- President's Council of Advisors on Science & Technology Report

2015

- *National Action Plan for CARB*
- White House Antibiotic Stewardship Forum
- Presidential Advisory Committee established

2016

- Congress appropriates funding to implement CARB activities
- U.S. engagement on UN General Assembly High Level Meeting on AMR

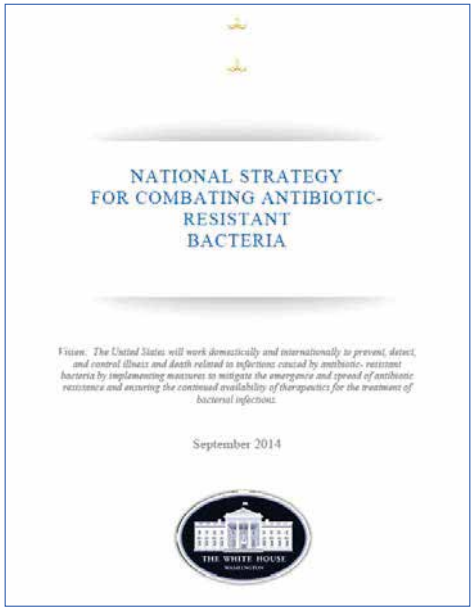
2017

- Executive Order reestablishes Presidential Advisory Committee
- Presidential Message on Antibiotic Awareness Week

2018

- Planned U.S. engagement on 2nd UN General Assembly High Level Meeting on AMR

National Strategy to Combat Antibiotic Resistant Bacteria, September 2014 – 5 Goals


NATIONAL STRATEGY
FOR COMBATING ANTIBIOTIC-
RESISTANT
BACTERIA

Vision. The United States will work domestically and internationally to prevent, detect, and control illness and death related to infections caused by antibiotic- resistant bacteria by implementing measures to mitigate the emergence and spread of antibiotic resistance and ensuring the continued availability of therapeutics for the treatment of bacterial infections.

September 2014

THE WHITE HOUSE

1. Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections
2. Strengthen National One-Health Surveillance Efforts to Combat Resistance
3. Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria
4. Accelerate Research to Develop New Antibiotics and Alternative Therapeutics, and Vaccines
5. Improve International Collaboration and Capacities for Disease Prevention and Surveillance and Antibiotic Research and Development

Fighting Antibiotic Resistance Where it Happens

Improving antibiotic use and infection prevention, with innovative and proven practices to control spread.

Rapidly identifying drug-resistant foodborne bacteria to stop and solve outbreaks and improve prevention.

Detecting, preventing, tracking and treating drug-resistant pathogens in the community.

Improving international collaboration and capacities for surveillance, infection control, prevention, stewardship, and public health research.

Exploring unanswered questions about AR and humans, animals, and the environment (e.g., surface water and soil).

CDC's Work in Antimicrobial Resistance

Laboratory & Diagnostics

DETECT & RESPOND

Communications & Guidance

PREVENT & CONTAIN

Insights for Practice

INNOVATE

Epidemiology & Surveillance

Improved Antibiotic Use

Research & Development

Accelerating & Implementing Innovations to Combat AR

Industry Partners

Synergies with Industry, e.g. CDC's Isolate Bank:

- *C. auris* diversity panel used by EPA to test disinfectants
- Isolates for development of new rapid diagnostics
- Environmental testing of antibiotics in pesticides

Leaders in Applied Research

Research on AMR in healthcare, food, and community, e.g.:

- New ways to detect AR and improve abx use
- Domestic and international AMR transmission and colonization
- Microbiome
- AMR in water systems, environment
- AMR data sources

Prevention Networks

Piloting and evaluating evidence-based prevention strategies in healthcare e.g.:

- Developing ways to model AR and HAI transmission
- Improving infection control interventions
- Assessing antibiotic stewardship and use

Academic & Healthcare Investigators

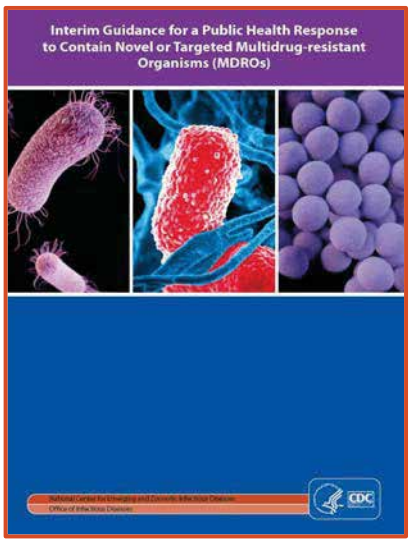
Discovering and scaling up new ways to protect people:

- Domestic and international HAI prevention research
- Research on environmental AMR
- Healthcare information technology development
- Veterinary healthcare quality improvement

CDC's Containment Strategy

Systematic approach to slow spread of novel or rare multidrug-resistant organisms or mechanisms—at a single case—through an aggressive response.

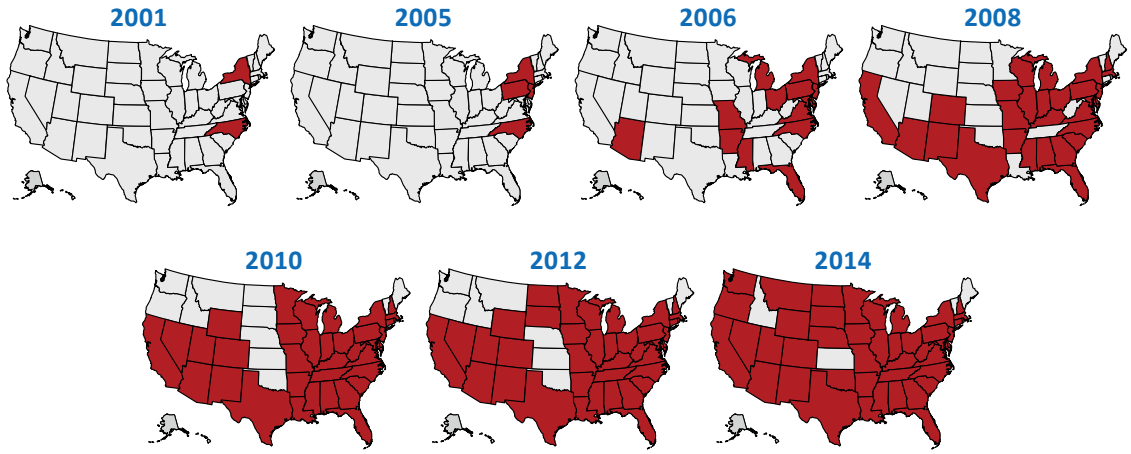
- **Targeted threats:** *mcr*, carbapenemase-producing organisms, pan-resistant organisms, *Candida auris*
- **Emphasis on settings** historically linked to amplification (e.g., LTC, LTAC, vSNF)
- **Main components:** Detection, infection control assessments, colonization screenings
- **Response tiers** based on threat



Guidance available on CDC's website:
www.cdc.gov/hai/outbreaks/mdro

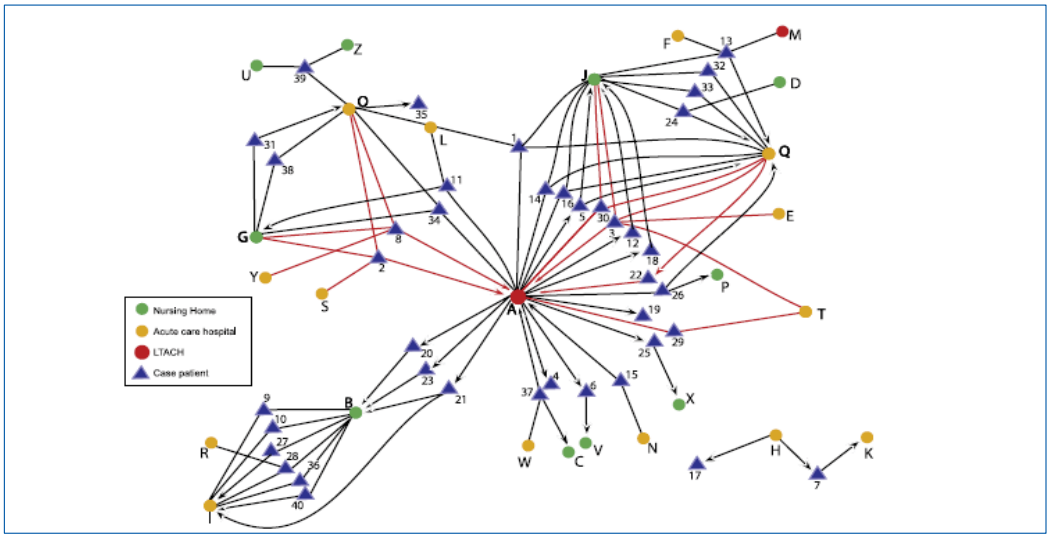
Why We Need a Containment Strategy

KPC, the first type of CRE found in the U.S., spread from 2 states in 2001 to 45 states, DC, and Puerto Rico in 13 years.



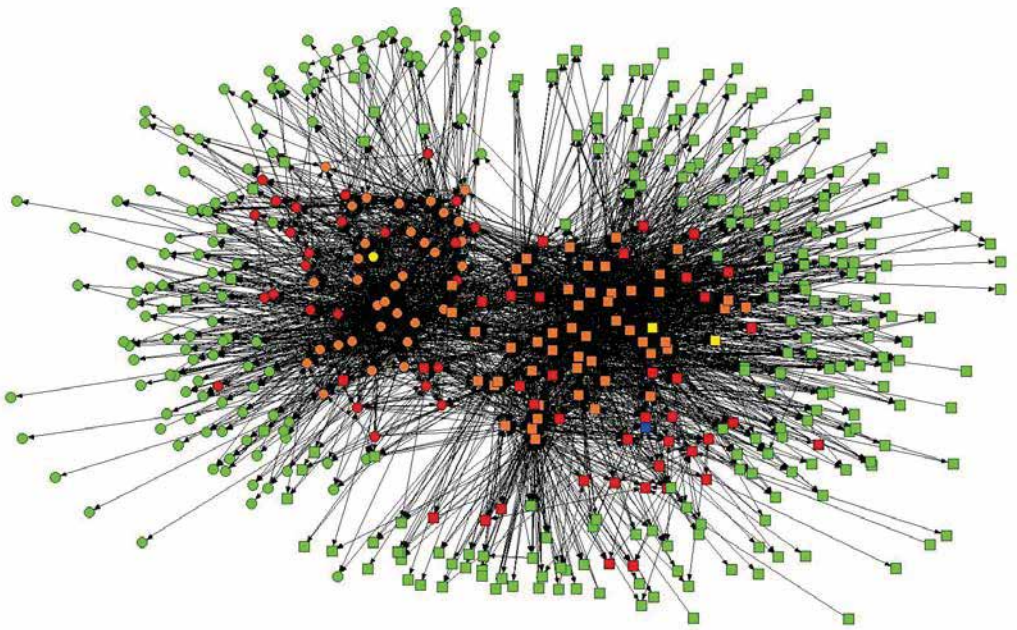
States with *Klebsiella pneumoniae* carbapenemase (KPC)-producing Carbapenem-resistant Enterobacteriaceae (CRE) confirmed by CDC

carbapenem-resistant Enterobacteriaceae (CRE) Outbreak: Several Healthcare Facilities in More than a County, Illinois, 2008



Won S, Munoz-Price S, Lolans K, Hota B, Weinstein R, Hayden M. for the Centers for Disease Control Prevention Epicenter Program. Rapid and Regional Spread of Klebsiella pneumoniae Carbapenemased CID 2011:53

Connectedness of Healthcare Facilities, Washington and Oregon



- Acute Care
- Critical Access
- Long-term acute care hospital
- Rehabilitation
- Skilled nursing facility

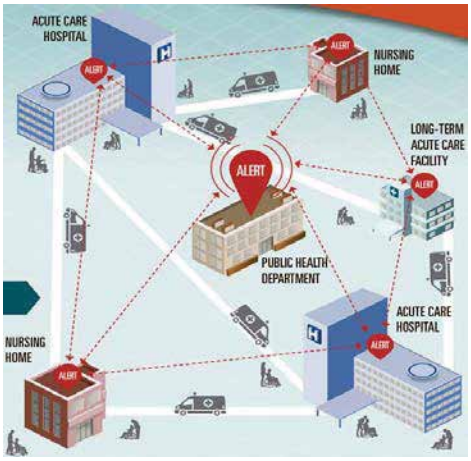
Prevention of *C. difficile,* MRSA, and Other MDROs: Need for Regional Prevention Approach

All state health departments are being funded by CDC to prevent healthcare-associated infections and antibiotic resistance.

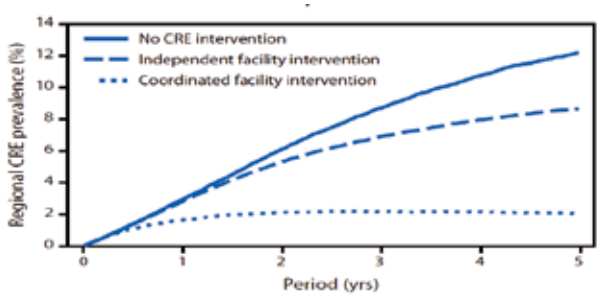
- **Traditional Approach**
  - Promotion of prevention efforts independently implemented by individual health care facilities
  - Does not account for inter-facility spread through movement of colonized/infected patients
  - Not effective for CDI and MDROs
- **Regional Approach**
  - Recognizes that individual facilities are components of integrated and dynamic networks connected via patient movement
  - Occurrences in one healthcare facility may affect many other healthcare facilities

<u>Prevention and Stewardship</u>

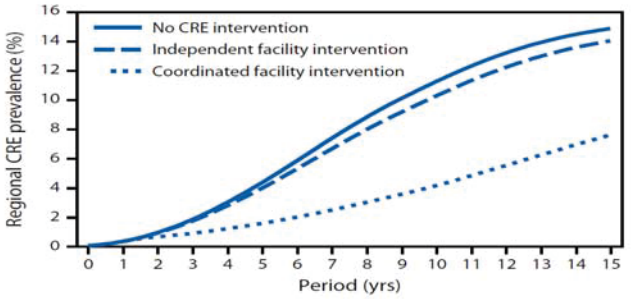
- In 27 states and 4 cities, CDC is aggressively expanding CRE, *C. difficile,* and other MDRO prevention and antibiotic stewardship programs



Projected Prevalence of CRE Based on Modeling



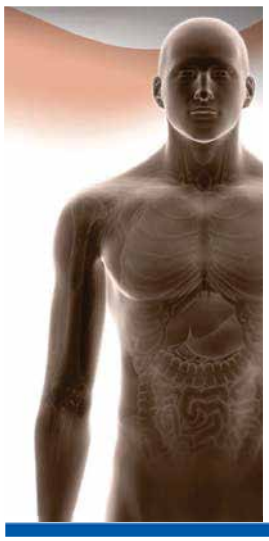
* Additional information available at http://www.cdc.gov/drugresistance/resources/publications.html. A video of the model simulations is available at http://www.cdc.gov/drugresistance/resources/videos.html.



* Additional information available at http://www.cdc.gov/drugresistance/resources/publications.html.

Conclusion: Coordinated prevention approaches assisted by public health agencies have the potential to more completely address emergence and dissemination of MDROS and in comparison to independent facility based efforts.

Thinking Holistically to Protect Patients



Prevent Infections	Early Detection	Appropriate Treatment
• Implement current recommendations • Innovation	• Diagnostic stewardship • Faster diagnostic tools • Sepsis	• Antibiotic Stewardship

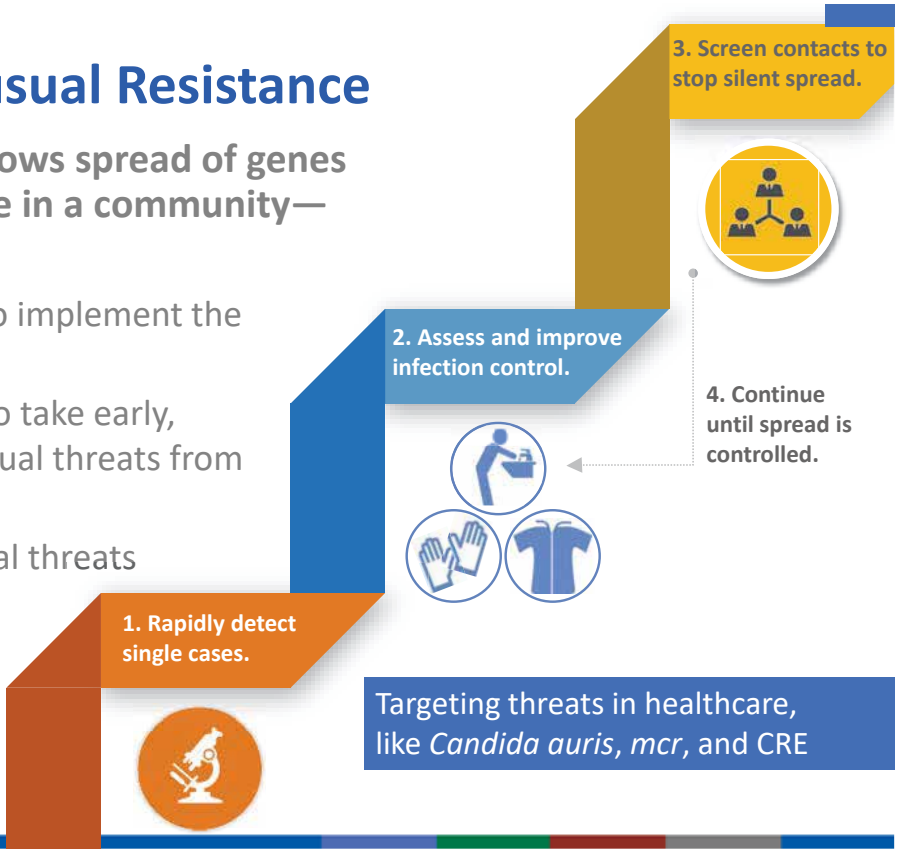
• Emerging Resistant Bacteria
• Inter-facility Transmission

Protecting Across the Patient Care Spectrum

Getting Ahead of Unusual Resistance

CDC's Containment Strategy slows spread of genes and germs that are new or rare in a community—even at a single case.

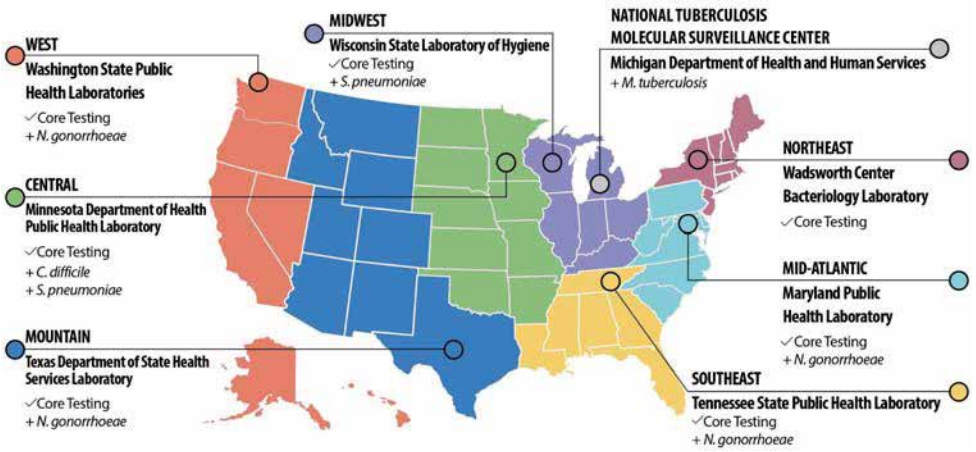
- Every state now has capacity to implement the Containment Strategy
- CDC works with local experts to take early, aggressive action to keep unusual threats from becoming common
  - More awareness of unusual threats
  - Improving response times
  - Stopping silent spread



Targeting threats in healthcare, like *Candida auris*, *mcr*, and CRE

Antibiotic Resistance Laboratory Network

National laboratory capacity to detect AR in healthcare, food, and community
Tracks resistance to identify outbreaks faster, stop spread, and protect people

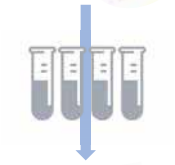


- CDC headquarters expertise and coordination
- 7 regional labs
- 1 National TB Molecular Surveillance Center
- 57 state and local labs

CDC & FDA Antibiotic Resistance Isolate Bank

New innovations can support earlier diagnoses and more effective treatment options that can slow antibiotic resistance.

CDC uses bacteria samples (isolates) from health departments, labs, and outbreak and surveillance activities.



CDC analyzes and sequences the bacteria's resistance and makes the data and sample available.

Researchers can use the bacteria and data to challenge, develop new diagnostic tests and antibiotics.

Laboratorians can validate lab tests to improve patient care.

BY THE NUMBERS
as of Nov. 1, 2017

CDC curated 15 panels from its 450,000+ isolate collection

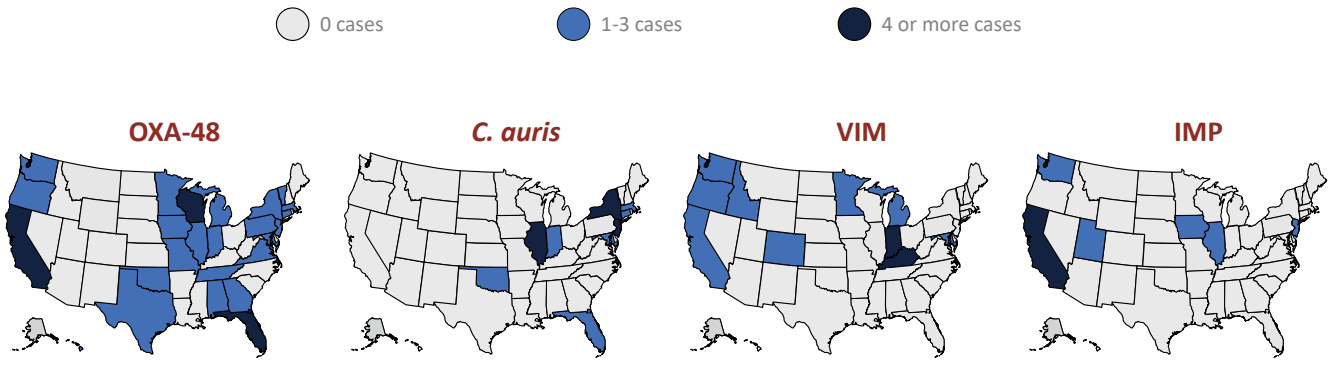
65,300 isolates shared since July 2015

570+ unique customers

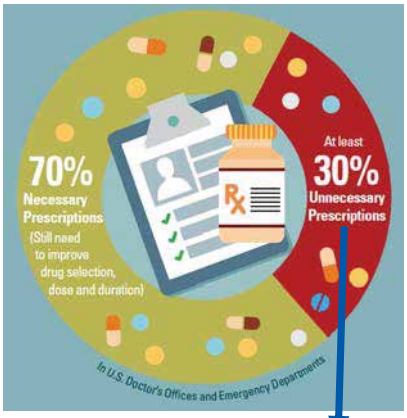
743 orders processed

CDC's Containment Strategy in Action

CDC and states have successfully contained many emerging threats, like *C. auris* and types of CRE, to single or few cases.

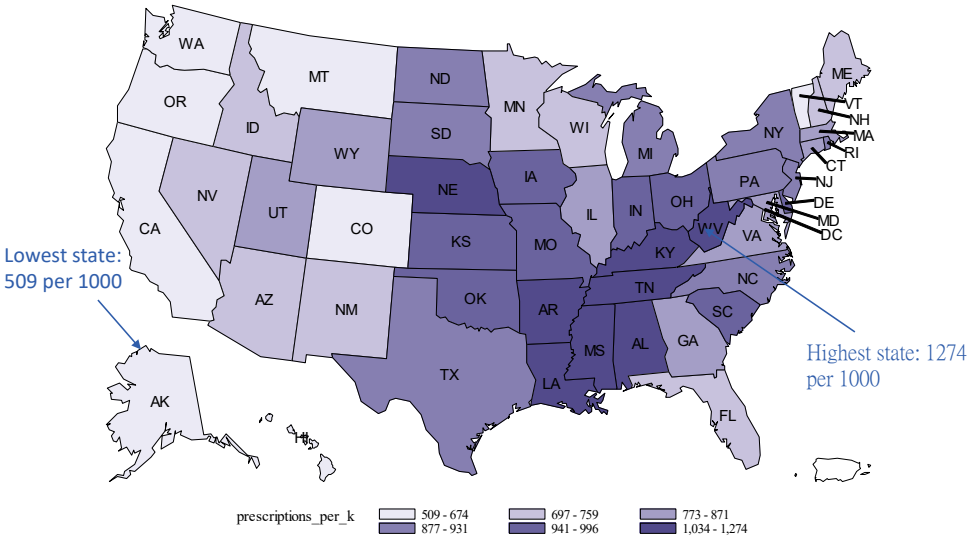


How much antibiotic use is unnecessary?



Represents unnecessary risks to patients of adverse drug events, *Clostridium difficile* infection and development of antibiotic resistance.

Fleming-Dutra et al. JAMA 2016;315(17): 1864-1873.



Hicks CID 2015: 60(9):1308-16; CDC. Outpatient antibiotic prescriptions — United States, 2013. Available via the internet: http://www.cdc.gov/getsmart/community/pdfs/annual-reportsummary_2013.pdf

Three Things Health Plans Should Know About Antibiotic Harms that Have Nothing to Do with Resistance

1. Antibiotic adverse events can be **severe**, examples:
   - Antibiotic-associated diarrhea (e.g., *C. difficile* infection)
   - Life-threatening allergic reactions (e.g., anaphylaxis)

2. Antibiotic adverse events can **cost** the health plan in **ER visits**
   - 1 in 1000 antibiotic prescriptions leads to an ER visit for an adverse event
     - **~200,000 estimated ER visits/year in U.S.**
   - Antibiotics: most common cause of drug-related ER visits in children

3. Antibiotic adverse events may have long-term consequences for **chronic disease**
   - Disruption of microbiota and microbiome linked to chronic disease

Linder. *Clin Infect Dis*. 2008 Sep 15;47(6):744-6 Shehab, et al. *Clin Infect Dis*. 2008 Sep 15;47(6):735-43. Shehab et al. *JAMA 2016*:316:2115-25. Bourgeois, et al. *Pediatrics.* 2009;124(4):e744-50. Vangay, et al. Cell host & microbe 2015; 17(5): 553-564.

Potential Impact of *C. difficile* Prevention

	Intervention Effectiveness			
	10%	25%	50%	75%
Cohort of 1,000 hospitalized Medicare beneficiaries ≥65 years old				
Total CDI infections averted over 5 years	7.36	18.59	36.94	56.06
Total CDI-attributed deaths averted over 5 years	1.20	2.93	5.91	8.97
Among all hospitalized Medicare beneficiaries ≥65 years old				
Total CDI infections averted over 5 years	101,000	257,000	509,000	773,000
Total CDI-attributed deaths averted over 5 years	**16,000**	**41,000**	**82,000**	**124,000**

National Perspective

- An intervention with 50% effectiveness would:
  - **Save $2.5 billion in direct medical costs** over 5 years.
  - **Save $689 billion in societal costs** over 5 years.

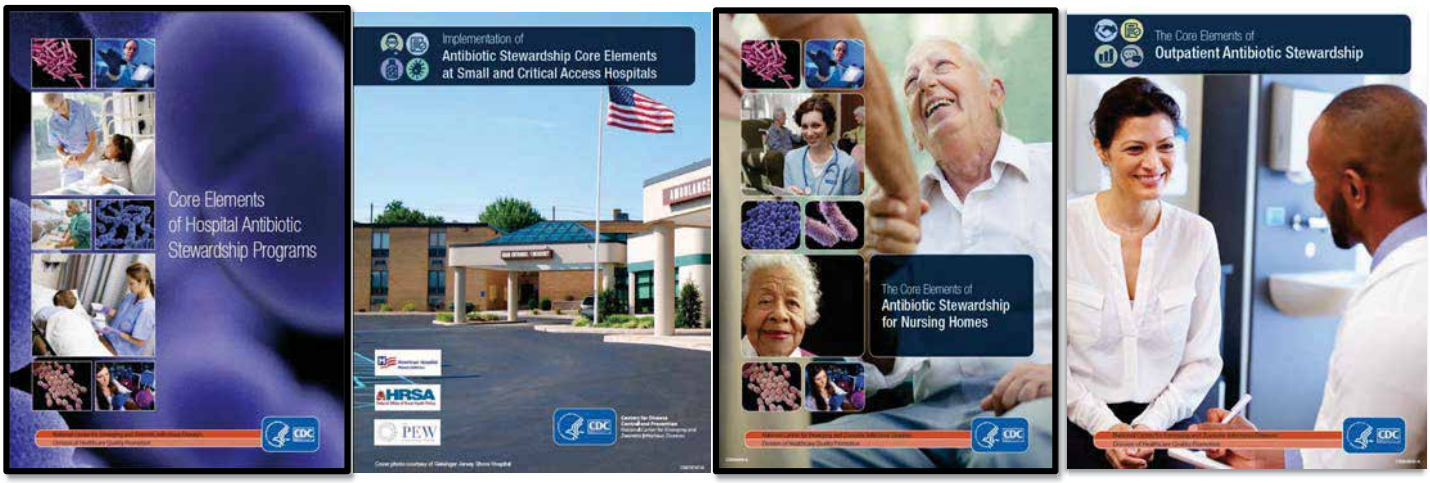
R Slayton, ICHE 2015; 36:681-687

Improving Education on Antibiotic Use

- New educational effort: Refining messaging and expanding to new target audiences.
  - Focus on patient safety: Unnecessary antibiotics cause preventable harm
  - Increased messaging for adult patients
  - New effort to reach hospitalists, nurse practitioners, physician assistants
- "U.S. Antibiotic Awareness Week"
  - November 12-19, 2018
  - Addresses key need to provide information on antibiotic use, especially to patients.

BE ANTIBIOTICS AWARE
SMART USE, BEST CARE

Working with Partners to Improve Stewardship Across All Healthcare Settings



https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html;
https://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html
https://www.cdc.gov/getsmart/community/improving-prescribing/core-elements/core-outpatient-stewardship.html
https://www.cdc.gov/getsmart/healthcare/implementation/core-elements-small-critical.html

Get Ahead of Sepsis

GET AHEAD OF SEPSIS

KNOW THE RISKS. SPOT THE SIGNS. ACT FAST.

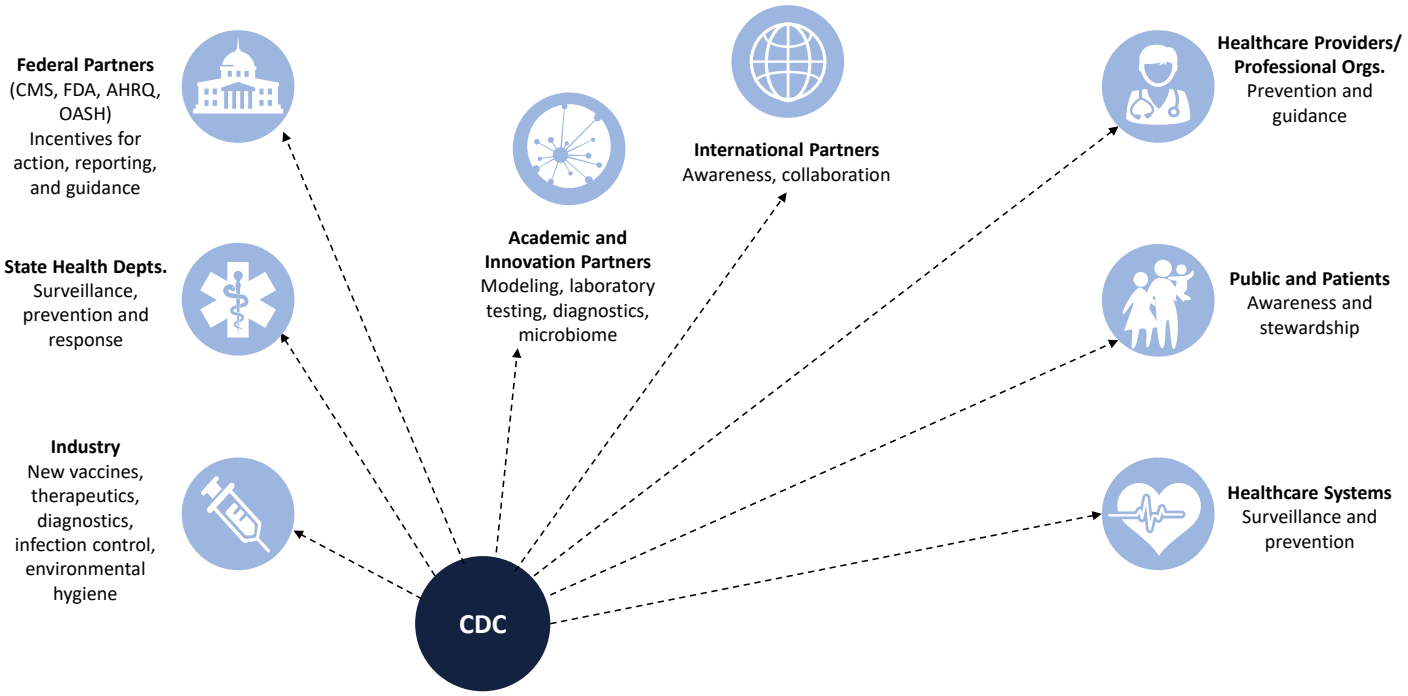
Goal

Emphasizes the importance of sepsis early recognition, timely treatment, reassessment of antibiotic needs, and prevention of infections that could lead to sepsis.

Anticipated Outcomes

- Increase awareness of need for early recognition and prompt treatment.
- Increase awareness of preventing infections that can lead to sepsis.

Partners are Critical



Examples of CDC's Global Work to Combat AR

Innovation & Infection Control in Vietnam

- **Piloting shorter-course preventive therapy** to reduce TB disease and slow development of resistant TB
- **Studying latent TB** management by offering testing and treatment before traveling to the United States.
- **Establishing national AR and HAI surveillance** network of 16 sites to generate critical data
- **Developing national infection control** expertise through a national Technical Advisory Group to reduce HAIs and improve containment

Improving TB Diagnostics in Mexico

- Linking patients diagnosed with TB to care and treatment

First National TB Program in China

- Strengthening the Chinese TB surveillance system and collaborating on lab quality assurance programs

Strengthening HAI/AR Programs in India

- **Implementing HAI and AR surveillance** in 30+ sites across country to better understand AR burden
- **Initiating programs** to prevent and reduce central line associated bloodstream infections
- **Assessing stewardship** programs to improve antibiotic use

Transformative Investments to Combat AMR

	Detect	Respond	Prevent	Innovate
Then	• Few state laboratories can detect CRE • CDC national reference laboratory • Late detection of threats	• Few states have AMR experts for outbreaks, infection control • CRE outbreaks go undetected	• Few states have local staff for prevention, infection control • Lack of coordination between facilities to stop spread	• Limited understanding of CRE reservoirs and transmission • Research efforts by Prevention Epicenters and CDC's laboratories
Now	• All states, 5 large cities, & PR detect local CRE • CDC, regional labs, TB centers test and track • Routinely detect AMR	• All states, 6 large cities, & PR have dedicated AMR staff • Dramatic improvement in response to CRE outbreaks	• State programs coordinate prevention between facilities • Greater understanding of transmission • More focus on abx use	• Intra/Extramural studies including environmental • Uncovering sources of AMR transmission • Measuring risk to people and prevention impact

ARLABnetwork

AMR Impacts Real People

Alicia Cole, CA

Nile Moss, CA

Dana Mirman, FL

Peggy Lillis, NY

Catherine Duff, Indiana

Joshua Nahum, Colorado

Thank you!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Session III
Infection Control Strategies to Contain Antimicrobial Resistance (AMR)

Moderator

Prof. Yin-Ching Chuang

Professor, Chi Mei Medical Center

Prof. David Chien Boon Lye

Associate Professor, Tan Tock Seng Hospital

Prof. Yin-Ching Chuang

Position: Professor

Department/organization: Chi Mei Medical Center

Economy: Chinese Taipei

Education Background

- Kaohsiung Medical College

Professional Career

- Chair Professor, Chi Mei Medical Center
- Honorary superintendent, Chi Mei Liouying Hospital
- Regional Commander of the Communicable Disease Control Medical Network of the CDC

Prof. David Chien Boon Lye

Position: Associate Professor

Department/organization: Tan Tock Seng Hospital

Economy: Singapore

Educational Background

- 1996 MBBS, University of Melbourne, Australia
- 2004 Fellow of Royal Australasian College Physicians
- 2009 Fellow, Academy of Medicine, Singapore,
- 2016 Fellow, Royal College of Physicians, Edinburgh

Professional Career

- 2011-2015 Chair, Chapter of Infectious Diseases, College of Physicians, Singapore
- 2012-2014 Treasurer, College of Physicians, Singapore
- 2014- Vice President, College of Physicians, Singapore
- 2015- President, Society for Infectious Diseases (Singapore)
- 2016- Bursar, Academy of Medicine, Singapore
- 2016- Board member, College of Clinician Scientists, Academy of Medicine, Singapore

Publications

- A Versporten, P Zarb, I Caniaux, M-F Gros, N Drapier, M Miller, V Jarlier, D Nathwani, H Goossens, on behalf of the Global-PPS network. First web-based Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (GLOBAL-PPS) in 53 Countries: results on hospitalized adults. Lancet Global Health 2018, in press.
- HL Htun, TW Yeo, CC Tam, J Pang, YS Leo, DC Lye. Metformin use and severe dengue in diabetic adults. Scientific Reports 2018, in press.
- K Saeed, S Esposito, I Gould, T Ascione, M Bassetti, E Bonnet, E Bouza, M Chan, JS Davis, G De Simone, M Dryden, T Gottlieb, K Hijazi, DC Lye, P Pagliano, C Petridou, E Righi, J Segreti, S Unal, AN Yalcin. Hot topics in necrotising skin and soft tissue infections. Int J Antimicrob Agents 2018, in press.

Session III
Infection Control Strategies to Contain Antimicrobial Resistance (AMR)

Speaker

Prof. Satoshi Hori

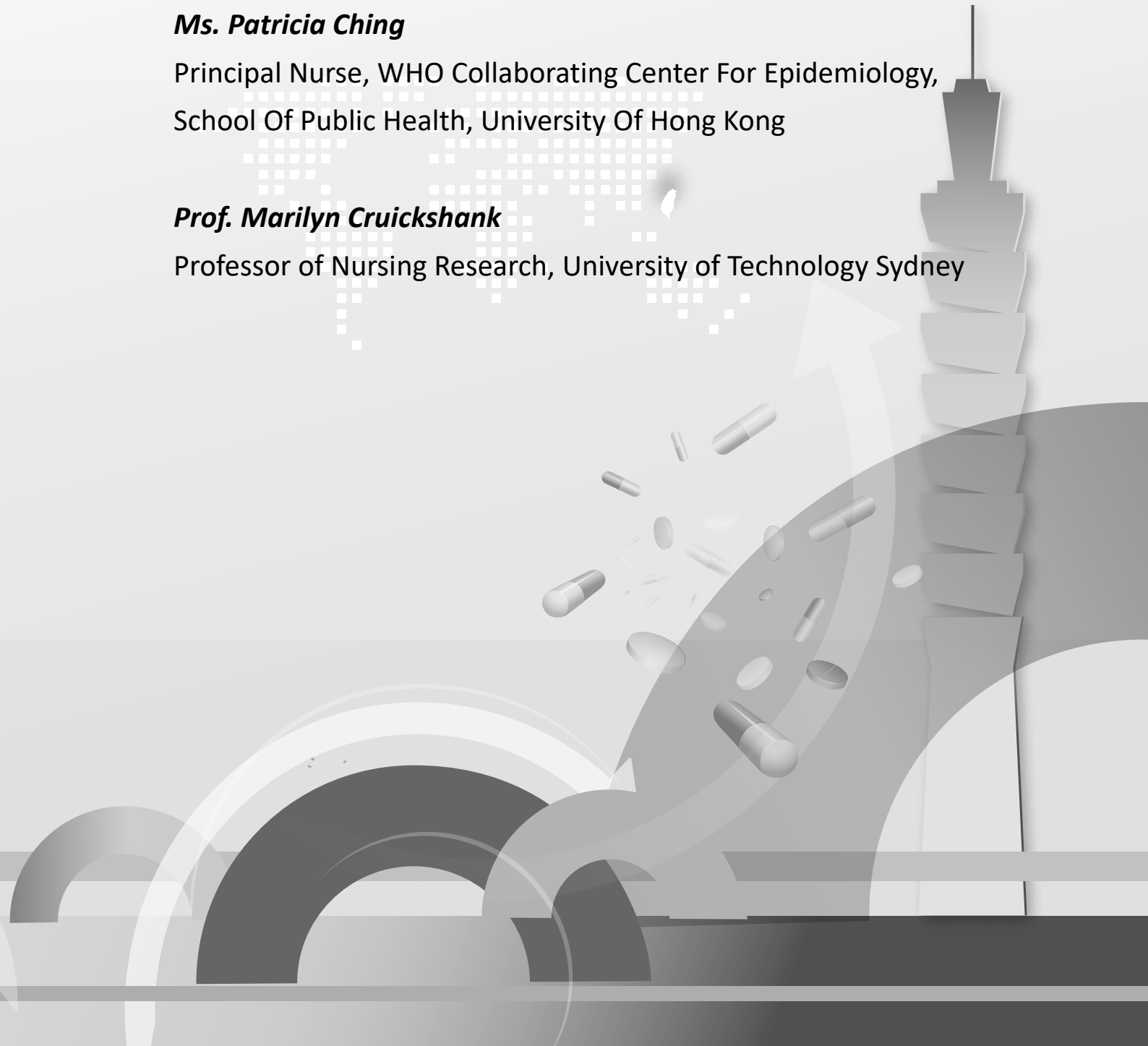
Professor, Department of Infection Control Science, Juntendo University

Ms. Patricia Ching

Principal Nurse, WHO Collaborating Center For Epidemiology, School Of Public Health, University Of Hong Kong

Prof. Marilyn Cruickshank

Professor of Nursing Research, University of Technology Sydney



Prof. Satoshi Hori

Position: Professor

Department/organization: Department of Infection Control Science, Juntendo University

Economy: Japan

Biography

Satoshi HORI gained his BS and MD from Juntendo University in 1991, PhD in 1994, DipHIC in 2001, and OHP in 2008. He has been appointed as the Professor of Infection Control Science and Medical Education in Juntendo Graduate School and the Director of Infection Control in 6 Juntendo University Hospitals.

He is a former council member of the Japanese Society for Infection Prevention and Control (JSIPC), and developed the guidelines of controlling influenza A H1N1 in hospitals (2009) and the guidance of controlling multi-drug resistant Gram negative organisms in hospital (2011). In 2011, He was awarded as the “Lobury Lecture” in the Healthcare Infection Society (UK), and as the “Best Article of the Tear” in the JSIPC.

He has investigated facility management and coordination in healthcare facilities and has been involved in many health building constructions. “Technical Award in building facilities” was granted by the Society of Heating, Air-Conditioning and Sanitary Engineering of Japan in 2018.

He is also editorial boards in the Lancet Infectious Diseases.

Speech Abstract

Ten Years Improvement in Infection Control Practice and Antimicrobial Optimization in The 29 Private University Hospitals in Japan

The main focus on AMR had been multidrug resistant GPC infections from mid-1980s. Since the huge outbreak of Multidrug resistant *Acinetobacter baumannii* (27 out of 46 MDRA positive patients died in 12 months) had occurred in one of a famous private university hospital in Tokyo in 2010, Japanese Association of Private Medical School (JAPMS) had launched the nationwide infection control network, called 'The Council for Infection Control (CIC)' in the same year.

The main activities are as follows; 1) an infection control practice cross-round between a pair of university hospitals using newly developed infection control audit tools for both practice and environment: 2) several common quality indicators (Qis) related with hand hygiene, optimal antimicrobial prescription, and antimicrobial resistance had been set, and each university hospital has tried to improve to the equivalent of the 'bench mark level': 3) several AMR data were referred as outcome indicators for those activities. Each achievement had been confirmed in the annual meeting of CIC.

After 9 years activities, mean alcohol-based hand rub consumption in hospitals has increased to 22.15 L/1,000 patient-days. The proportion of MRSA in *Staphylococcus aureus* blood steam isolates slightly declined from 43.1 to 41.0%. The proportion of MRSA with MIC level of vancomycin was 4 and more, decreased from 0.23 to 0.00%. In Gram negative bacilli, the proportions of carbapenem resistance were slightly decreased from 14.1 to 13.62% in *Pseudomonas aeruginosa*, and from 2.51% to 0.89% in *Acinetobacter spp*.. The proportion of Extended spectrum beta-lactamase producers increased from 16.60 to 23.10% in *Escherichia coli*, and from 6.55 to 6.86% in *Klebsiella pneumoniae*.

Although the proportions of resistant isolates have not been significantly improved, the number of infection cases which were difficult to be treated, such as MDRA an MRSA with vancomycin MIC >4 may decreased. In recent years, the proportion of ESBL/carbapenemase producers in the community is increasing. The AMR movement should be encouraged both in the hospitals and the community.

Ms. Patricia Ching

Position: Principal Nurse

Department/organization: WHO Collaborating Center for Epidemiology, School Of Public Health, University of Hong Kong

Economy: Hong Kong, China

Educational Background

- Diploma of Nursing Administration (1989 at the Hong Kong Polytechnic).
- Certified Practitioner of Healthcare Quality (CPHQ) since 1997
- Honorary Fellow Member in Infection Control, conferred by the Hong Kong Academy of Nursing, May 2018

Professional Career

- Principal Nurse of WHO Collaborating Centre for Infectious Disease Epidemiology and Control, The University of Hong Kong
- Senior Nurse, WHO Collaborating Centre Hospital Authority Hong Kong for infection control, outbreak, education and research. (2010-2012)
- Senior Nurse adviser, Infection Control, Hong Kong Baptist Hospital (2012 till present)
- Senior Nurse adviser, Infection Control, Hong Kong Evangel Hospital (2017 February till present)
- Nurse consultant, Accreditation, Hong Kong University Shenzhen Hospital, Shenzhen, China.

Publications

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Speech Abstract

Strategies to Prevent and Control AMR Infection in Hong Kong

The resistance profiles of multiple drug resistant organisms (MDROs) have been closely monitored in public hospitals under the Hospital Authority in Hong Kong. Among the concerned MDROs, Gram positive organisms include methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE). Gram negative organisms include extended spectrum beta-lactamase producing *Enterobacteriaceae* (ESBL-E) and the WHO top priority organisms of carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA). There are a total of 53 hospitals in Hong Kong, 80% (n=42) are public while 20% (n=11) are private hospitals. The private hospital are equipped with ample of single rooms and therefore pledged to be MDRO free. However isolation rooms in the public hospitals are lacking and therefore controlling strategies require prioritization. As MRSA and ESBL are already endemic and with insufficient single rooms thus patients are cared in general ward with standard precautions emphasizing hand hygiene compliance and dedicated care equipment such as BP cuff and stethoscopes. Patients infected or colonized with VRE, CRE, CRAB and CRPA are cared in single rooms and implementing contact precautions. When upsurge of new cases or outbreaks occurs, patients with similar organisms will be cohorted in a multiple bedded room or cubicle applying contact precautions. Active surveillance screening is only done for identifying VRE and CRE, while others are screened when there is clustering or outbreaks. Environmental hygiene and cleaning is presently improved as a strategy for preventing the spread of MDRO. Disposable cleaning clothes impregnated with 2-in-one disinfectant detergent are used for cleaning and disinfection of the patients' environment daily and also terminally after discharge. The focus is the high touch areas such as bed rails, bed tables, door handle , switches etc that are usually contaminated by healthcare workers' hand. In time of outbreak, new room non-touch room disinfection machines with vaporized hydrogen peroxide are used to terminate hospital outbreaks. The strategies for controlling MDRO in Hong Kong are: 1. Prioritize MDRO of significance using search and destroy approaches. 2. Cohort of same MDRO when upsurge of cases and outbreak. 3. Improve on environmental cleaning and disinfection using disposable wipes. The strategies has been proven effective during the VRE outbreak in Hong Kong in 2013-2014.

Strategies for Preventing Healthcare-Associated MDRO infections in Hong Kong

PTY Ching

WHO CC

Hong Kong

Health Facts of Hong Kong

2017 Edition

Health Facilities (End 2016)	
Number of Public Hospitals and Institutions under Hospital Authority	42
Number of Private Hospitals	11
Number of Nursing Homes	63
Number of Hospitals under Correctional Institutions	21
Number of Hospital Beds in Hospitals in Hospital Authority	28 126
Number of Hospital Beds in Private Hospitals	4 226
Number of Hospital Beds in Nursing Homes	5 858
Number of Hospital Beds in Correctional Institutions	880

Organization chart of the Centre for Health Protection

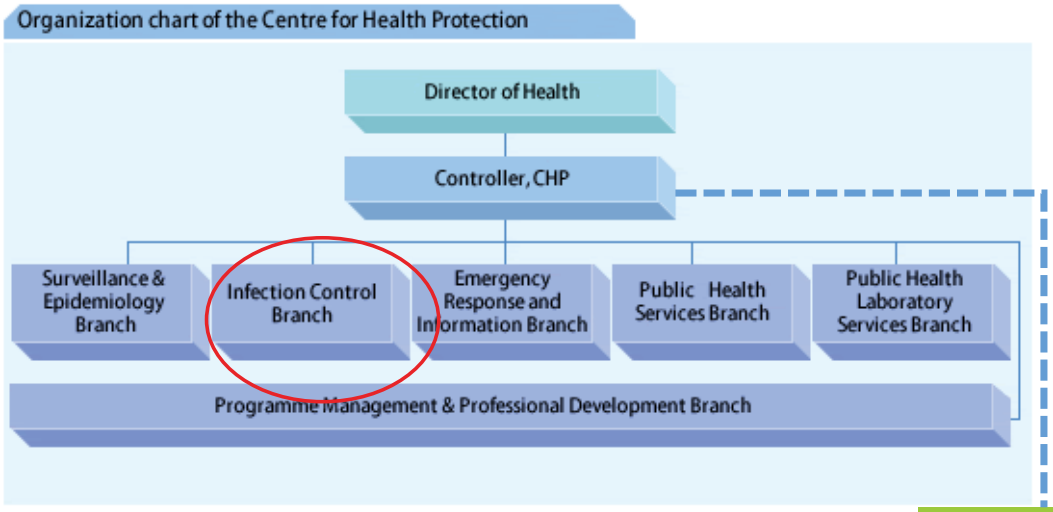


Table 1 - Prevalence of infections.

Prevalence	Overall Infection % (95% C.I.)	CAI % (95% C.I.)	HAI % (95% C.I.)	OHAI % (95% C.I.)
2010	15.0 (14.5-15.5)	11.9 (11.5-12.4)	2.7 (2.5-2.9)	0.5 (0.4-0.6)
2007	15.2 (14.7-15.7)	11.4 (11.0-11.8)	3.2 (2.9-3.4)	0.8 (0.7-0.9)

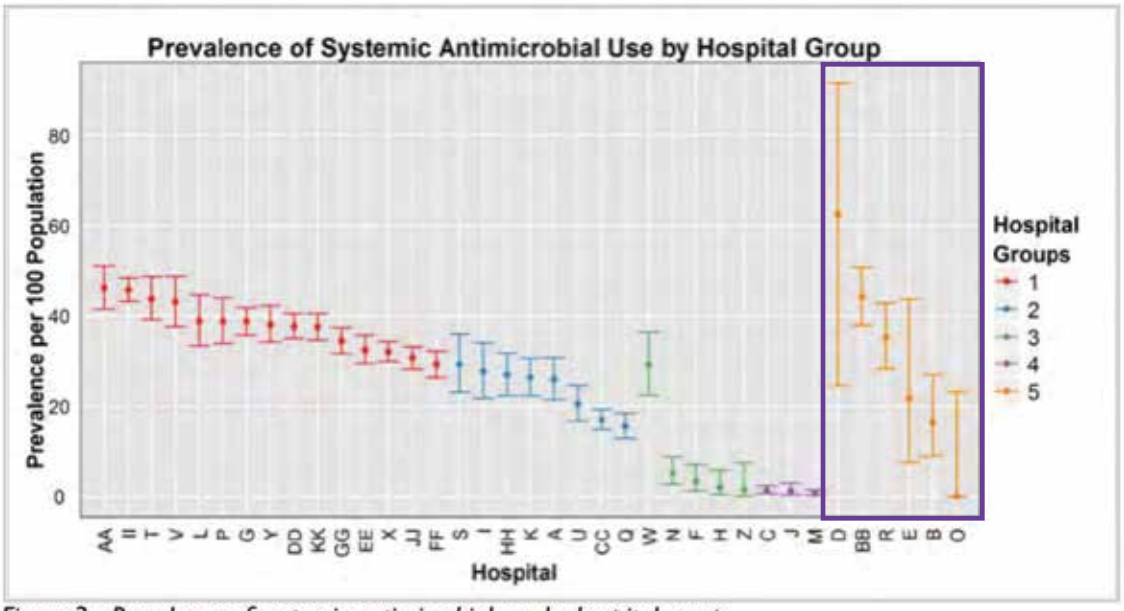


Figure 3 - Prevalence of systemic antimicrobial use by hospital group.

The most common systemic antimicrobials used were **augmentin (11.8%)**, followed by **cefuroxime (2.7%)** and **levofloxacin (2.4%)**. The pattern was similar to 2007. The overall prevalence of systemic antimicrobial use was **higher in 2010** compared to 2007 (26.6%; 95% C.I.: 26.0%-27.2%)

Group 1 – general acute hospitals
Group 2 – hospitals with mixture of acute/ non-acute beds;
Group 3 – hospitals with non-acute/infirmary beds
Group 4 – psychiatric hospitals
Group 5 – acute hospitals of special nature.

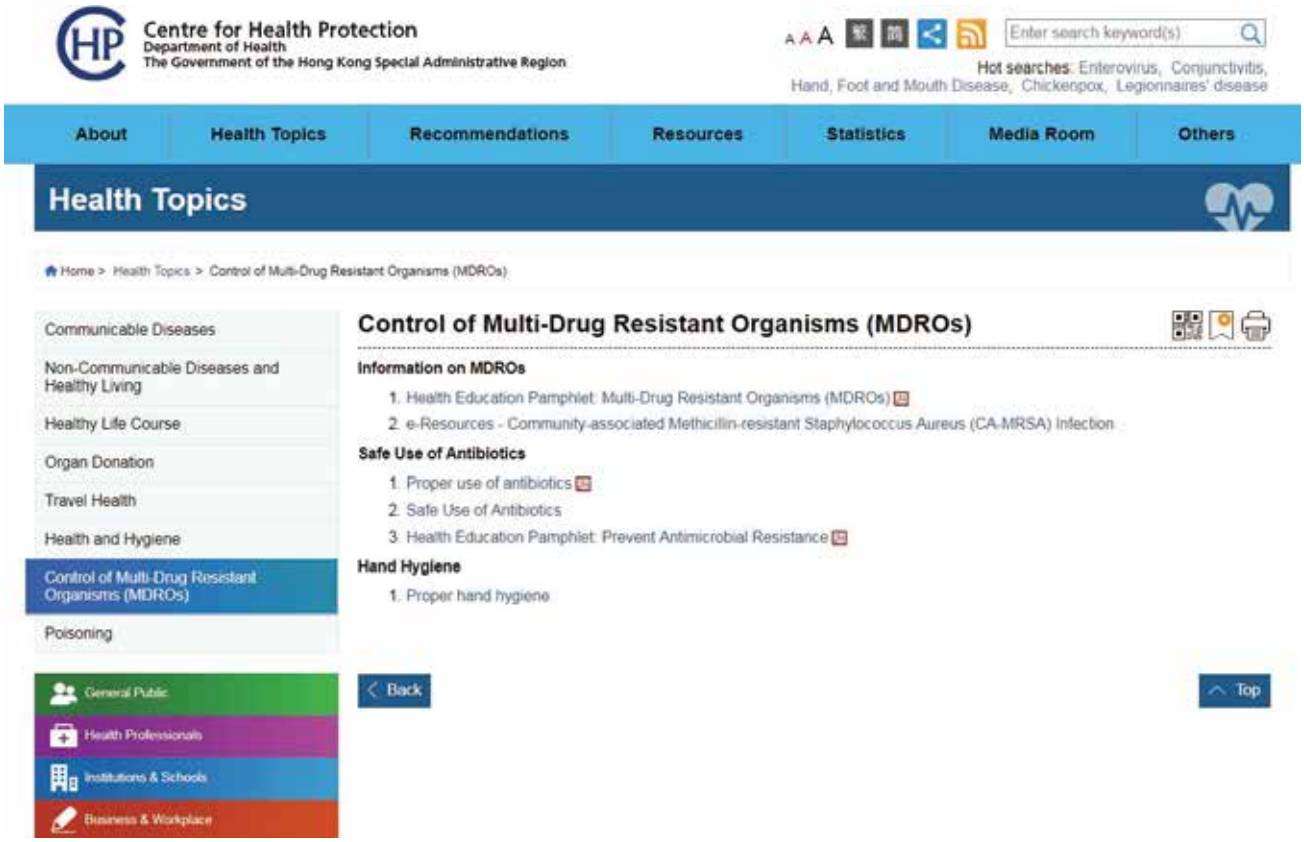
Infection Control Challenges and Opportunities

IN

CONTROLLING OF MDRO

Challenges and Opportunities

- Prioritize MDRO
- Modify Isolation Facilities
- Improve Environmental Cleaning



MDRO in HA hospitals Hong Kong

		2012	2013	2014	2015	Change
MRSA / all S. aureus		43.6%	46.3%	45.7%	46.1%	→
MRSA BSI *per 1,000 acute bed days*	**Overall**	0.138	0.146	0.143	0.146	→
	≥ 2 days of admission	0.059	0.062	0.059	0.057	→
VRSA		0%	0%	0%	0%	→
VRE		0.34%	1.26%	0.74%	0.25%	↘
ESBL producing Enterobacteriaceae (*E.coli* and *Klebsiella* spp. only)		24.3%	23.9%	23.3%	23.2%	→
CRE/CPE Carbapenemase producing Enterobactericeae (E.coli & Klebs total isolates)		36	33	108 (105,993)	132 (110,858)	↑
MDRA		10.4%	18.6%	24.9%	15.9%	↘
MRPA		0.07%	0.09%	0.06%	0.02%	↘

MRPA=concomitant R to Imipenem, Ceftazidime. Amikacin and Ciprofloxacin
MDRA= concomitant R to Fluoroquinolones, Aminoglycosides, Cephalosporins and BL/BLase inhibitor combinations

MDRO in HA hospitals

	2014	2015	2016	2017	Change
MRSA / all S. aureus	**45.7%**	**46.1%**	**43.5%**	**43.1%**	↘
MRSA BSI *per 1,000 acute bed days*	**0.143**	**0.146**	**0.158**	**0.144**	→
VRSA	**0%**	**0%**	**0%**	**0%**	none
VRE	**0.74%**	**0.25%**	**0.18%**	**0.15%**	↘
ESBL producing Enterobacteriaceae (*E.coli* and *Klebsiella* spp. only)	**23.3%**	**23.2%**	**22.4%**	**22.0%**	↘
CPE Carbapenemase producing Enterobacteriaceae (E.coli & Klebs total isolates)	**0.10%**	**0.12%**	**0.30%**	**0.40%**	↑
MDRA	**24.9%**	**15.9%**	**11.7%**	**8.6%**	↘
MRPA	**0.06%**	**0.02%**	**0.02%**	**0.06%**	→

MRPA=concomitant R to Imipenem, Ceftazidime. Amikacin and Ciprofloxacin
MDRA= concomitant R to Fluoroquinolones, Aminoglycosides, Cephalosporins and BL/BLase inhibitor combinations

Year		2011	2012	2013	2014	2015	2016	2017
No of new cases		19	36	33	108	134	340	473
Imported case		10 (53%)	27 (75%)	26 (79%)	48 (44%)	41 (31%)	79 (23%)	127 (27%)
Imported from: Hospitalization history outside HK (Since 1 October 2016, the criteria has been extended from 6 months to 12 months)		China 9 USA 1	China 23 Thailand 2 Chinese Taipei 1 Burma 1	China 16 India 4 Pakistan 2 Indonesia 1 Cambodia 1 Korea 1 Thailand 1	China 42 India 4 Vietnam 1 Germany 1	China 31 India 6 Nepal 3 Thailand 1	China 63 India 7 Nepal 2 Vietnam 2 Pakistan 2 Indonesia 1 Bail 1 Cambodia 1	China 101 India 8 Thailand 5 Vietnam 3 America 1 Bangladesh 1 Cambodia 1 Nepal 1 Pakistan 1 Singapore/Kuala lumpur 1 Spain 1 Chinese Taipei 1 UK/India 1 Ukraine 1
Type of specimen	Clinical specimen	9 (47%)	13 (36%)	3 (9%)	11 (11%)	21* (15%)	45 (13%)	46 (10%)
	Screening	10 (53%)	23 (64%)	30 (91%)	97 (89%)	114* (85%)	295 (87%)	427 (90%)

Data Source: Hospitals reported to CICO office **1 patient had positive results in both clinical and screening specimens*

CPE Statistic

Year		2011	2012	2013	2014	2015	2016	2017 (1Q)	2017 (2Q)
No of new cases		19	36	33	108	134	330	96	85
Imported case		10 (52.6%)	27 (75%)	26 (78.79%)	48 (44%)	41 (30.6%)	79 (58.6%)	15 (15.8%)	31 (36.4%)
Imported from: Hospitalization history outside HK (Since 1 October 2016, the criteria has been extended from 6 months to 12 months)		China 9 USA 1	China 23 Thailand 2 Chinese Taipei 1 Burma 1	China 16 India 4 Pakistan 2 Indonesia 1 Cambodia 1 Korea 1 Thailand 1	China 42 India 4 Vietnam 1 Germany 1	China 31 India 6 Nepal 3 Thailand 1	China 63 India 7 Nepal 3 Vietnam 2 Pakistan 2 Indonesia 1 Bail 1 Cambodia 1	China 11 Thailand 2 India 1 Bangladesh 1	China 24 Thailand 2 India 2 UK & India 1 Spain 1 Ukraine 1
Type of specimen	Clinical specimen Sterile	1 bile	0	0	2 (1 blood, 1 bile)	1 (peritoneal swab)	6 (3 blood, 2 bile, 1 hydrosalpinx asp.)	0	1 blood
	Clinical specimen Non sterile	8 (3 urine, 4 sputum, 1 pus swab)	13 (8 urine, 3 sputum, 2 wound)	3 (MSU, CSU, hand abscess wall tissue)	9 (5 CSU, 2 sputum/ETA, 1 thigh tissue, 1 knee wound)	20* (10 urine, 2 sputum, 5 wound, 1 tissue, 1 peritoneal dialysis fluid, 1 pus swab)	39 (26 urine, 8 TA/ETA/Sputum, 1 tubal drain fluid, 4 wound)	8 (4 urine, 1 sputum, 1 stool, 1 peritoneal dialysis fluid, 1 IV Catheter)	9 (7 urine, 2 ETA/Sputum)
	Screening	10 (52.6%)	23 (63.9%)	30 (90.9%)	97 (89%)	114* (85.07%)	295# (86.8%)	88 (91.7%)	75 (88.2%)
PCR result	NDM	2	10	18	48	101	190	47	60
	KPC	4	7	7	36	19	52	34	9
	IMI	1	1	1	1	0	5	1	2
	IMP	10	14	4	11	9	67	8	7
	VIM	1	1	0	0	1	0	0	0
	OXA	0	1	0	3	1	21	6	5
	NDM+IMP	1	0	1	1	0	0	0	0
	NDM+OXA	0	2	0	5	1	3	0	2
	KPC+IMP	0	0	2	3	2	0	0	0
	NDM + IMI	0	0	0	0	0	1	0	0
	OXA + IMP	0	0	0	0	0	1	0	0
Age	0	2	3	1	1	0	8	2	2
	1-4	1	2	2	0	1	4	2	3
	5-14	0	0	2	1	2	2	0	1
	15-24	0	0	0	3	4	4	3	4
	25-34	1	1	3	3	7	11	6	7
	35-44	0	2	1	9	12	26	8	8
	45-54	1	1	4	11	18	32	4	8
	55-64	3	8	4	23	24	53	10	7
	65-80	7	9	8	40	34	106	26	24
	>=81	4	8	8	17	32	94	35	21

Data Source: Hospitals reported to CICO office **1 patient had positive results in both clinical and screening specimens*

To show the PCR typing

1. NDM
2. KPC
3. IMI

"Usually accepted that eradication would be unlikely in the highly endemic setting"

< 20 cases	100% elimination
20-39 cases	79% elimination
>39 cases	10% elimination

Marshall et al, JHI 2004:56:253
Boyce JM: ICHE 1991:12:36

Still we should try to lower the incidence…

Overcrowding in Hong Kong Public Hospital

Influenza Winter Peak 2018
occupancy of 120-150% - camp beds

Search and Destroy for Low prevalent MDRO

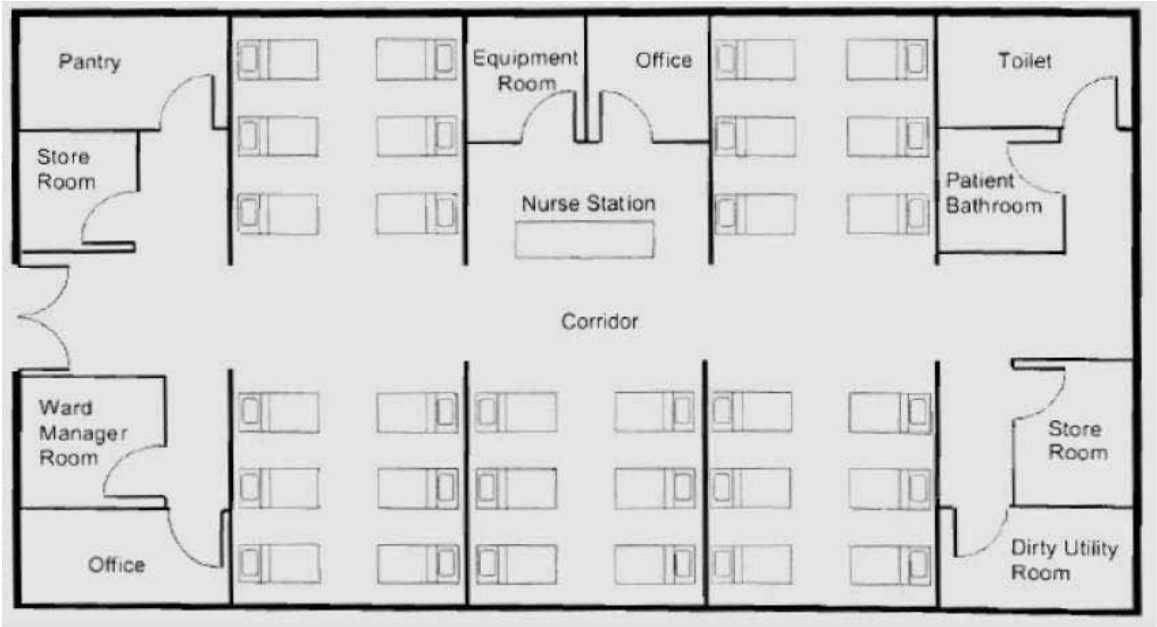
Isolation Policies in Hospital Authority – Hong Kong

IC tactics	MRSA	VISA/ VRSA	VRE	ESBL	CRE	CRAB/ MDRA	CRPA/ MRPA
Single room	No	Yes	Yes	No	Yes	If available (MDRA)	Yes (MRPA-XDR)
PPE, HH, EnH, Deq	HH	Yes	Yes	HH	Yes	Yes	Yes
CMS alert	No	Yes	Yes	No	Yes	MDRA	Yes
Discharge to RCHE	Allowed	2 –ve culture	2 –ve culture	Allowed	2 –ve culture	Allowed	MRPA: 2 –ve culture
Send isolate to reference lab	No	Yes	Yes	No	Yes	No	No
Notify Dept Health	No	Yes	Yes	No	No	No	MRPA: Yes

Isolation for ALL MDRO in Private Hospitals

Challenges in isolation facilities

- Not enough single room isolation
- Increase manpower when patients are nursed in single room



Layout of general patient ward

Resolution: Single cohort (Specific MDRO patients)
Group cohort (patient with same diagnosis)

- Single cohort ante room - Existing site constraint issue

Resolution: Shared ante room with interlocking doors

MDRO in HA hospitals

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MRSA BSI *per 1,000 acute bed days*	0.143	0.146	0.158	0.144	→
VRSA	0%	0%	0%	0%	none
VRE	0.74%	0.25%	0.18%	0.15%	↘
ESBL producing Enterobacteriaceae (*E.coli* and *Klebsiella* spp. only)	23.3%	23.2%	22.4%	22.0%	↘
CPE Carbapenemase producing Enterobacteriaceae (E.coli & Klebs total isolates)	0.10%	0.12%	0.30%	0.40%	↑
MDRA	24.9%	15.9%	11.7%	8.6%	↘
MRPA	0.06%	0.02%	0.02%	0.06%	→

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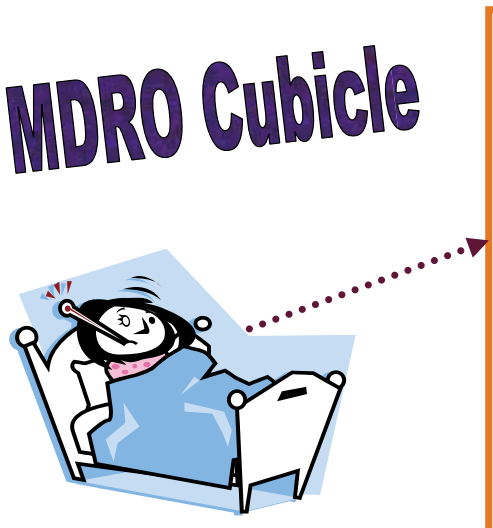
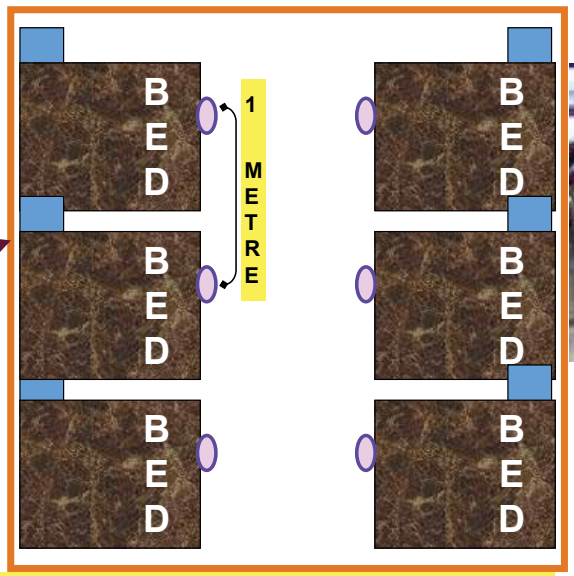
Isolation Policies in Hospital Authority – Hong Kong

IC tactics	MRSA	VISA/ VRSA	VRE	ESBL	CRE	CRAB/ MDRA	CRPA/ MRPA
Single room	No	Yes	Yes	No	Yes	If available (MDRA)	Yes (MRPA-XDR)
PPE, HH, EnH, Deq	HH	Yes	Yes	HH	Yes	Yes	Yes
CMS alert	No	Yes	Yes	No	Yes	MDRA	Yes
Discharge to RCHE	Allowed	2 –ve culture	2 –ve culture	Allowed	2 –ve culture	Allowed	MRPA: 2 –ve culture
Send isolate to reference lab	No	Yes	Yes	No	Yes	No	No
Notify Dept Health	No	Yes	Yes	No	No	No	MRPA: Yes





1.Beds separated by 1 m apart
2.Sufficient supply of PPEs
3.Alcohol hand rub at each bedside
4.Individual patient care items –BP cuff, stet
5.Cohort same MDRO in one room or cubicle

CORRIDOR
TO EXIT

Alcohol hand rub

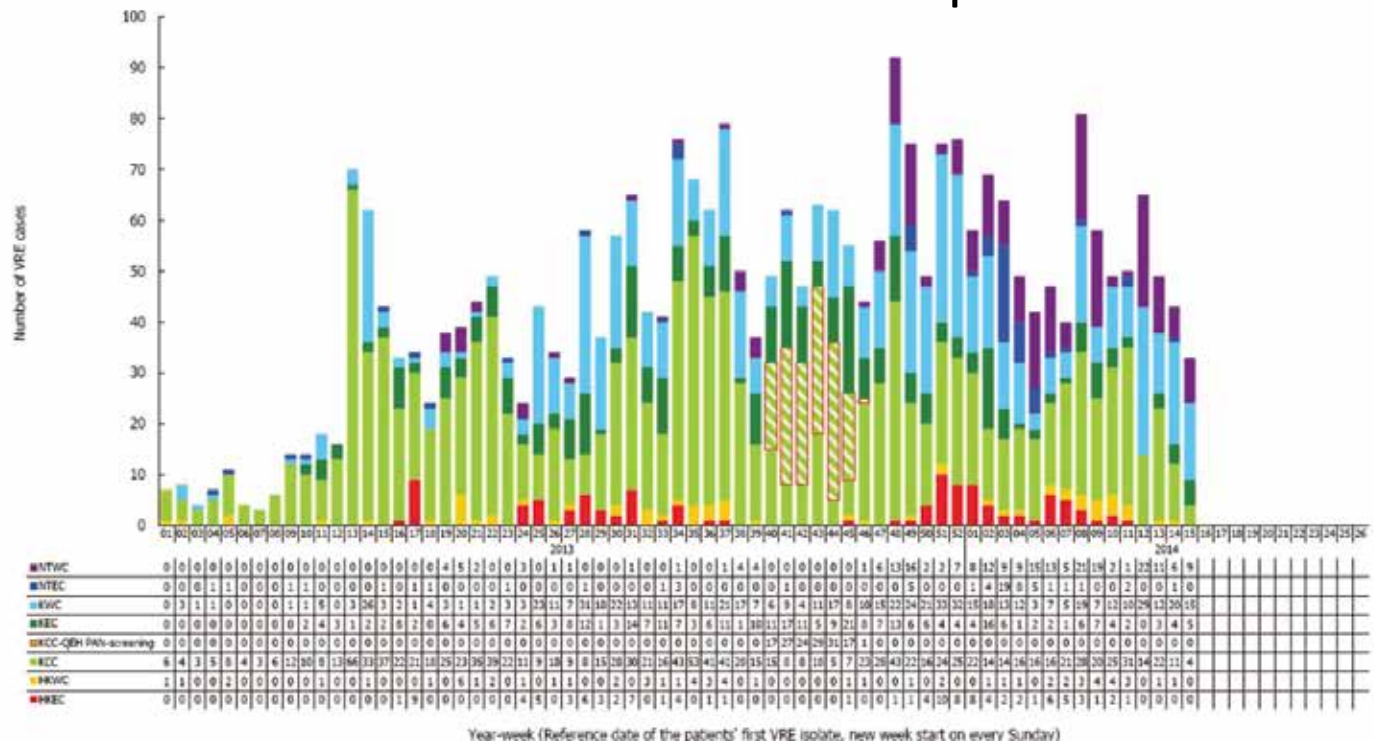
Nurses station is a clean zone. Medical charts stay here. No gowns or gloves allowed. Mask not really needed if not going in to see patients.

Challenges and Opportunities

Environmental cleaning

Using reusable wash clothes -spreading MDRO and OSH concern

New VRE cases in HA hospitals



Cleansing of the Environment

HA guideline Hong Kong	CDC	WHO	AUS	NHS	Canada
when the environment is visibly soiled or contaminated;	✓	✓	✓	✓	✓
General housekeeping surfaces - according to housekeeping cleaning schedule			✓	✓	✓
HTA in General clinical area - cleaned with detergent and water at least once daily	more frequent schedule	✓	✓	✓	✓
HTA in Contact Precautions - cleaned and disinfected at least twice daily.	more frequent schedule	At least daily	(Base on Risk level, e.g. Outbreak)	(Base on Risk level, e.g. ICU, AED)	(Base on Risk level, e.g. VRE, C. diff)

Meeting the challenge of VRE outbreak

Improvement on environmental cleaning

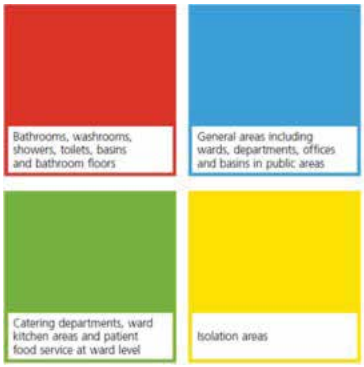
From reusable wash clothes → disposable jay clothes

From disposable jay clothes → single use disinfectant wipes

Plus non-touch environmental disinfection machines

Manual Cleaning :

- Standardize cleaning protocols in clinical areas
- Designated team for EH
- Training
- Onsite coaching and return demonstration regular monitoring of cleanliness
- Use of dedicated equipment
- Disposable wipe
- 2:1 disinfectants



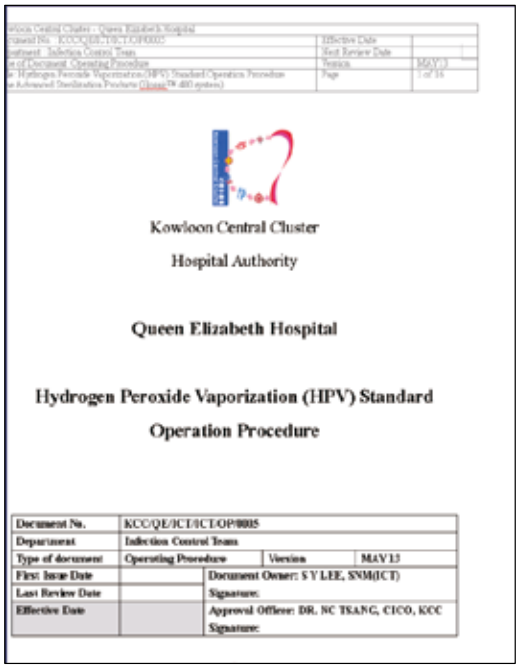
Disposable Wipes

Wipes

Cotton, Disposable, Microfiber, Nonwoven Spunlace

Wipe should have sufficient wetness to achieve the disinfectant contact time. Discontinue use of a disposable wipe if it no longer leaves the surface visibly wet for ≥ 1min

New technology for the control of MDROs



Kowloon Central Cluster

Hospital Authority

Queen Elizabeth Hospital

Hydrogen Peroxide Vaporization (HPV) Standard Operation Procedure

Document No.	KCC/QE/ICT/ICTOP/0005		
Department	Infection Control Team		
Type of document	Operating Procedure	Version	MAY13
First Issue Date		Document Owner: S Y LEE, SNM(ICT)	
Last Review Date		Signature:	
Effective Date		Approval Officer: DR. NC TSANG, CICO, KCC Signature:	

MDRO in HA hospitals

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Turning Challenges to Opportunities

- Difficulties in controlling MDRO
  - Prioritize MDRO for contact precautions
  - Emerging MDRO implement “search and destroy”
- Coping with insufficient isolation facilities
  - Prioritize emerging MDRO for contact precautions
  - Cohorting SAME mdro with special droplet precautions
- Ineffective environmental cleaning
  - Convert old practice to most up-to-date practices
  - Changed to disposable wipes and non-touch environment disinfection machine

Thank You!!!

Prof. Marilyn Cruickshank

Position: Professor of Nursing Research

Department/organization: University of Technology Sydney

Economy: Australia

Educational Background

- Registered Nurse, Royal Alexandra Hospital for Children
- Neurological and Neurosurgical Nursing, Royal Prince Alfred Hospital
- Paediatric Intensive Care Nursing, NSW College of Nursing
- Emotional & Behavioural Problems of Childhood, NSW Institute of Psychiatry
- Paediatric HIV Nursing, Newark Children's Hospital New Jersey USA
- Bachelor of Arts, University of New England Australia
- Bachelor of Arts Honours - Class I, University of New England Australia
- PhD, University of Technology Sydney

Professional Career

- Director, Australian national healthcare associated infection program Chair, Australian Antimicrobial Resistance Standing Committee
- Designer and co-author, National Surveillance and Reporting of Antimicrobial Resistance and Antibiotic Usage for Human Health in Australia
- Co-editor, Antimicrobial stewardship in Australian hospitals
- Appointed Professor Faculty, Nursing and Midwifery, Griffith University, in recognition of professional activities in healthcare associated infection and antimicrobial resistance
- Appointed Professor of Nursing (Research), University of Technology Sydney to lead research initiatives with the Sydney Children's Hospitals Network.
- President, Australasian College of Infection Prevention and Control

Publications

- Grayson ML, Stewardson AJ, Russo PL, Ryan KE, Olsen KL, Havers SM, Greig S, Cruickshank M. The Australian National Hand Hygiene Initiative after 8 years - a successful potential blueprint for sustained national action. The Lancet Infectious Diseases 2018
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- Stewardson AJ, Stuart RL, Marshall C, Cruickshank M and Grayson ML. More doctor-patient contact is not the only explanation for lower hand-hygiene compliance in Australian emergency departments. Infection Control and Hospital Epidemiology,. 2017; 38: 502-4.
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Speech Abstract

Carrot or Stick?
Building Capacity in ASP and Infection Control Through Quality Accreditation

Building and operating robust systems for the surveillance and reporting of antimicrobial resistance and antibiotic usage requires comprehensive recognition and integration of the relevant technical, scientific, governance, policy, financial and jurisdictional levers and constraints. A number of strategies have been demonstrated to enhance appropriate use of antibiotics and reduce their use overall. To enhance and increase the potential for sustainability of these strategies – the "carrots", regulation is required – the "stick" is required.

Scientifically, antimicrobial resistance is a complex and important issue; no one action alone will provide an effective response. The situation is exacerbated by the ability of many bacteria to share genetic material and pass on resistance genes, and the inadvertent Antimicrobial stewardship (AMS) is one of the most important and effective interventions in promoting appropriate use. In some countries AMS is maturing in the hospital sector but stewardship strategies need to be developed and enhanced for antimicrobial use in the community, including residential aged care facilities.

AMS refers to coordinated actions designed to promote and increase the appropriate use of antimicrobials and is a key strategy to conserve the effectiveness of antibiotics. In health care settings, AMS programmes have been shown to improve the appropriateness of antibiotic use; reduce institutional rates of resistance, morbidity and mortality; reduce health care costs, including pharmacy costs; and reduce the adverse consequences of antibiotic use, including toxicity.[1]

An example of such regulation is the National Safety and Quality Health Service (NSQHS) Standards introduced 2013 by the Australian governments which form the basis of mandatory accreditation. The NSQHS require every Australian hospital and day procedure service to implement infection prevention and antimicrobial stewardship programs. With the introduction of the Standards, Australia has mandated requirements for infection prevention and control and antimicrobial stewardship in hospitals and day procedure services. The Standards have laid the basis for a significant role in helping to improve the appropriateness of antimicrobial usage

[1] Duguid M, Cruickshank M (eds). Antimicrobial Stewardship in Australian Hospitals. Australian Commission on Safety and Quality in Health Care, Sydney, 2010

in Australian hospitals. Hospital accreditation criteria for AMS in Australia include

- have an AMS program in place
- provide prescribing clinicians with access to current therapeutic guidelines
- undertake monitoring of antimicrobial use and resistance
- take action to improve the effectiveness of AMS

Reducing antimicrobial usage is one element of a comprehensive national approach to preventing and containing the spread of AMR and requires collaboration between experts, regulatory authorities, and producers, and integrated monitoring of the effects of interventions is essential.

Carrot or stick? Building capacity in ASP and infection control through quality accreditation

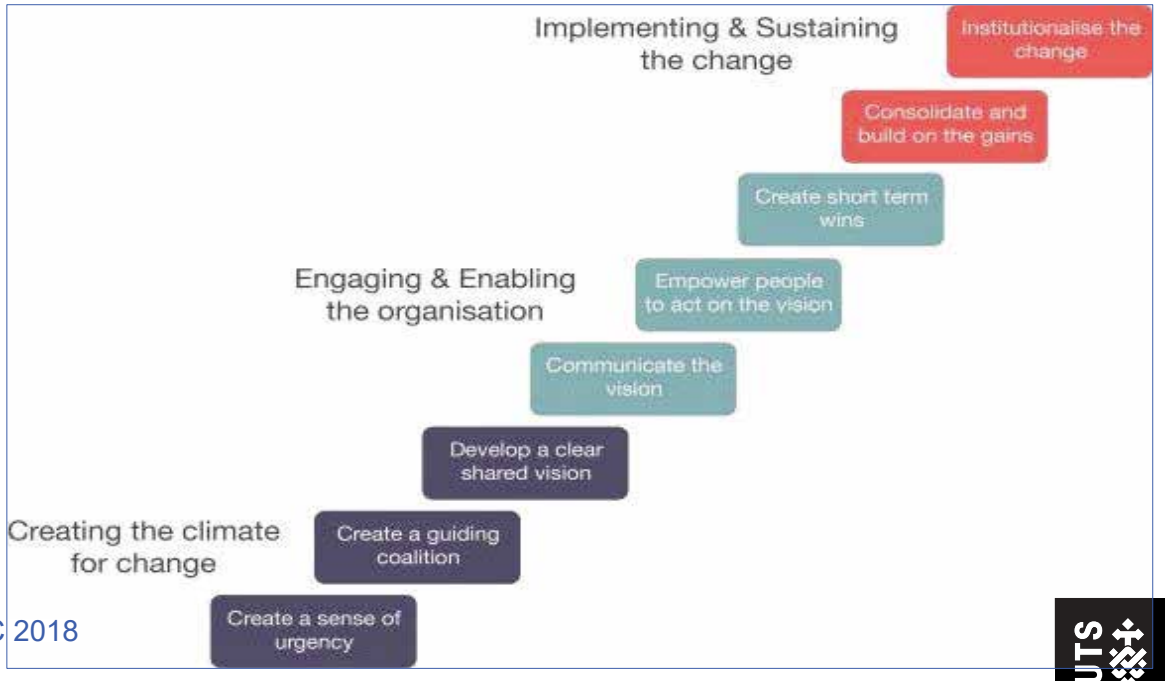
Professor Marilyn Cruickshank
APEC
September 2018

Where to start?

The phrase "**carrot** and **stick**" is a metaphor for the use of a combination of reward and punishment to induce a desired behaviour. It is based on the idea that a cart driver might activate a reluctant horse by dangling a **carrot** in front of it and smacking it on the rear with a **stick**.

The carrots

Kotter's 8-step change model



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urgency

stakeholders

vision

communicating the vision

short term wins

consolidating

institutionalise

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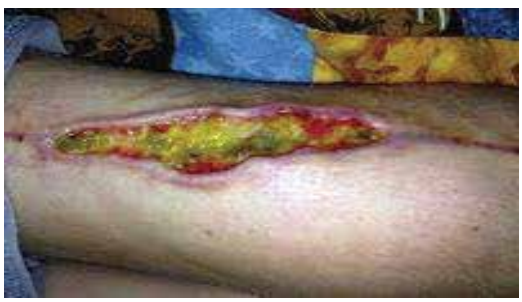
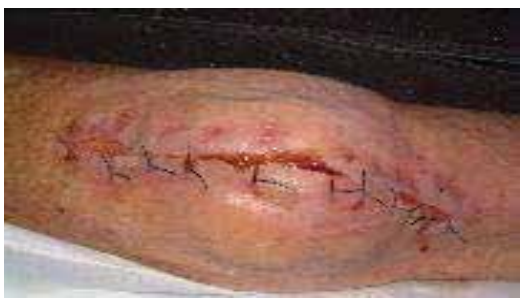
Do HAI matter?

Pain, suffering and possible death for patients

More work for health staff

Increase LOS, costs, available beds etc





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Who is at risk of HAI?

The old

The young

The very sick

Patients who have had surgery

Patients with IV lines

Patients with drains

Patients who are immunocompromised

Patients with central lines, dialysis catheters

Patients with urinary catheters

Patients with increased LOS

Patients with co-morbidities

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Where to start?

Priorities:

Quick wins

Unify professionals – voice, action,

Bring 8 jurisdictions on board – save time and $$$

Standardisation

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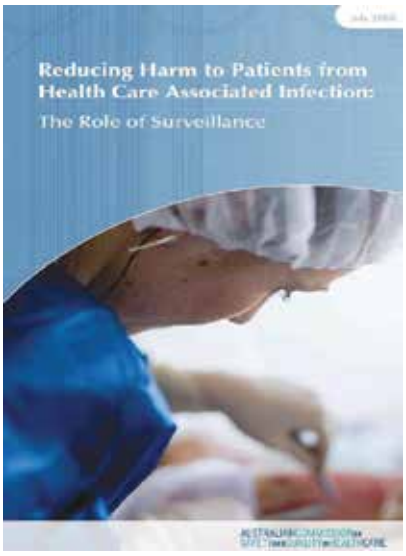
Initial (small) steps in national HAI Surveillance



- 51 co-authors
- (limited) recommendations from experts
- top 3
  - surveillance
  - hand hygiene
  - infection control guidelines

endorsed by health ministers

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Putting good practice into policy and good policy into practice

What should a national program look like?

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Engaging with experts – Implementation Advisory Committee

The committee brought clinical, academic, professional, research and government expertise with geographical representation across Australia:

Think national!!

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National data

Only from large data sets can decisions be made on some HAI measures.

- local and state surveillance data bases do not contain sufficient data to reliably plot trends eg antimicrobial usage
- to inform and update infection control guidelines, national programs
- guide national policy and priorities
- monitor national trends

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AAA Infections Audit Annually,
Additional Isolation Precautions,
Additional Precautions Audit
Aged care infection control practice audits,
air sampling in theatre
all clinical areas.
Antibiotic prophylaxis
BBSE cause & effect
Blood and Body F
Blood fridge,
Care of patient eq
central devices
central IV access
central line
CJD questionnaire
Clinical Audits
Clinical waste & s
Clinical waste ma
Cold chain,
Correct waste disp
customer focus su
Decubitus Ulcers
Drinking water
Education Attenda
Engineering and E
engineering,
Environment,
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Environmental Hy
Environmental sw
environmental/house keeping audit
equipment e.g. IV pumps.
Equipment Reprocessing Annually
Eye Infections and
flash steriliser use in theatres;
flash steriliser,
food handling,
Food safe
food safe program
food services,
Food storage,
Food temperature
Fridge temp record immunisations
Fridge temperatures monitored
Gastroscopes (GESA guidelines),
general infection control audit
glutaraldehyde management
GOR/CSD/

hand hygiene compliance competency
Hand hygiene solution audit by company rep
hand hygiene station audit,
hand washing audit

mortuary audit;
motor vehicle audit,
MRO compliance audits
MRO documentation audits
MRO,
MRSA audits
MRSA documentation
N95/P2 fir checking competency
needle stick body fluid,

in clinical areas annually
PPE knowledge/donning & doffing assessment;
processsing of equipment.
proper disposal of waste
RADIOLOGY,
Rain water (Dialysis),
Rain water (drinking),

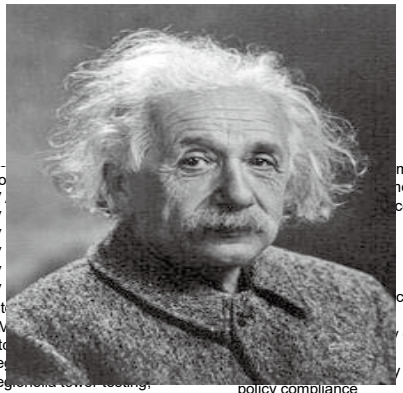
site audit annually
specimen collection
SSI audit,
SSI prophylaxis
staff compliance to uniform i.e. jewellery, hair, nails
staff immunisation audit,
staff knowledge of infection control
standard & additional precautions ,

"Not everything that can be counted counts,

and

not everything that counts can be counted"

Albert Einstein



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of aged care
twice year,

scope cleaning
Sharp disposal
sharps
Sharps and clinical waste management
sharps and sharps containers.
Sharps Audit
sharps bins audits.
sharps compliance,
Sharps container audit
Sharps containers: audit disposal practices and safety
sharps control
Sharps disposal
Sharps information audit
sharps management,
sharps safety & biohazard injuries
sharps safety,

Ward/Department based IC audits (all principles audited),
warm water
Warm water / Legionella
waste
Waste Compliance;
Waste disposal,
Waste management
WASTE,
water testing
Wound Drains

policy compliance
Post Body Fluids Audit annually
PPE audit
PPE Availability Audits 3 monthly,
PPE compliance audits
PPE Compliance.

Legionella water testing of patient/staff use areas legionnaire
H20 testing 3 monthly
linen,
maintenance
mask fit testing annually

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Infections – what are healthcare associated infections (HAI)?

- Infections patients get as the result of health care

CA- Community Associated	HO- Hospital Onset	HACO- Healthcare-Assoc. Community Onset

d1 adm date; d2; d3; d4; d5; d6 d/c date

i.e. 72-96 hrs post adm

Primary category			Codes	
CA	No admission within 365 days	Subclassify	CA	
	Was not admitted from residential care address		CA-OS	Where overseas exposure recorded within previous 6 months
HO		Subclassify	HO-HNE	HNE LHD hospital onset
			HO-nonHNE	Non-HNE LHD hospital onset
HACO	ONE or more of:	Subclassify	HACO-HNE	Specify HNE LHD hospital that was the last prior location
	Admission within 365 days		HACO-nonHNE	Specify non-HNE hospital that was the last prior location
	Residential care resident at time of detection		HACO-OS	Where HACO exposure(s) were in a foreign location without more recent hospital exposure

HNE= Hunter New England Local Health District

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Need for standardisation

National Cumulative Hospital Antibiogram

Standardisation of laboratory reporting

Second National Survey of Clostridium Difficile Infection (CDI)

Antibioti

Antimicr

National

"Flexible standardisation"

Multi Resistant Gram Negative (MRGN) Taskforce

HAI Technical Working Group

National safety and quality health service standards

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Aims for AMS Forum

Snapshot of current state of AMS across Australia

Be inspired by examples of successful/innovative programs

What are the likely barriers to implementing the recommendations?

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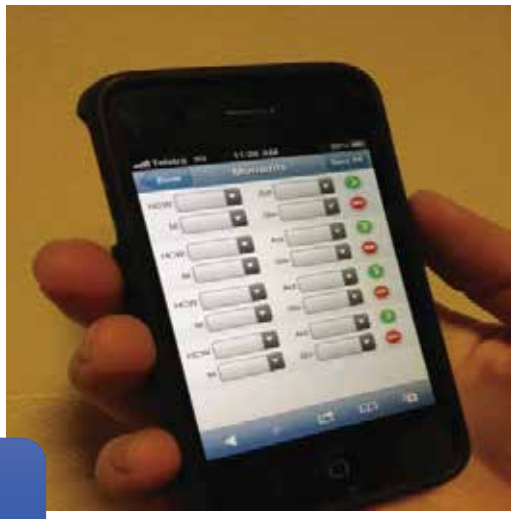
Making change easy - Collection by HHApp

Central HH database

New direct-entry HH compliance App

- i-Phones, other Smartphones
- Benefits:
- Reduces data management time by 50%
- No duplicate data entry and errors
- Potential – WHO, NZ, Singapore



Platform and database - potentially huge

I'm here to help!

The Clinical Care Standard for AMS

Implementation happens at the bedside

Infection Control Guidelines

Australian Guidelines for the Prevention and Control of Infection in Healthcare based on:

- Best available current scientific evidence
- International guidelines (CDC, EPIC II)
- Best practice / expert opinion

Guidelines don't implement themselves

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AMS in different settings


Standard 3: Preventing and Controlling Healthcare Associated Infec

Table 2 provides suggestions for ways in which strategies to support antimicrobial stewardship (AMS) implemented in different settings.

Table 2: Options for implementation of antimicrobial stewardship in different facilities

One size does not fit all

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Rural and regional hospitals

About 1/3 of hospitals in Australia are < 20 beds

Depend on GP visiting medical officers

Lack of access to ID physicians, clinical microbiology, pharmacists or pathology services

Lack of access to education and training

Difficulty in retaining experienced clinicians

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Private hospital sector

> 40% of all hospital care and > 60% of surgery

Limited scope to introduce restrictions, prescribing policies,

No inherent hierarchy in private hospitals – but some influence by peers

Doctors are the “customers”

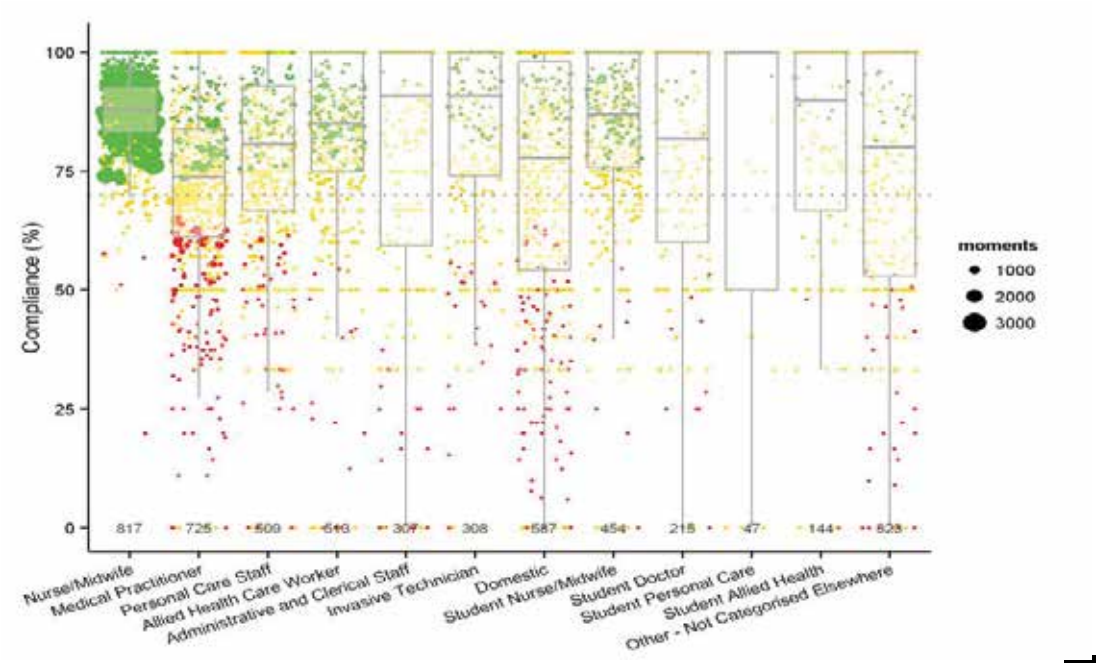
Nurses often follow doctors protocols rigidly

ID physicians involved at patient rather than hospital level

Doctor - Patient

Hospital ≠Patient

Hand Hygiene Performance: by Profession



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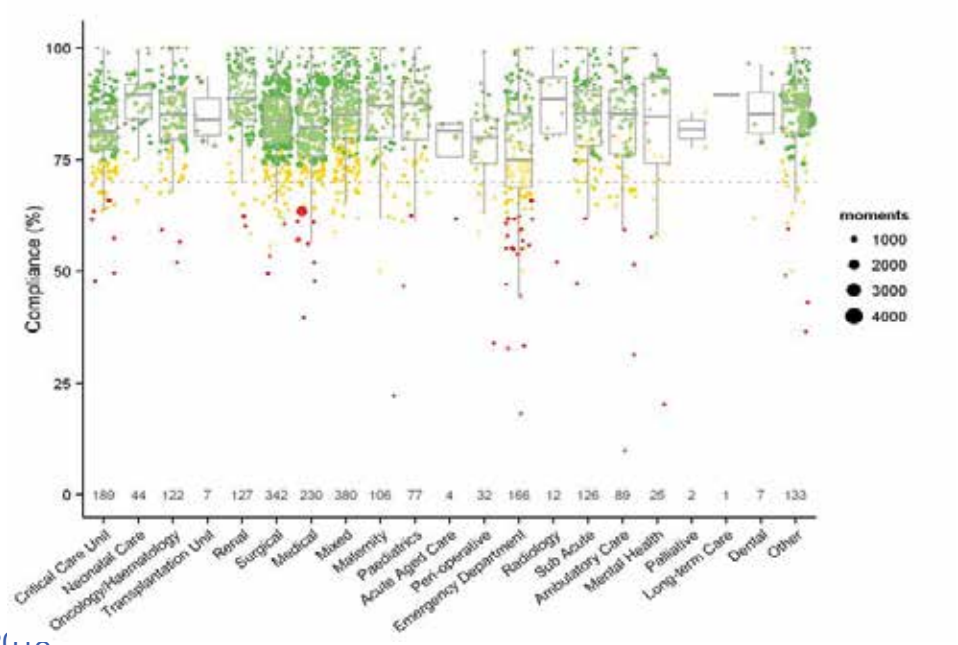
Hand Hygiene Performance: Department Type



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The stick

Priorities for Standard 3

Having an effective governance framework

Identifying what is working well

Knowing your risks and/or gaps

Having systems to gather, review and report evidence

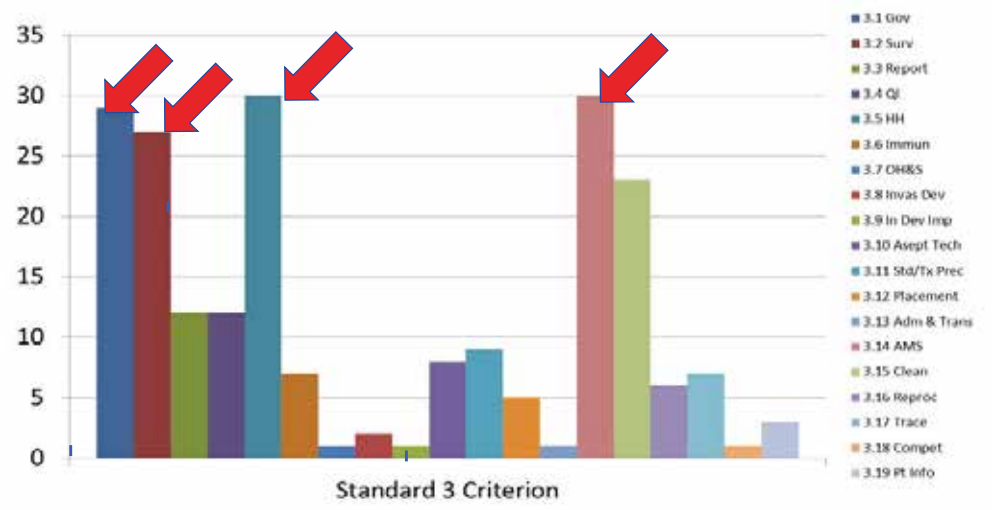
Having a plan to address risks and respond

Aiming for the best (either 0 or 100%)

Demonstrating progress/improvement

Engaging with others in the organisation

Met with Merit
Health service accreditation



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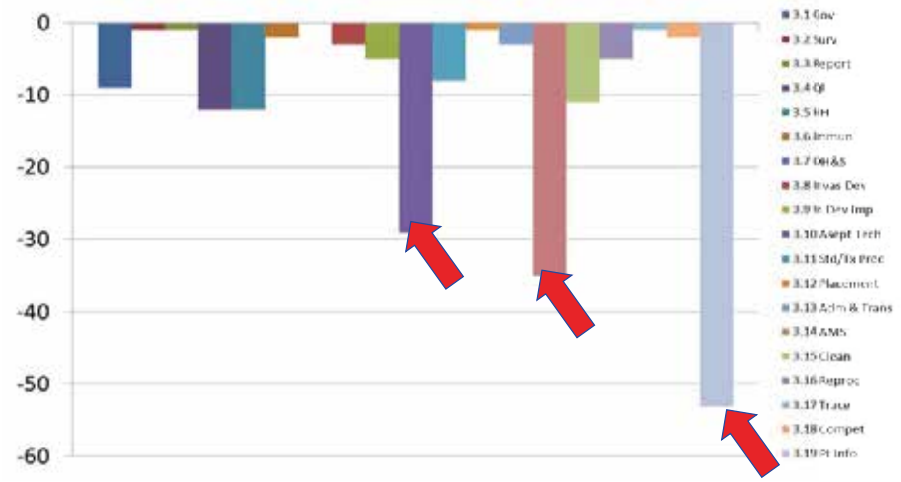
Not Met
Health service accreditation



March-December 2013

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Steps to national roll out

It's wasn't easy!

- involve key stakeholders in design and implementation
- agreed organisational objectives
- use trained personnel to collect and manage data, and provide them with appropriate information technology support
- use definitions of surveillance events that are unambiguous, practical, specific and can be validated
- use reliable and practical methods for detecting events

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Closing Remarks

Dr. Jih-Haw Chou

Director-General, Centers for Disease Control

Dr. Jih-Haw Chou

Position: Director-General

Department/organization: Centers for Disease Control

Economy: Chinese Taipei

Educational Background

- MPH (Environmental Toxicology), University of California at Berkeley
- MPH (Epidemiology), National Taiwan University
- DDS, Taipei Medical College
- LLB, Fu Jen Catholic University

Professional Career

- Deputy Director-General, CDC.
- Health Commissioner, Taipei County Health Department
- Deputy Health Commissioner, Taipei County Health Department
- Director, Div. Research, Planning and Development, Taipei City Health Department
- Branch Chief, National Quarantine Service, Department of Health
- Specialist, Bureau of Communicable Disease Control, Department of Health

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List of Participants

Australia

- Marilyn Cruickshank
Professor of Nursing Research
University of Technology Sydney
marilyn.cruickshank@uts.edu.au

Chile

- Mrs. María Aldunate
Chief of Drug information section
Institute of Public Health
faldunate@ispch.cl

Hong Kong, China

- Miss Patricia Ching
Principal Nurse
WHO Collaborating Center For Epidemiology, School Of Public Health, University Of Hong Kong
chingpty@yahoo.com.hk

- Prof. Wing Hong Seto
Co-Director
WHO Collaborating Centre for Infectious Disease Epidemiology and Control, The University of Hong Kong
whseto@hku.hk

Indonesia

- Dr. Triya Novita Dinihari
Head
Section for early warning,
DG for Diseases Prevention and Control,
Ministry of Health
tndinihari@yahoo.com

- Miss Bunga Dian Kurniati
Pharmacist
National Agency of Drug and Food Control
bunga_dian_k@yahoo.com

Japan

- Prof. Satoshi Hori
Professor
Department of Infection Control Science,
Juntendo University
shori@juntendo.ac.jp

- Dr. Junko Sato
Director
Office of International Cooperation,
Pharmaceuticals and Medical Devices Agency
sato-junko@pmda.go.jp

- Mr. Takahiro Shirakawa
Inspector
National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries
takahiro_shirakaw140@maff.go.jp

- Prof. Kazuhiro Tateda
President
Japanese Association for Infectious Diseases
kazu@med.toho-u.ac.jp

- Miss Yoko Nakata
Health Policy Senior specialist
MSD K.K (Japan)
yoko.nakata@merck.com

Malaysia

- Dr. Noor Amelia Abdrasid
Principal Assistant Director
Medical Development Division, Ministry of Health
dramelia_ar@moh.gov.my

- Dr. Suraya Amir Husin
Senior Principal Assistant Director
Medical Development Division, Ministry of Health
drsurayaamirhusin@gmail.com

- Prof. Victor Lim
Pro Vice-Chancellor
International Medical University
victor_lim@imu.edu.my

Peru

- Mr. Victor Fiestas Solórzano
Infectious Disease Specialist
National Institute Health
vfiestas@ins.gob.pe

- Mr. Luis Fernando Donaires Toscano
Infectious Disease Specialist
National Institute Health
fernandod1225@gmail.com

The Philippines

- Dr. Irene Florentino-Farinas
Medical Officer IV
Department of Health
ayeenfarinasmd@gmail.com

Republic of Korea

- Mr. Damon Ihm
Policy Manager
Merck Sharp & Dohme
damon.ihm@merck.com

- Miss Young Jin Nah
Sr. Market Access Specialist
Merck Sharp & Dohme
young.jin.nah@merck.com

Singapore

- Dr. Claudia Adler
Regional Commercial Lead
MSD Asia Pacific
claudia.adler@merck.com

- Prof. David Chien Boon Lye
Associate Professor
Tan Tock Seng Hospital
david_lye@ttsh.com.sg

- Miss Hui Ling, Esther Ng
Director, Market Access Asia Pacific
MSD International GmbH
esther.ng@merck.com

Switzerland

- Prof. Didier Pittet
Chief Medical Officer, University hospitals of Geneva
didier.pittet@hcuge.ch

Thailand

- Dr. Mintra Lukkana
Veterinarian
National Bureau of Agricultural Commodity and Food Standards, Ministry of Agriculture and Cooperatives
l.mintra@gmail.com

- Miss Rathar Benchapalanont
Pharmacist
Food and Drug Administration, Ministry of Public Health
raththar.b@gmail.com

USA

- Dr. Michael Bell
Deputy Director
Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention
zzb8@cdc.gov

- Mrs. Lynn Cinelli
Director
Merck Sharp & Dohme
lynn.cinelli@merck.com

- Mr. Silas Holland
Director
Merck Sharp & Dohme
silas.holland@merck.com

- Mr. Michael Schmitz
Director
C&M International
mschmitz@crowell.com

Vietnam

- Mr. Hung Thai Cao
Deputy Director
Department of Medical Service Administration, Ministry of Health
thai_caohung@yahoo.com

- Mrs. Thi Minh Chau Nguyen
Deputy Director
The International Cooperation Department, Ministry of Health
chautinotina@yahoo.com

Chinese Taipei

- Prof. Feng-Yee Chang
Professor
Tri-Service General Hospital, National Defense Medical Center
fychang@ndmctsgh.edu.tw

- Miss Hsiao-Ling Chang
Deputy Director
Division of Infection Control and Biosafety, Centers for Disease Control
hlchang@cdc.gov.tw

- Prof. Shan-Chwen Chang
Dean
College of Medicine, National Taiwan University
changsc@ntu.edu.tw

- Mrs. Shu-Ling Chang
Nurse
Division of Infection Control and Biosafety, Centers for Disease Control
ling@cdc.gov.tw

- Miss Ching-I Chen
Assistant
Agricultural Technology Research Institute
1052073@mail.atri.org.tw

- Mrs. Hsiu-Chu Chen
Pharmacist
Taichung Veterans General Hospital
kiku@vghtc.gov.tw

- Dr. Li-Kuang Chen
Chief of Laboratory Diagnosis Section
Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation
lkc@tzuchi.com.tw

- Dr. Shih-Chung Chen
Minister
Ministry of Health and Welfare

- Dr. Yao-Shen Chen
Chief
Department of Internal Medicine, Kaohsiung Veterans General Hospital
yschen@vghks.gov.tw

- Prof. Yee-Chun Chen
Professor
Department of Internal Medicine, National Taiwan University Hospital and College of Medicine
yeechunchen@gmail.com

- Miss Yu-Wen Chen
Pharmacist
Shionogi
kylie@shionogi.com.tw

- Dr. Chun-Wen Cheng
Medical doctor
Division of Infectious Diseases, Linkou Chang Gung Memorial Hospital

- Miss Wan-Hsin Cheng
Chief
Public Health Bureau Tainan City Government
dc13@tncghb.gov.tw

- Prof. Wen-Jin Cherng
Superintendent
Linkou Chang Gung Memorial Hospital

- Miss Chia-Wen Chiang
Nurse
China Medical University Hospital
2jdiagxl@yahoo.com.tw

- Dr. Chuen-Sheue Chiang
Associate Researcher
Center for Diagnostics and
Vaccine Development,
Centers for Disease Control
cschiang10@cdc.gov.tw

- Dr. Shih- Ming Johnson Chiang
President
World Veterinary Association (WVA)
jvh125@gmail.com

- Miss Hui-Yi Chien
Public Health Officer
Division Of Planning and Coordination,
Centers for Disease Control
ivy0311@cdc.gov.tw

- Dr. Li-Jung Chien
Section Chief
Division of Infection Control and
Biosafety, Centers for Disease Control
jung@cdc.gov.tw

- Dr. Chien-Shun Chiou
Principal Investigator
Center for Diagnostics and Vaccine
Development,
Centers for Disease Control
nipmcsc@cdc.gov.tw

- Prof. Cheng-Hsun Chiu
Professor
Department of Pediatrics, Chang Gung
Memorial Hospital
chchiu@adm.cgmh.org.tw

- Dr. Jih-Haw Chou
Director General
Centers for Disease Control

- Mrs. Wei-Hui Chou
Specialist
Division of Infection Control and Biosafety,
Centers For Disease Control
weihui@cdc.gov.tw

- Dr. Yu-Ju Chou
Medical Officer
Northern Regional Center,
Centers for Disease Control
awuxawu@gmail.com

- Mr. Chien-Hua Chu
Specialist
Division of Infection Control and
Biosafety, Centers for Disease Control
olin0725@gmail.com

- Mrs. Sun Chin Chuan
Commissioner
Taipei Tzu Chi Hospital
wagdar@ms39.hinet.net

- Miss Hsin-Tzu Chuang
Pharmacist
Shionogi
meredith@shionogi.com.tw

- Mr. Pei-Hua Chuang
Associate Technical Specialist
Food and Drug Administration
cph@fda.gov.tw

- Prof. Yin-Ching Chuang
Professor
Chi Mei Medical Center
secretary@mail.chimei.org.tw

- Mr. Yuan-Zong Gu
Medical Technologist
Taipei Veterans General Hospital
tmub8604008@pchome.com.tw

- Mrs. Li-Yuan Ho
Registered Nurse
Nursing Department,Rueifang Miner Hospital
leann35311@yahoo.com.tw

- Miss Hsuan-ling Hsiao
Clinical Pharmacist
Linkou Chang Gung Memorial Hospital
ellisa@adm.cgmh.org.tw

- Miss Yi-Chen Hsieh
Public Health Inspector
Department of Health, Taipei City Government
lizzie248@health.gov.tw

- Mrs. Mia-Hui Hsu
ICN
Nursing Department,Rueifang Miner Hospital
cefiros@ms25.hinet.net

- Miss Wei-Ting Hsu
Assistant Technical Specialist
Division of Infection Control and Biosafety,
Centers For Disease Control
wthsu@cdc.gov.tw

- Mr. Wen-Chien Hsu
Medical Technologist
Tri-Service General Hospital Songshan Branch
ymdarwins@gmail.com

- Miss Chi Hsuan
Section Chief
Public Health Bureau, Ping Tung County Government
pthchihsuan@ksmail.mohw.gov.tw

- Miss Yi-Jen Hung
Medical Technologist
Taipei Municipal Gan-Dau Hospital
lily80053131@gmail.com

- Dr. Chen-Hua Huang
Doctor
Cathy General Hospital
infection@cgh.org.tw

- Dr. Chin-Cheng Huang
Deputy Minister
Council of Agriculture

- Miss Jing-Fang Huang
Assistant Researcher
Agricultural Technology Research Institute
hcf@mail.atri.org.tw

- Prof. Kao-Pin Huang
Professor
China Medical University Hospital
kapihw@gmail.com

- Miss Li-Jung Huang
Secretary General
Taiwan Society Of Health-System Pharmacists
lijung8819@gmail.com

- Prof. Yhu-Chering Huang
Attending Physician
Chang Gung Memorial Hospital
ychuang@cgmh.org.tw

- Miss Yu-Chin Huang
Nurse
Ruefang Miner Hospital
vive@ms4.hinet.net

- Dr. Chieh Ju
Doctor
New Taipei City Hospital
hopeliu@ms26.hinet.net

- Miss Yu-Fen Ke
Senior Technical Specialist
Division of Infection Control and Biosafety, Centers for Disease Control
kyf@cdc.gov.tw

- Dr. Shu-Chen Kuo
Attending Physician and Assistant Investigator
National Health Research Instiutes
ludwigvantw@gmail.com

- Prof. Wen-Chien Ko
Chief of Division of Infectious Diseases
Division of Infectious Diseases, Department of Internal Medicine, National Cheng Kung University Hospital
winston3415@gmail.com

- Miss An-Chi Lai
Section Chief
Division of Planning and Coordination, Centers for Disease Control
angellai@cdc.gov.tw

- Mr. Wei-Fan Lai
Medical Laboratory Scientist
Hope Doctor Hospital
k223930@yahoo.com.tw

- Dr. Susan Shin-Jung Lee
Chief, Division of Infectious Diseases
Kaohsiung Veterans General Hospital
ssjlee28@yahoo.com.tw

- Miss Yi-Ting Lee
Pharmacist
Shionogi
annie_lee@shionogi.com.tw

- Yuan-Ti Lee
Director of Infection Disease
cshy521@csh.org.tw

- Miss Rachel Li
Stationed Agent
Division of Infection Control and Biosafety, Centers for Disease Control
fabail@cdc.gov.tw

- Dr. Ching-Len Liao
Director
National Institute of Infectious Diseases and Vaccinology
chinglen@gmail.com

- Mr. Wei-Tsen Laio
Associate Coordinator
Joint Commission of Taiwan
wt.liao@jct.org.tw

- Miss Chien-Yuan Lin
Director
Division of Planning and Coordination, Centers for Disease Control
hscylin@cdc.gov.tw

- Dr. Chii-Jeng Lin
President
Joint Commission of Taiwan

- Mr. David Lin
Country Manager
Pfizer Limited

- Dr. Huan-Po Lin
Visiting Doctor
Country Hospital
jameslin@url.com.tw

- Miss Le-Hau Lin
Nursing Home Director
Population Hospital
sf7324742@Gmail.Com

- Dr. Stephen Sheng-Fong Lin
Pfizer Limited
APAC Regional Medical Therapeutic Area Lead
stephen.lin@pfizer.com

- Mrs. En-Chi Liu
Infection Control Nurse
Chang Gung Memorial Hospital
angel20050714@adm.cgmh.org.tw

- Mr. KevinLiu
Director
Pfizer Limited
kevin.Liu@pfizer.com

- Miss Li-Ling Liu
Counselor
Ministry of Health and Welfare

- Miss Tsui-Ping Liu
Supervisor
Linkou Chang Gung Memorial Hospital
blue1010@adm.cgmh.org.tw

- Dr. Yung-Ching Liu
Chief Infection Disease
Taipei Medical University --Shuang Ho Hospital
08682@s.tmu.edu.tw

- Dr. Hsiu-Jung Lo
Investigator
National Health Research Institutes
hjlo@nhri.org.tw

- Dr. Yi-Chun Lo
Deputy Director-General
Centers for Disease Control
loyichun@cdc.gov.tw

- Mrs. Hui-Li Lu
Medical Technologist
Taichung Armed Forces General Hospital
lulu803m2005@yahoo.com.tw

- Mrs. Ying-Ping Ma
Specialist Animal Health Inspection Division
Bureau of Animal and Plant Health Inspection
and Quarantine Council of Agriculture
v019009@mail.baphiq.gov.tw

- Mr. Jasper Macslarrow
Director, International Affairs-Asia
Pfizer Limited
jasper.macslarrow@pfizer.Com

- Dr. Jung-Jung Mu
Research Fellow
Center for Diagnostics and
Vaccine Development,
Centers for Disease Control
Jjmu@cdc.gov.tw

- Prof. Sung-Ching Pan
Doctor
National Taiwan University Hospital
scpbpan@gmail.Com

- Miss Wan-Chen Shen
Pharmacist
Taipei Medical University –Shuang Ho Hospital
16323@s.tmu.edu.tw

- Mrs. Yi-Ting Shen
Professional Nurse
Office of Preventive Medicine,
Centers for Disease Control
beckeyshen@cdc.gov.tw

- Dr. Chung-Liang Shih
Director General
Ministry of Health and Welfare

- Dr. Tai-Hwa Shih
Deputy Director General
Bureau of Animal and Plant Health Inspection and Quarantine (BAPHIQ)
hcshih@mail.baphiq.gov.tw

- Miss Yu-Yen Shih
Senior Specialist
Division of Infection Control and Biosafety,
Centers for Disease Control
yyshih@cdc.gov.tw

- Mr. Chen-Yi Su
Doctor
Tan Chai Hospital
sujohn789@yahoo.com.tw

- Dr. Chih-Kuang Su
Attending Physician
Xinzhuang Yingren Hospital
thome666@yahoo.com.tw

- Dr. Ying-Shih Su
Medical Officer
Eastern Regional Center,
Centers for Disease Control
sih0818@cdc.gov.tw

- Dr. Cheng-Sheng Tai
Attending Doctor Taipei Veterans General Hospital,Taitung Branch
t7612217@gmailcCom

- Miss Chun-His Tai
Infection Control Medical Technician
Taichung Veterans General Hospital
taichun1209@hotmail.com

- Miss Kuei-Lien Tien
Registered Nurse
Center for Infection Control, National Taiwan University Hospital
kltien@ntuh.gov.tw

- Miss Chia-Shan Tsai
Pharmacist
Taipei Medical University – Shuang Ho Hospital
10587@s.tmu.edu.tw

- Miss Chia-Yin Tsai
Public Health Inspector
Department of Public Health Taoyuan

- Miss Ching-Hua Tsai
Asso. Market Access Director
Merck Sharp & Dohme
yvette.tsai@merck.com

- Dr. Chin-Shiang Tsai
Attdening Physician
National Cheng-Kung University Hospital
jasonmammal@gmail.com

- Tsai-Ling Yang Lauderdale
Investigator
National Institute of Infectious Diseases and Vaccinology
lauderdale@nhri.org.tw

- Miss Wan-Hsuan Tsai
Assitant Technical Specialist
Division of Infection Control and Biosafety, Centers for Disease Control
washt@cdc.gov.tw

- Dr. Shu-Hui Tseng
Director
Division of Infection Control and Biosafety, Centers for Disease Control
tsengsh@cdc.gov.tw

- Dr. Tsung-Pei Tsou
Medical Officer
Division of Preparedness and Emerging Infectious Diseases,
Centers for Disease Control
tsungpei@cdc.gov.tw

- Miss Kai-Hao Wang
Sr. Public Affairs/Policy Manger
Pfizer Limited
kai-hao.wang@pfizer.com

- Dr. Kung-Ching Wang
Medical Officer
Central Regional Center,
Centers for Disease Control
kcwang35@cdc.gov.tw

- Prof. Kwua-Yun Wang
Vice President
Taiwan Nurses Association
twna@twna.org.tw

- Mr. Cheng-Hao Wu
Program Coordinator
Division of Planning and Coordination,
Centers for Disease Control
collinwu@cdc.gov.tw

- Dr. Chi-Jung Wu
Assistant Investigator and Attending Physician
National Health Research Institutes
wucj@nhri.org.tw

- Dr. Hao-Hsin Wu
Medical Officer
Division of Infection Control and Biosafety,
Centers for Disease Control
wuahushing@cdc.gov.tw

- Mrs. Hsiu-Hui Wu
Assistant Researcher
Agricultural Technology Research Institute
hhwu@mail.atri.org.tw

- Dr. Jiunn-Shyan Julian Wu
Section Chief
Division of Infection Control and Biosafety,
Centers for Disease Control
delight@cdc.gov.tw

- Dr. Mai-Szu Wu
Superintendent
Taipei Medical University --Shuang Ho Hospital maiszuwu@gmail.com

- Dr. Yi-Chun Wu
Division Director
Division of Quarantine,
Centers for Disease Control
wuyj@cdc.gov.tw

- Miss Hsiang-Yin Yeh
Associate Technical Specialist
Ministry of Health and Welfare
mdime@mohw.gov.tw

- Dr. Muh-Yong Yen
Director
Taipei City Hospital
myyen1121@gamil.com