# Antibiotic Resistance:
# National One Health Initiative


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***Department of Medicine***

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# New superbug found in two patients here

BY POON CHIAN HUI

A NEWLY found superbug from India that has been making news around the world infected two patients here early this year – before anyone knew what they were dealing with – but was successfully dealt with and contained.

The Ministry of Health (MOH) told The Straits Times that the patients had infections from bacteria with the New Delhi metallo-beta-lactamase-1 (NDM-1) gene identified last month.

The gene has the ability to shield bacteria from all antibiotics, turning them into drug-resistant superbugs.

It was found in the samples from the two patients last month, after hospitals went back and tested past samples.

"Following reports of NDM-1 in other countries and the availability of newer and more sensitive tests, our hospitals found two cases from the beginning of this year that were positive for NDM-1," said an MOH spokesman.

resistant bacteria when they showed signs of illness besides the one they had gone in for – an indication they might also be infected with a superbug.

Both were quickly isolated from other patients after bacteria in their urine samples were found to be resistant to drugs.

MOH said they were moved to single-bed rooms and had limited contact with visitors.

Health-care staff who attended to

**Both cases successfully contained as experts urge health officials to track deadly bacteria**

that strict hospital infection control measures are the key to fighting superbugs.

One measure is the retroactive testing

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NDM-1 made the headlines after a study published on Aug 11 in The Lancet medical journal said the gene was detected in British patients in 2007, and appeared to have originated from India. So far, it has occurred mainly in two gut bacteria – *Escherichia coli* (E. coli) and *Klebsiella pneumoniae*.

The news triggered a global reaction as NDM-1 is able to resist even the most powerful class of antibiotics known as carbapenems.

Cases have now been reported in places such as the United States, France, Germany, Australia, Hong Kong and Japan. Last month, a Belgian man became the first known fatality.

On Monday, scientists at the International Conference on Antimicrobial Agents and Chemotherapy urged the health authorities to track bacteria with the gene.

The conference in the United States, which ended yesterday, is the world's largest gathering of infectious disease specialists, attracting about 12,000 people.

Drug-resistant superbugs are not new and include methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*.

MRSA is a serious infection found mostly in hospital settings, while the latter usually infects the lungs.

The NDM-1 gene is a part of a bigger problem of drug resistance brought about by the abuse of antibiotics worldwide.

To fight the spread of these bugs, local hospitals have comprehensive infection control measures.

Hospital staff practise strict hand hygiene and are audited regularly.

Inpatients are also screened for existing superbugs such as MRSA.

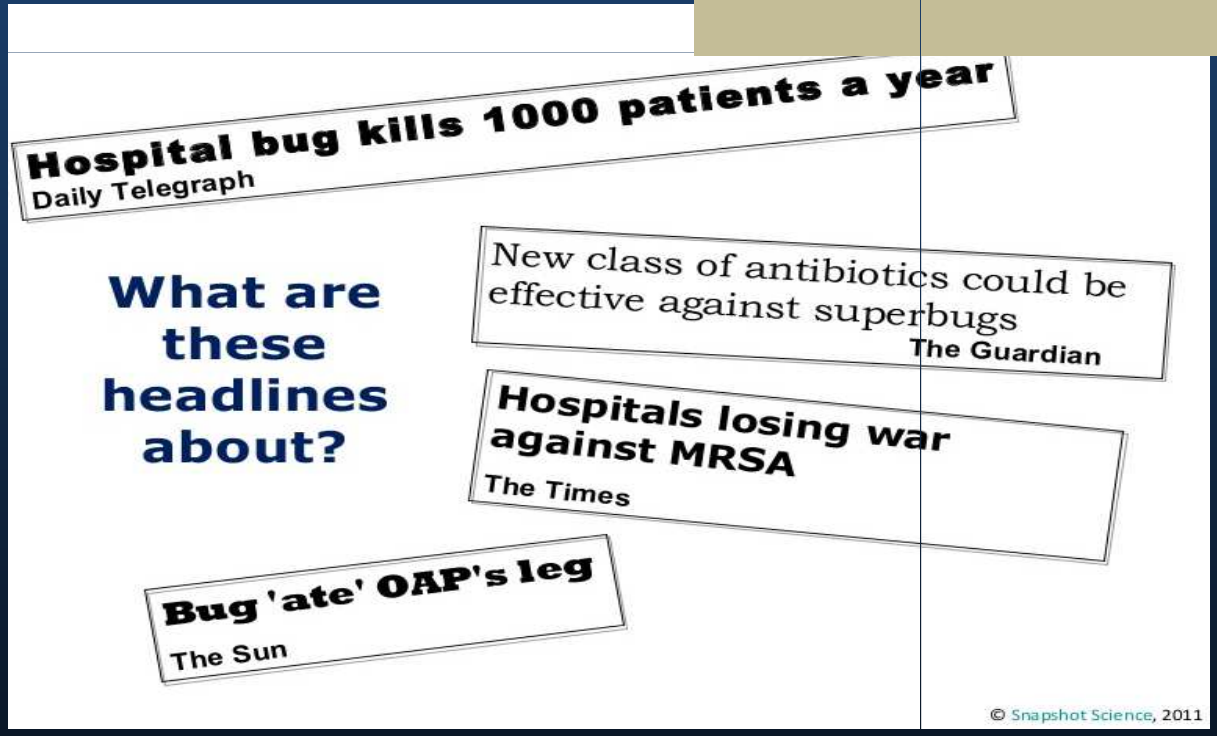
There are also antibiotic stewardship programmes to help doctors prescribe the right type and dosage of antibiotics to minimise the rise of drug resistance.

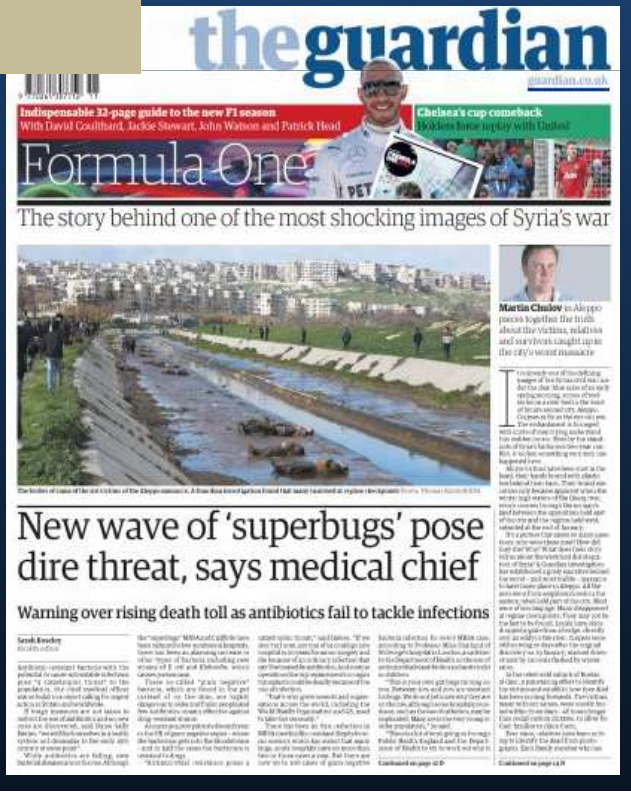
chpoon@sph.com.sg

More in tomorrow's edition of Mind Your Body

The Straits Times

**AMR making the Worldwide News!**



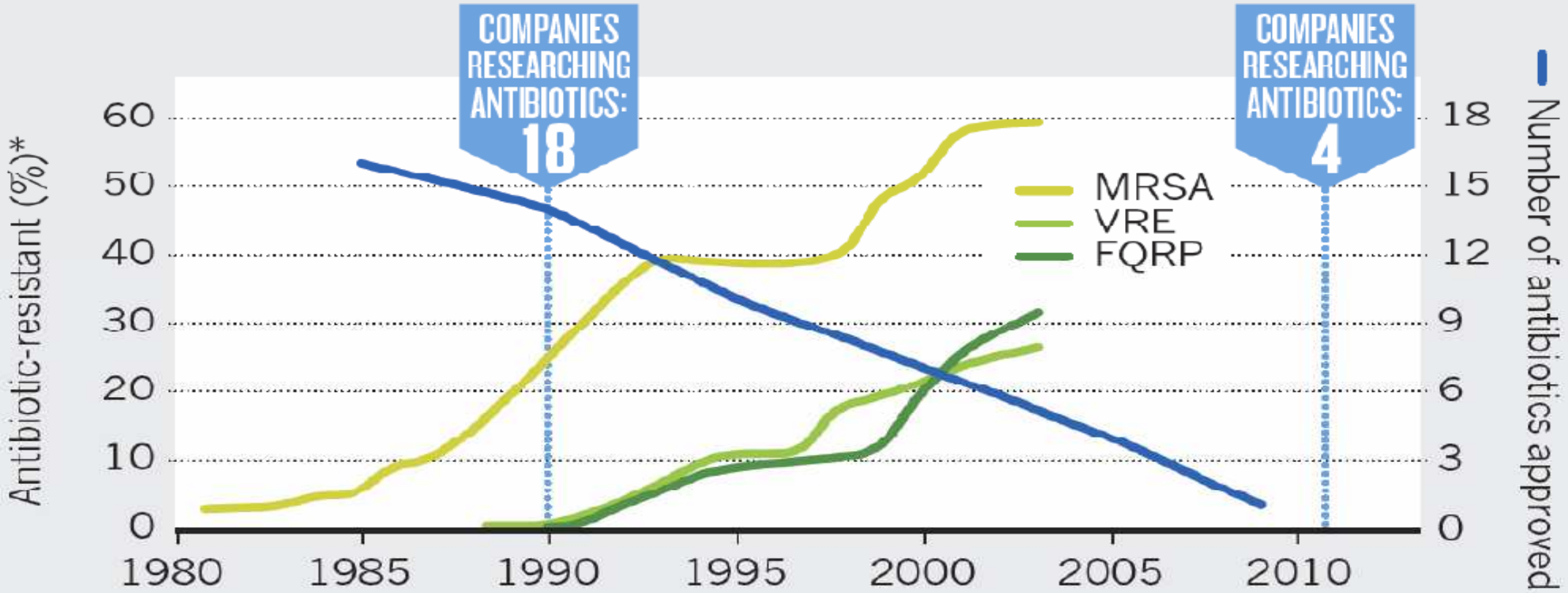
## *Klebsiella pneumoniae* antimicrobial resistance, US 1998–2010.




Sanchez et al. EID, Vol 19, No 1—Jan 2013

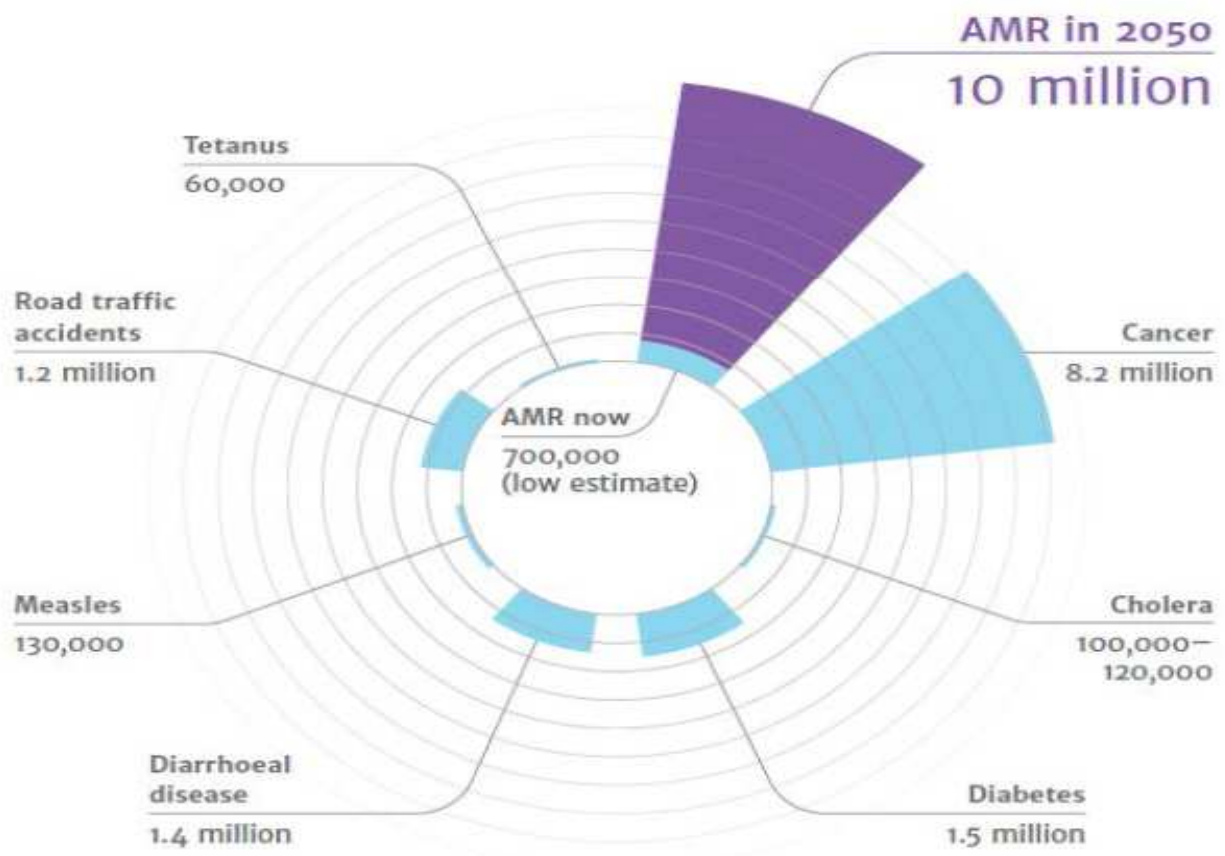
# A PERFECT STORM

As bacterial infections grow more resistant to antibiotics, companies are pulling out of antibiotics research and fewer new antibiotics are being approved.




*Proportion of clinical isolates that are resistant to antibiotic. MRSA, methicillin-resistant *Staphylococcus aureus*. VRE, vancomycin-resistant *Enterococcus*. FQRP, fluoroquinolone-resistant *Pseudomonas aeruginosa*.

# DEATHS ATTRIBUTABLE TO AMR EVERY YEAR




Review on Antimicrobial Resistance

Cumulative economic impact of $100 trillion

**O'Neill Report**

# Crisis in Antimicrobial Resistance

## Local, national, global problem

Theme for
World Health Day
April 7, 2011

# Antimicrobial Resistance

Urgent local, national and global challenge

Implications for

- Human health, Animal health, Environmental health

Threat to

- Public health
- Animal health
- National and global security
- National and global economy

Complex, multifaceted problem

- requiring multidisciplinary collaboration and cooperation and national and global commitment and support

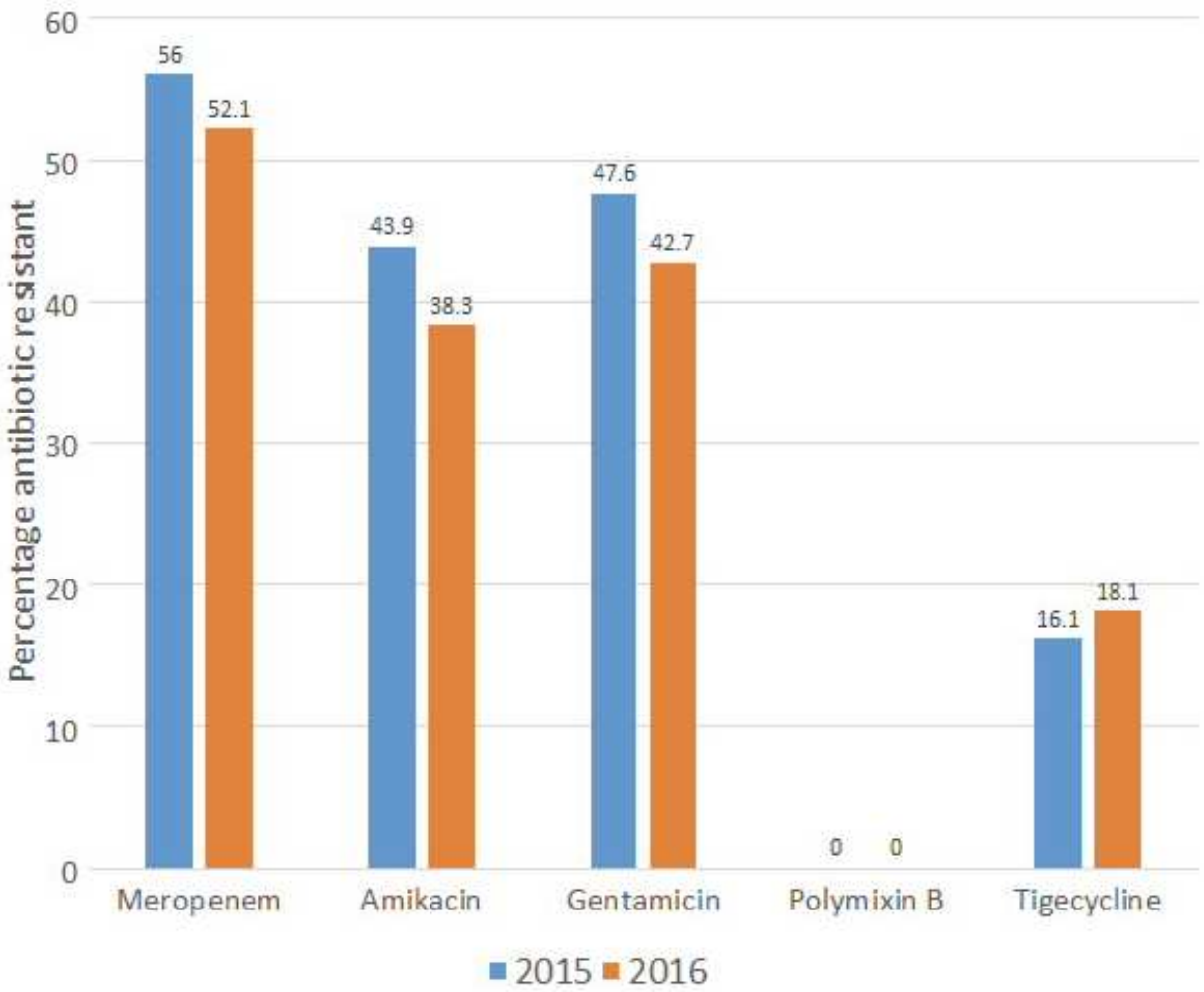
# Introduction

- A total of 41 hospitals contributed their Antibiotic Sensitivity data i 2016, compared to 39 hospitals in 2015
- The data was analysed based on one patient per isolate
- A total of 352,485 isolates were tested and analysed in 2016

# *Percentage Acinetobacter baumanii* isolated from blood, resistant to antibiotics

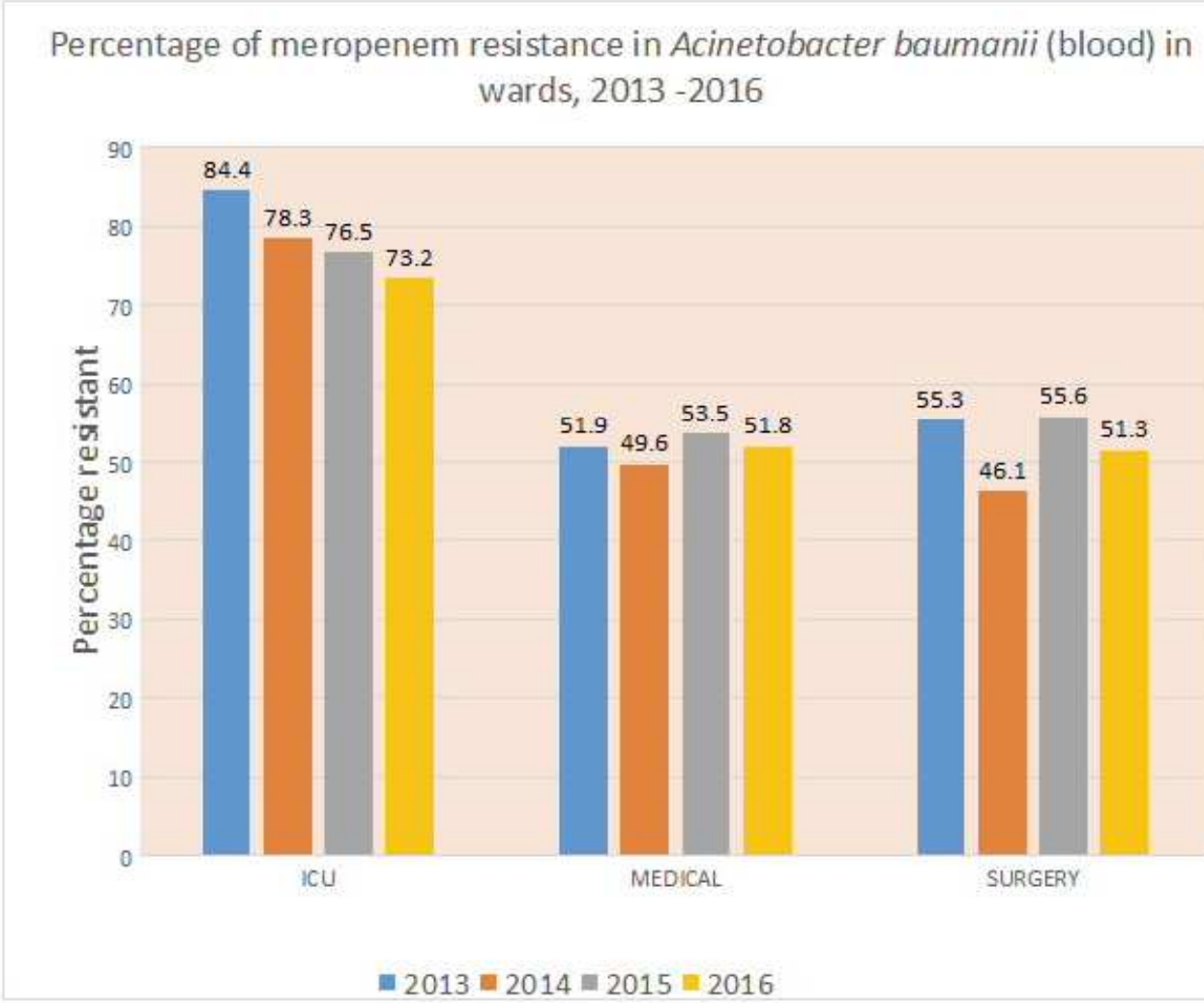
- High resistance rates were observed for meropenem, amikacin and gentamicin

- However, decreasing resistance rates were observed in 2016 for the tested antibiotics (except tigecycline)



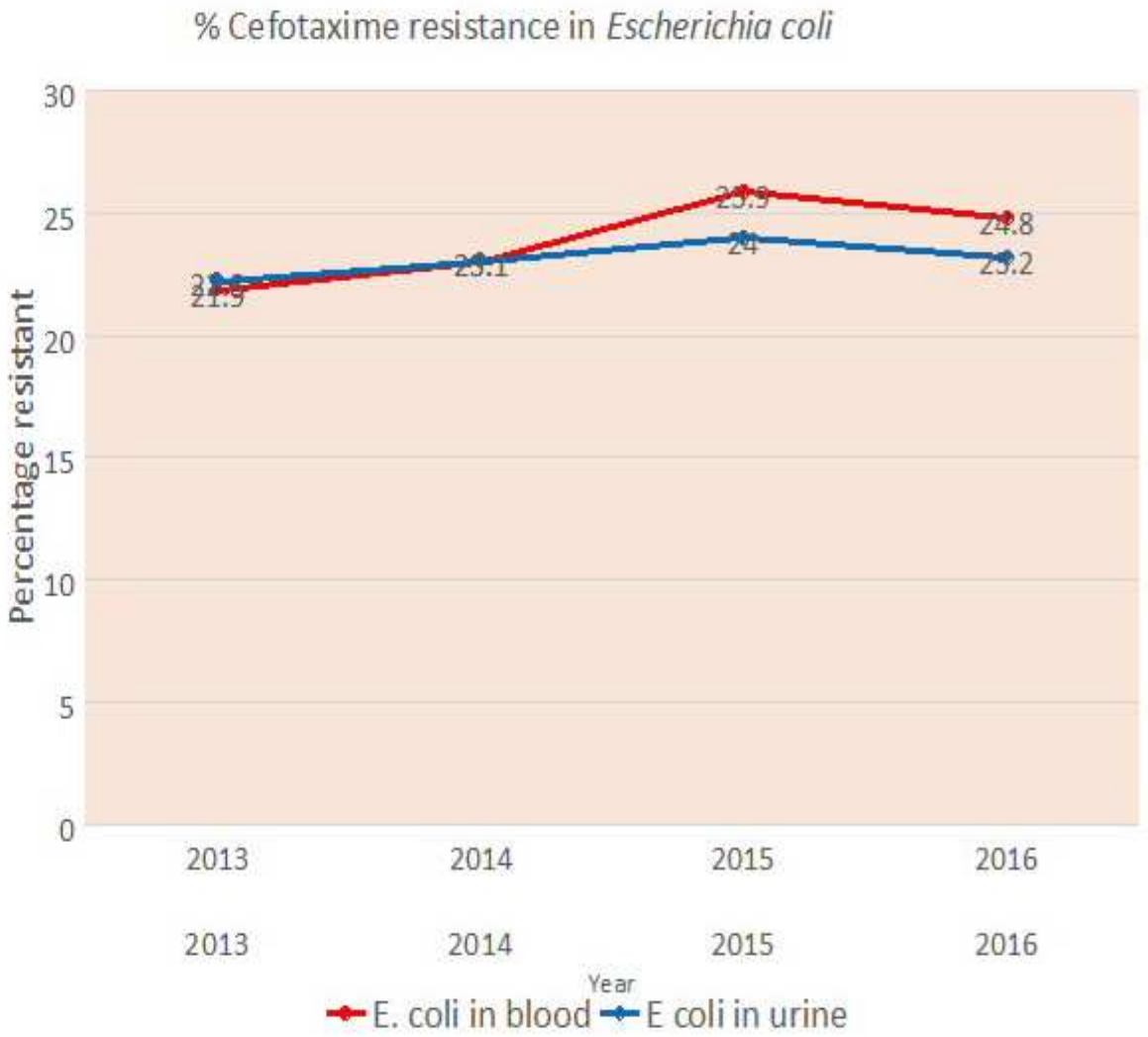
# Meropenem resistance in *A. baumanii* isolated from blood, by wards

- High meropenem resistance rates was observed in ICU compared to medical and surgical wards
- The resistance rates are > 70% in ICU
- However, a decreasing trend in resistance is observed in ICU



# Cefotaxime resistance in *Escherichia coli*

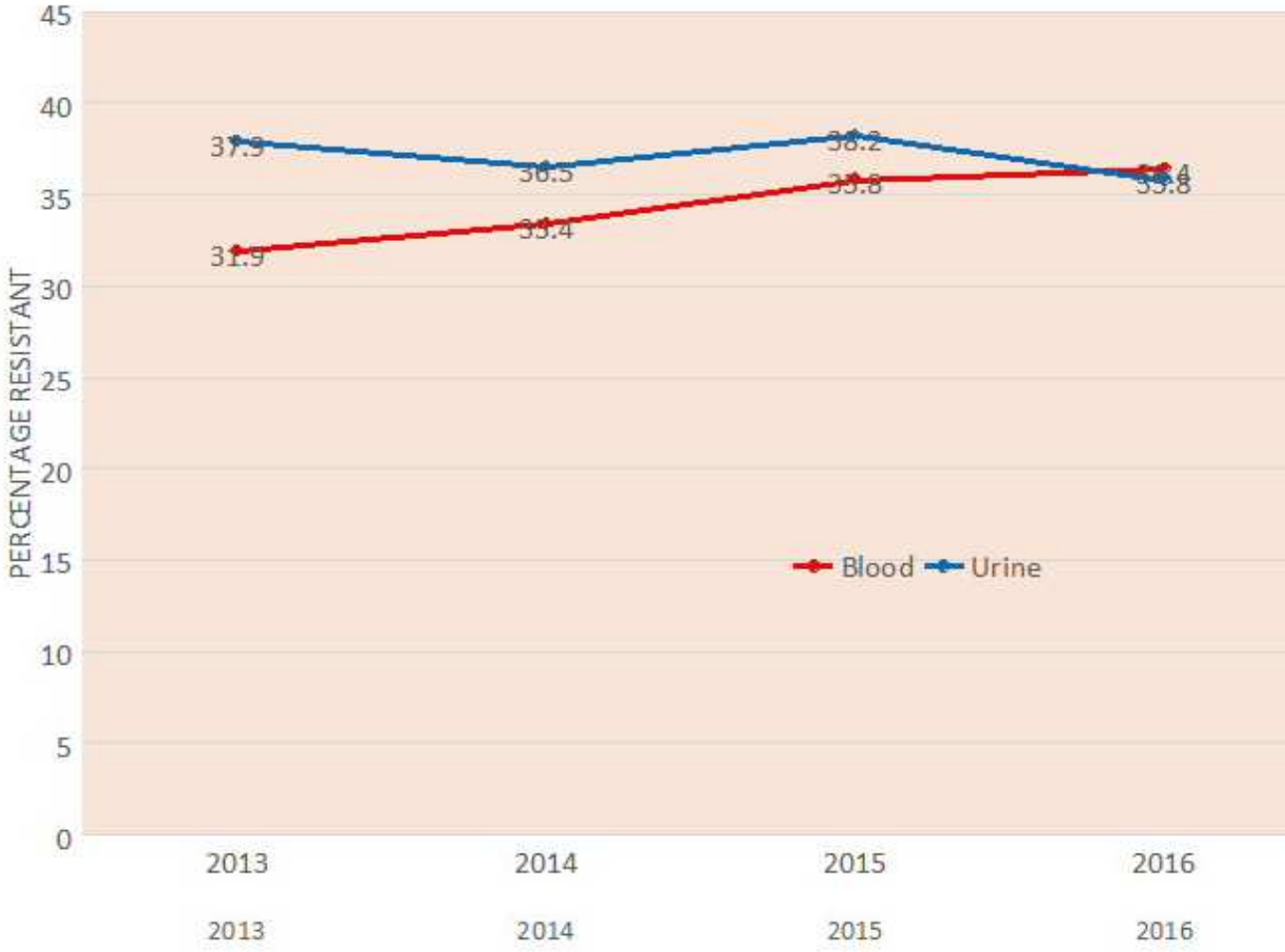
- Cefotaxime resistance in more than 20% in *E. coli*
- A slight decrease in cefotaxime resistance was noted in 2016 for both blood and urine isolates



# Cefotaxime resistance of *Klebsiella pneumoniae* isolated from blood & urine

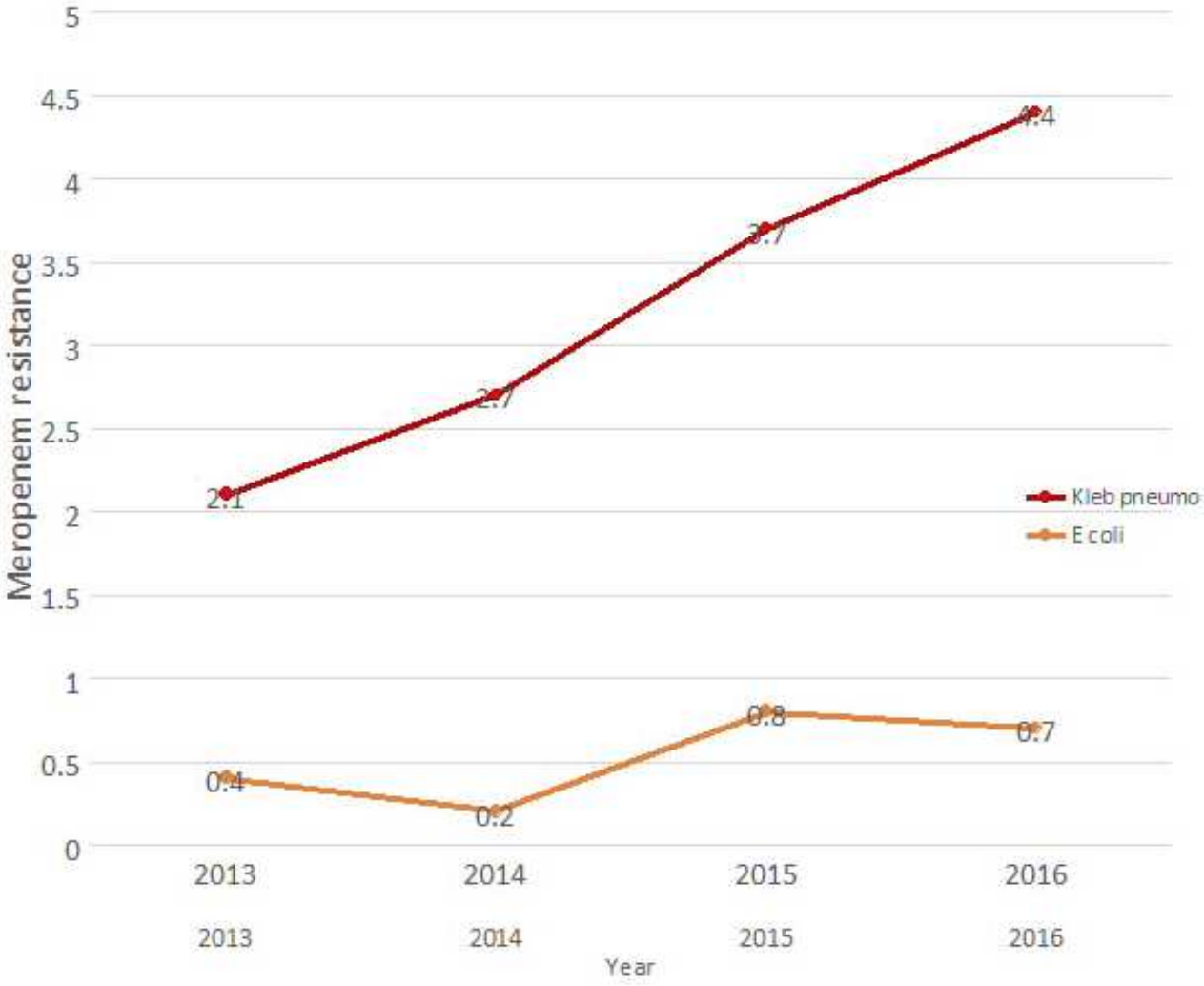
Cefotaxime resistance is higher in *Kleb pneumoniae* compared to *E. coli*

An increasing trend of cefotaxime resistance was observed for *Kleb. pneumoniae* isolated from blood



# Meropenem resistance in *Klebsiella pneumoniae and Escherichia coli* isolated from blood

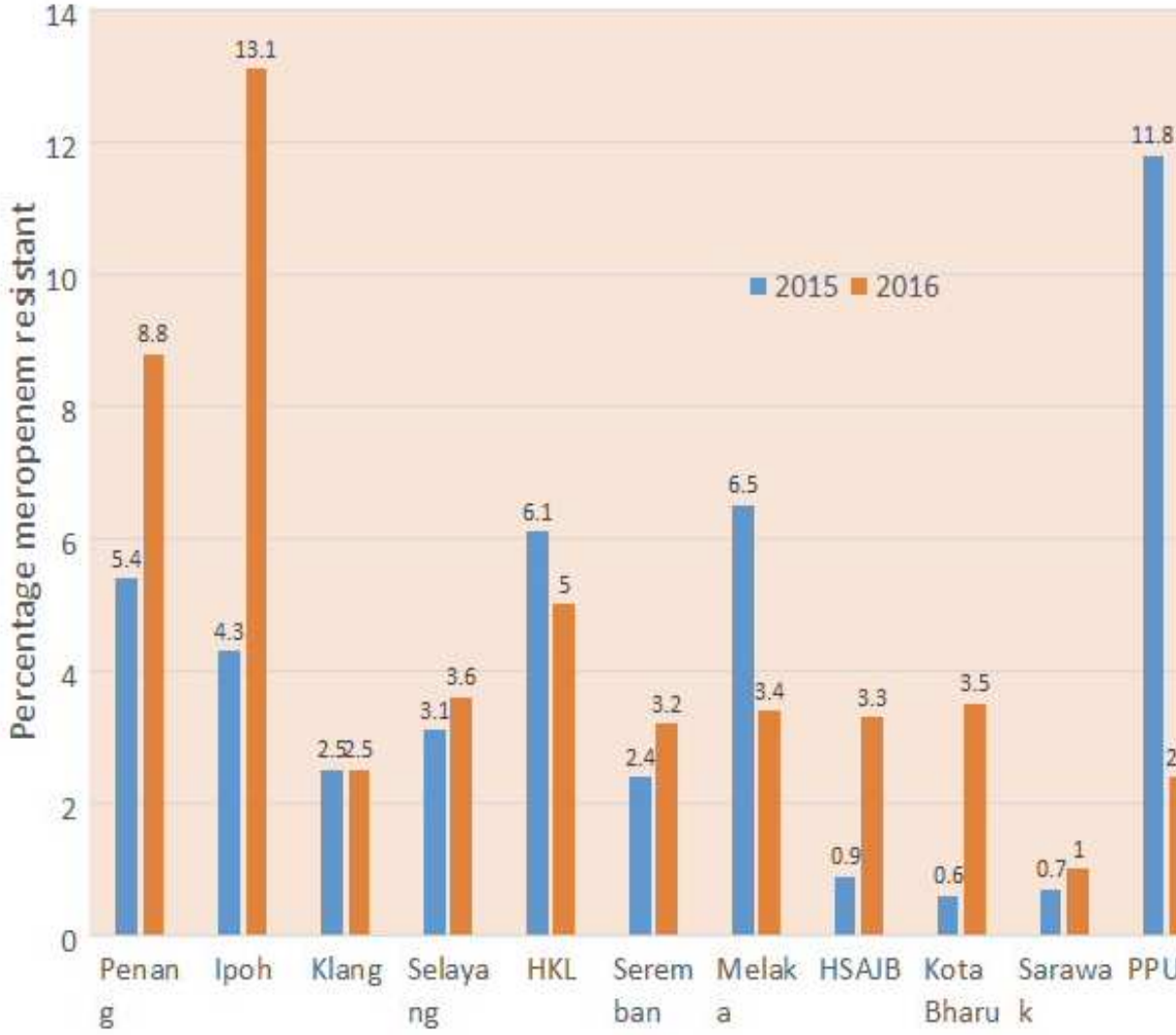
- An increasing trend in meropenem resistance was observed in *Klebsiella pneumoniae*
- For *E. coli* the resistance rates remain fairly stable at less than 1%



# Meropenem resistant *Kleb. pneumoniae* isolated from blood in hospital >900 beds

- Ipoh Hospital showed an increase in meropenem resistant *Kleb. pneumoniae*, followed by Penang, Kota Bharu and HSAJB

- A reduction in meropenem resistance was observed in PPUM.



Lancet Infect Dis 2015

# Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu*, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen

## Summary

**Background** Until now, polymyxin resistance has involved chromosomal mutations but has never been reported via horizontal gene transfer. During a routine surveillance project on antimicrobial resistance in commensal *Escherichia coli* from food animals in China, a major increase of colistin resistance was observed. When an *E coli* strain, SHP45, possessing colistin resistance that could be transferred to another strain, was isolated from a pig, we conducted further analysis of possible plasmid-mediated polymyxin resistance. Herein, we report the emergence of the first plasmid-mediated polymyxin resistance mechanism, MCR-1, in Enterobacteriaceae.

Lancet Infect Dis 2015
Published Online
November 18, 2015
http://dx.doi.org/10.1016/S1473-3099(15)00424-7
See Online/Articles
http://dx.doi.org/10.1016/S1473-3099(15)00463-6

During the writing of this report, we noted that five *E coli* DNA contigs containing *mcr-1*-like genes from Malaysia have been recently submitted to the European Molecular Biology Laboratory (GenBank accession number JWKG01000081.1, JWKF01000084.1, JUJZ01000081.1). Although no additional information is available, the possibility that *mcr-1*-positive *E coli* have spread outside China and into other countries in southeastern Asia is deeply concerning.

Chicken spleen and chicken liver

# MCR-1 positive CRE

| | 1st case | 2th case | 3nd case | 4th case | 5th case |
|---|---|---|---|---|---|
| Date | 23/2/15 | 19/1/16 | 19/10/16 | 29/11/16 | 30/12/16 |
| Hospital | HKL | Sult. Bahiyah | Seberang Jaya | Kota Bharu | Penang |
| Gender | Female | Male | Female | Female | Female |
| Age (yrs) | 46 | 50 | 67 | 76 | 45 |
| Diagnosis | Chronic renal failure | Severe head injury (ICU) | Pneumonia | Infected pressure sore | Acute myeloid leukemia with sepsis |
| Bacteria | *Escherichia coli* | *Escherichia coli* | *Escherichia coli* | *Escherichia coli* | *Escherichia coli* |
| Source | Rectal swab | Tracheal aspirate | Blood | Pus | Blood |
| Outcome | Died | Died | Died | Died | Alive |

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Hot Topic

# Emergence of colistin-resistant bacteria in humans without colistin usage: a new worry and cause for vigilance

ARTICLE INFO

*Keywords:*
Enterobacteriaceae
Cationic antimicrobial peptides
Veterinary

ABSTRACT

Colistin is currently regarded as one of the 'last-resort' antibiotics used for the treatment of critical infections caused by multidrug-resistant Gram-negative pathogens. There have been numerous reports of the emergence of colistin resistance in patients, most of whom had previously received colistin therapy or with acquisition via nosocomial transmission. However, there are also ample reports of colistin resistance in humans who have not received the drug previously or without nosocomial transmission. We have also observed a similar occurrence in our study involving colistin resistance from several countries along with a similar phenomenon being reported by researchers. The observation of colistin resistance in humans without prior colistin exposure is of particularly great clinical importance and concern because of the current importance of colistin in clinical medicine. Colistin use and colistin-resistant bacteria in animals have been recently reported, suggesting that animals could also be a source of transmission of colistin-resistant bacteria to humans. This is a real worry and calls for clinicians to be aware and vigilant of this phenomenon and of the possibility of independent resistance to colistin in some patients.

# Global trends in antimicrobial use in food animals

Thomas P. Van Boeckel[a,1], Charles Brower[b], Marius Gilbert[c,d], Bryan T. Grenfell[a,e,f], Simon A. Levin[a,g,h,1], Timothy P. Robinson[i], Aude Teillant[a,e], and Ramanan Laxminarayan[b,e,j,1]

[a]Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544; [b]Center for Disease Dynamics, Economics & Policy, Washington, DC 20036; [c]Universite Libre de Bruxelles, B1050 Brussels, Belgium; [d]Fonds National de la Recherche Scientifique, B1000 Brussels, Belgium; [e]Princeton Environmental Institute, Princeton, NJ 08544; [f]Fogarty International Center, National Institutes of Health, Bethesda, MD 20892; [g]Beijer Institute of Ecological Economics, 10405 Stockholm, Sweden; [h]Resources for the Future, Washington, DC 20036; [i]International Livestock Research Institute, 00100 Nairobi, Kenya; and [j]Public Health Foundation of India, New Delhi 110070, India

- **For Brazil, Russia, India, China and South Africa, antimicrobial consumption for animals is expected to grow by 99% by 2030 (13% for humans).**

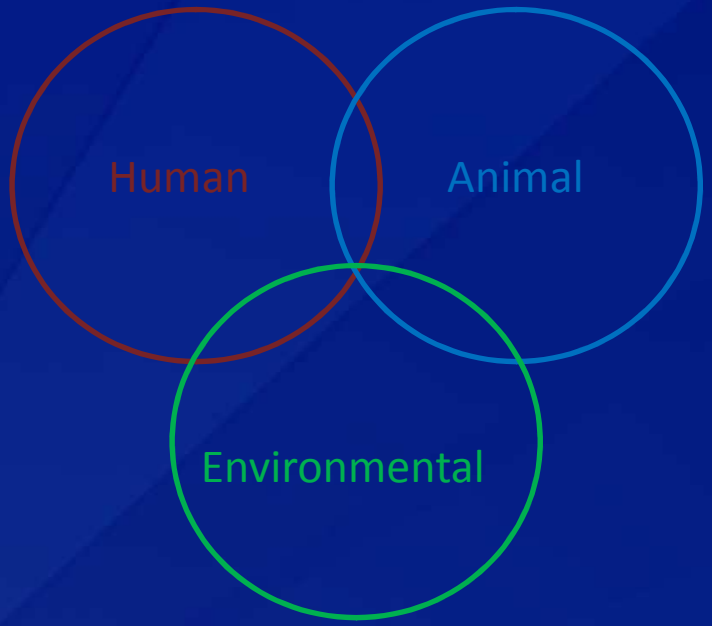
**Intensification is a given, but the bad parts that lead to overuse /need for antibiotics must be unravelled**

# Definition of One Health

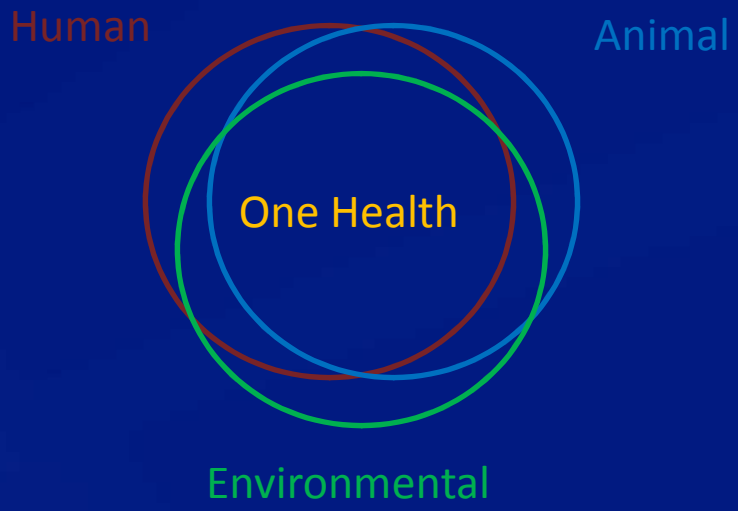
One Health is the collaborative effort of multiple health science professions, together with their related disciplines and institutions -- working locally, nationally, and globally – to attain optimal health for people, domestic animals, wildlife, plants, and our environment

# What is One Health?

**A one health approach recognizes the relationships between the human, animal, and environmental health, and applies interdisciplinary tools to solve complex public health problems**



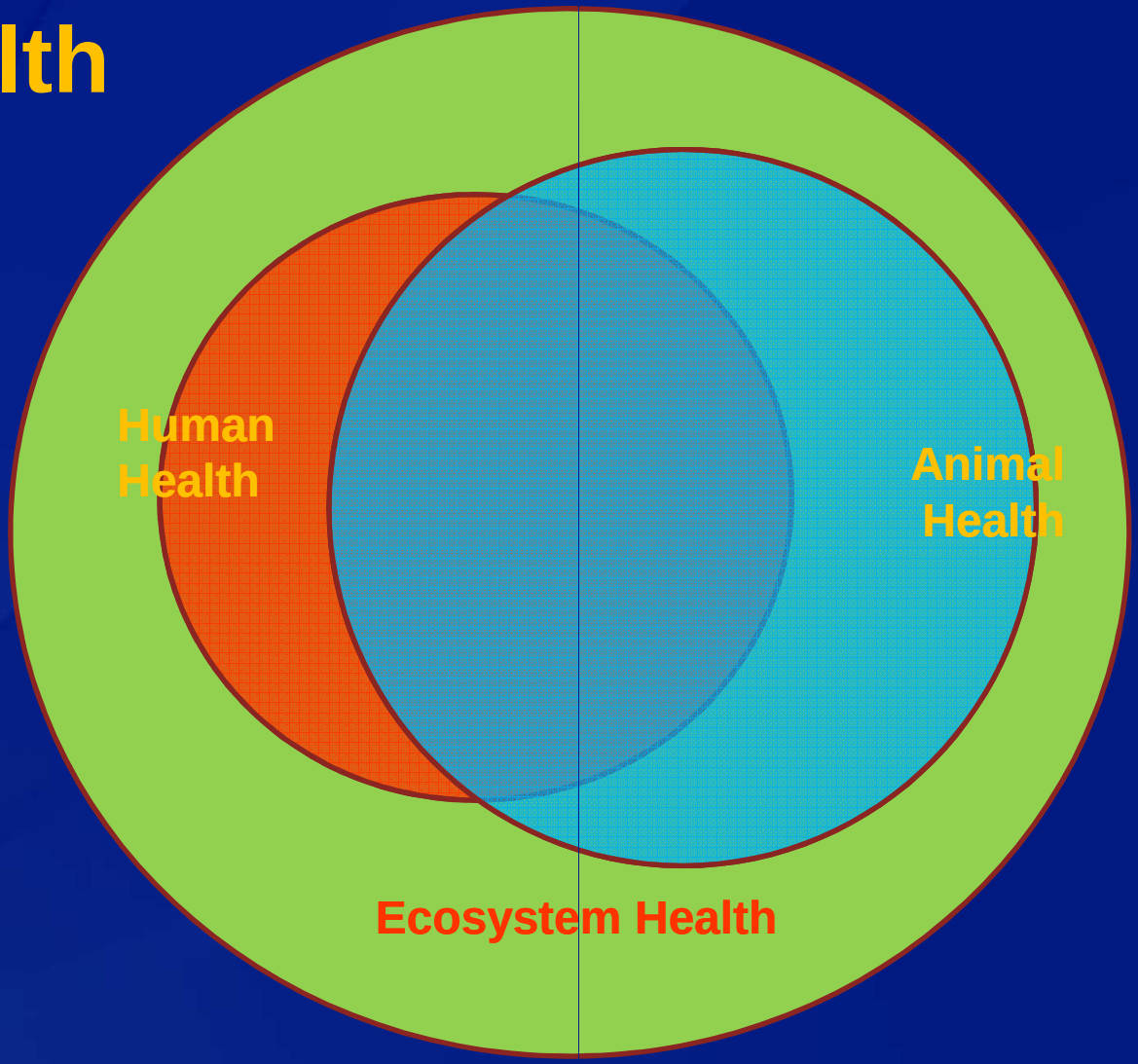

TRADITIONAL PUBLIC HEALTH MODEL



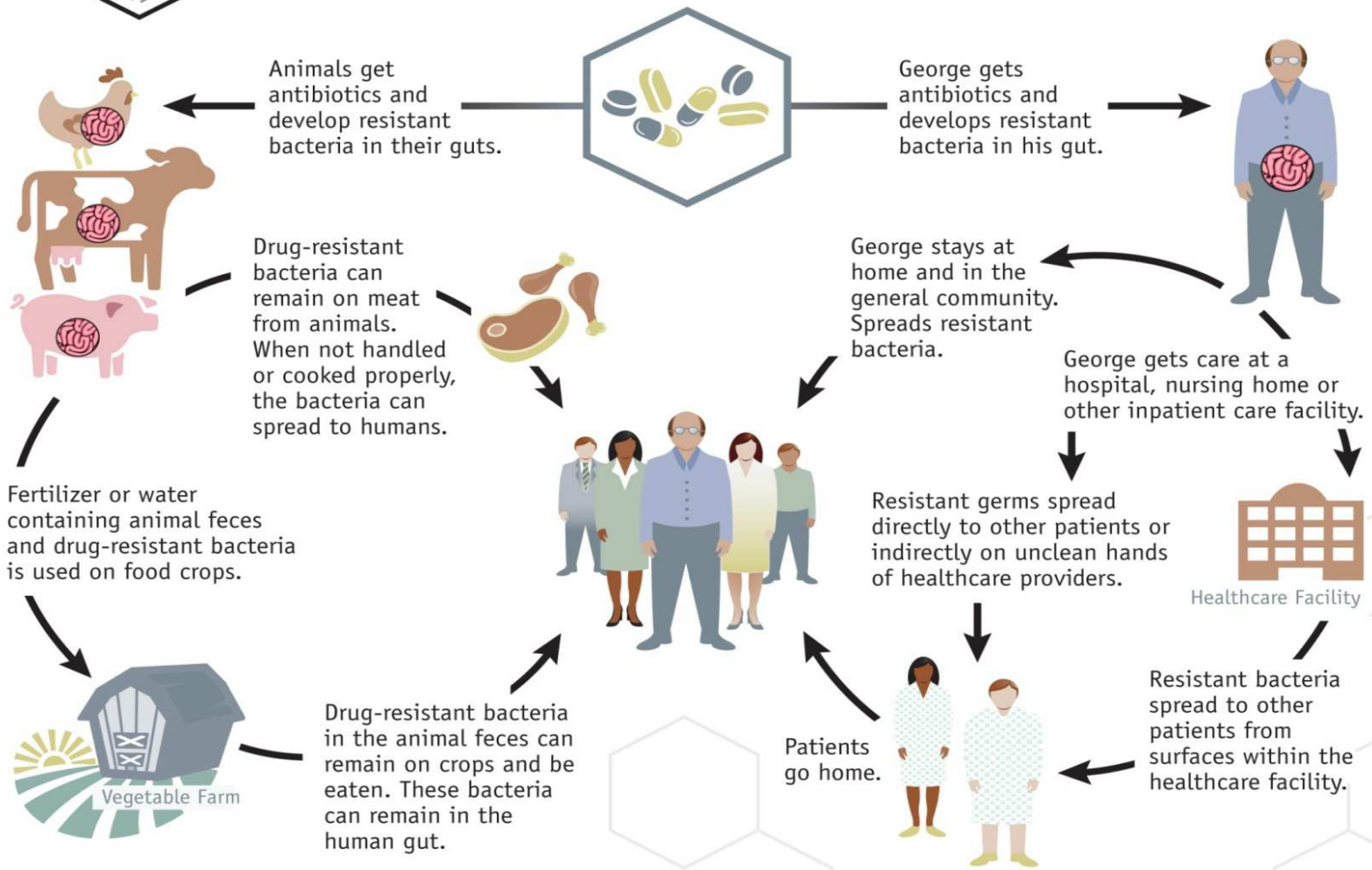

ONE HEALTH APPROACH

Source: Gael Lamielle

# One Health



# Examples of How Antibiotic Resistance Spreads




**Simply using antibiotics creates resistance. These drugs should only be used to treat infections.**

# Antimicrobial resistance – the biggest One Health issue on the globe

Death from bacterial infections in pre-AB era was between 40-50% and in the antibiotic era <10% with an increased life expectancy of 20 years.

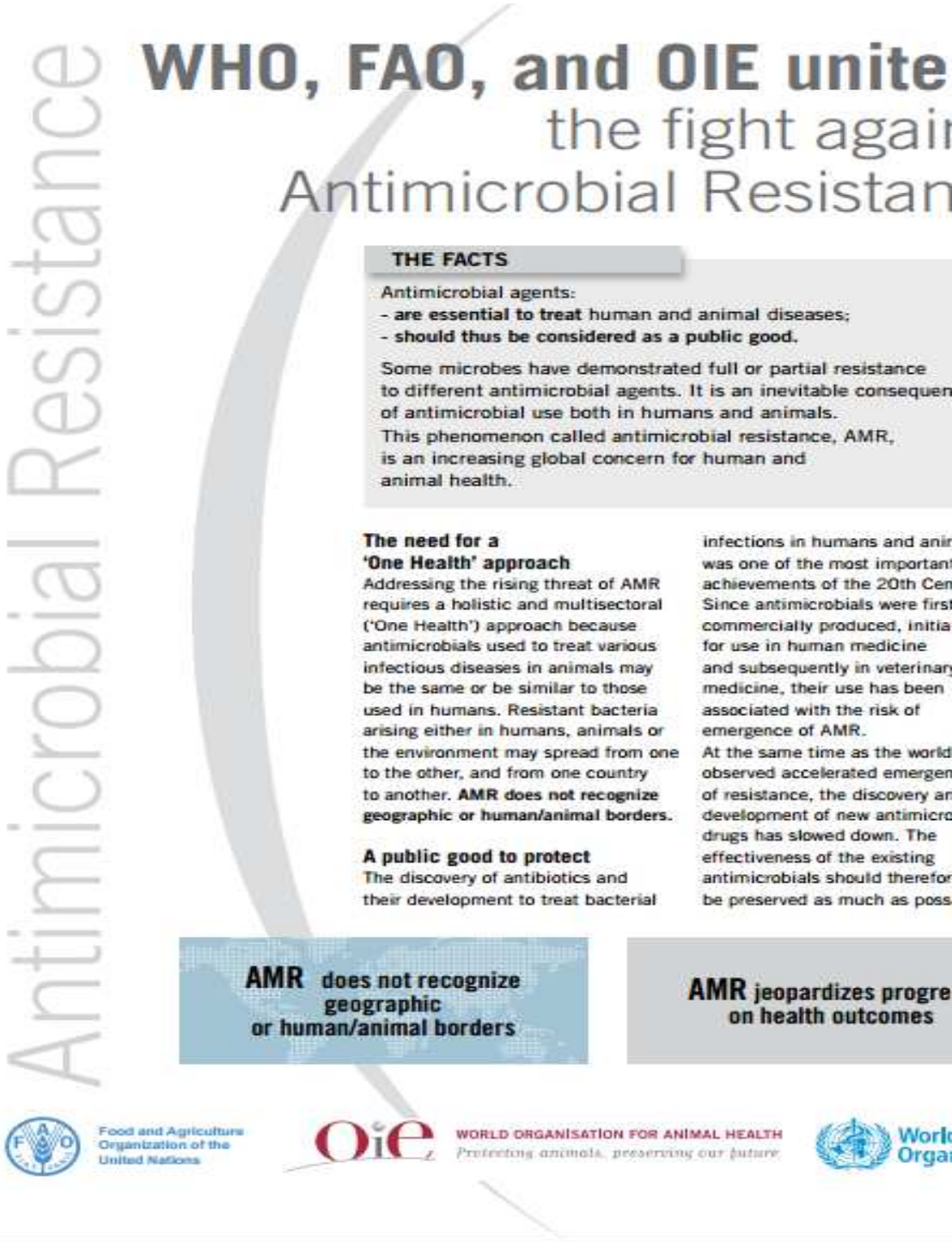
By 2050, AMR is estimated to lead to 10 million deaths per year, and lost output worth US $100 trillion across the world

No new class of antibiotics has been discovered since 1987

# Tripartite collaboration

**FAO-OIE-WHO Tripartite Agreement/Vision, Mexico October 2011**

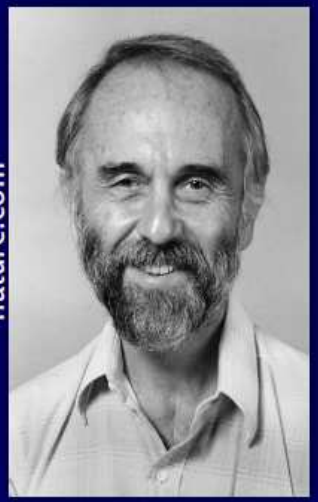
- Holistic and coordinated management of AMR across the animal, food and human sectors in different ecosystems and geographic locations



CALVIN SCHWABE ONE HEALTH PROJECT

UCDAVIS VETERINARY MEDICINE

"Human and animal health are inextricably linked. They always have been. They always will be."

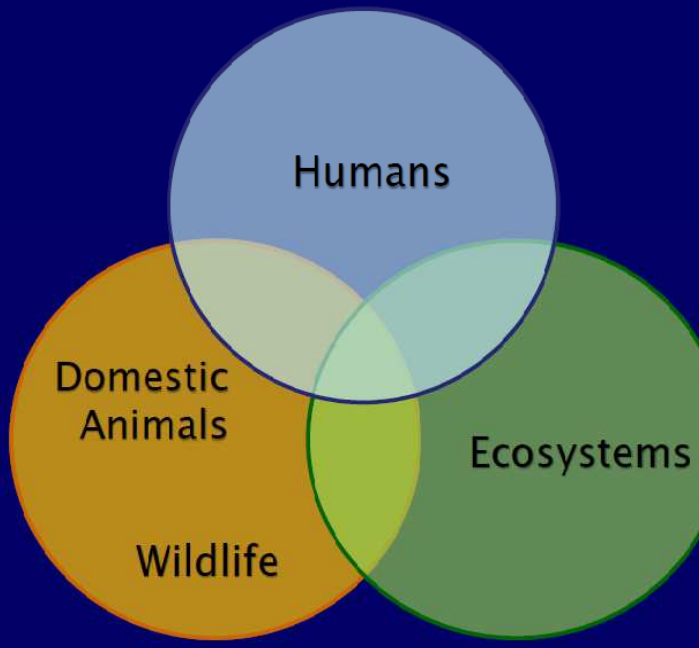



**Calvin Schwabe**
1927 – 2006
Professor of Veterinary Medicine

**James H. Steele**
1913 – 2013
Chief, Veterinary Public Health Division, CDC
Assistant Surgeon General for Veterinary Affairs, USPHS

## The Opportunities

## "One Health"



# Restriction on the use of colistin

SAVC
SOUTH AFRICAN VETERINARY COUNCIL

## Colistin use by veterinarians

nber

**mmended that Colistin not be used in food producing animals at all, unless the veterinarian can justify its use at the hand of a sensitivity test and as a very last resort**
**l. Any conduct to the contrary would be regarded by Council as unprofessional conduct.**

d the message from the Registrar of Medicines addressed to all veterinarians.

narian

## What we need to do

## The Animal Health Pillars

Review on Antimicrobial Resistance

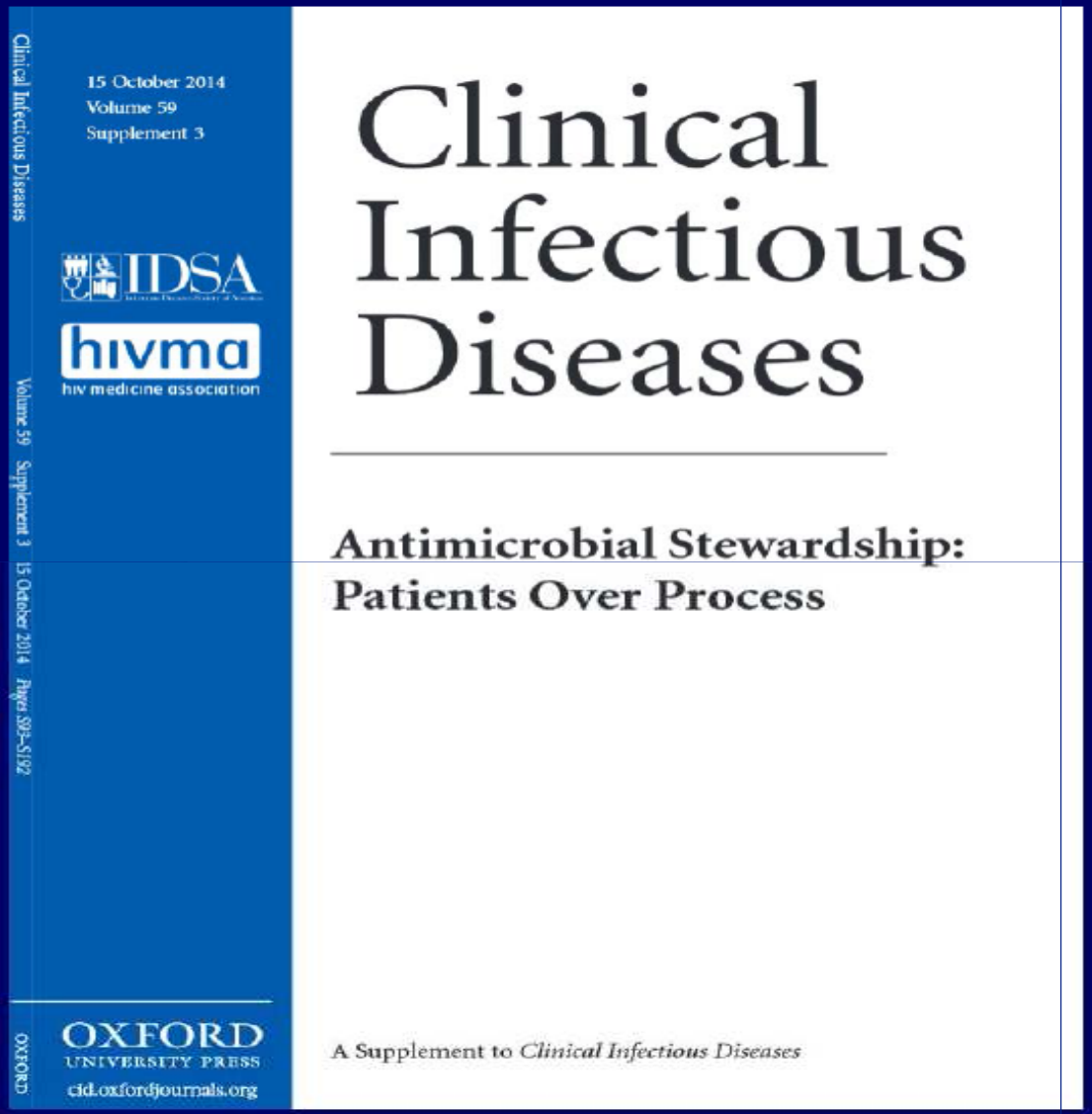
We propose three broad steps to improve this situation:

1. **10-year targets to reduce unnecessary antibiotic use in agriculture, introduced in 2018 with milestones to support progress consistent with countries' economic development.** In order to reduce global use of antibiotics in agriculture there is a strong case for targets on use at the country level, taking into account countries' production systems.

2. **Restrictions and/or bans on certain types of highly critical antibiotics.** Too many antibiotics that are last-line drugs for humans are being used in agriculture, sometimes without even professional oversight. These need to be the prime focus of efforts to reduce consumption in animals and action should be taken on this now.

3. **Improve transparency** from food producers on the antibiotics used to raise the meat that we eat, to enable consumers to make more informed purchase decisions.

**O'Neill Report**




# Core Elements

- Leadership commitment
- Accountability (single leader)
- Drug expertise (pharmacist)
- Action (recommendation implementation)
- Surveillance (usage and resistance
- Education (prescribers)
- Data sharing

# National Action Plan on Antimicrobial Resistance (AMR)

# Objective 1: Improve awareness and understanding of AMR through effective communication, education and training

Potential measures of effectiveness: extent of reduction in national human consumption of antibiotics and reduction in the volume of antibiotic use in food production

**Strategy 1:** Increase national awareness of AMR through public communication programmes in human health, animal health and agricultural practice.

**Strategy 2:** Establish AMR as a core component of professional education, training, certification and development for the health and veterinary sectors

**Strategy 3:** Include AMR in school curricular in order to promote better understanding and awareness

**Strategy 4:** Provide the public media with accurate and relevant information on AMR .

## bjective 2: Strengthen the knowledge and evidence base throug urveillance and research

otential measure of effectiveness: extent of reduction in the prevalence of AMR, based on data llected through integrated programmes for surveillance of AMR throughout country.

**rategy 1:** Develop a national surveillance system that includes a core set of organisms and timicrobial medicines from both health care facilities and the community

**rategy 2:** Develop a national surveillance system for antimicrobial resistance that uses ndardized tests for identification of resistant microorganisms and operating to agreed quality ndards

**ategy 3:** Develop a national surveillance system for antimicrobial resistance that strengthens veillance in animal health

**ategy 4:** Establish a comprehensive One Health Surveillance System for AMR that promotes rticipation in regional and global networks and sharing of information

**ategy 5:** Develop a national surveillance system for antimicrobial resistance that has the capaci detect and report newly emerged resistance that may constitute a public health emergency of ernational concern (PHEIC)

**ategy 6:** Implement research to promote responsible use of antimicrobial medicines; defining proved practices for preventing infection in human and animal health

## Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

Potential measures of effectiveness: extent of reduction in the prevalence of preventable infections, and in particular the incidence of drug-resistant infections in health care settings

**Strategy 1:** Implement and strengthen hygiene and infection prevention and control; To include training and education in hygiene and infection prevention and control as core (mandatory) content in training and education for health care and veterinary professionals and in their continuing professional development and accreditation or registration.

**Strategy 2:** Strengthen national policies and standards of practice regarding infection prevention and control activities in health facilities.

**Strategy 3:** To strengthen national surveillance on healthcare associated infections prevalence.

**Strategy 4:** Strengthen animal health through implementation of the standards published in the OIE.

**Strategy 5:** 3.5. Promote vaccination as a method of reducing infections in human and food animals.

## Objective 4: Optimize the use of antimicrobial medicines in human and animal health

Potential measure of effectiveness: extent of reduction in national human consumption of antibiotics and the consumption of antibiotics used in food production (terrestrial and aquatic livestock, and other agricultural practices), and the use of medical and veterinary antimicrobial agents for applications other than human and animal health

**Strategy 1:** Activities of distribution, prescription & dispensing of antimicrobials are carried out in accordance with national legislation.

**Strategy 2:** Marketing authorization is given only to antimicrobial agents that are quality assured safe & efficacious.

**Strategy 3:** To develop & implement the national & institutional essential medicines lists guided by the WHO Model Lists of Essential Medicines & standard treatment guidelines to guide purchasing & prescribing of antimicrobial medicines & regulation & control of promotional practices by industry.

**Strategy 4:** Laboratory capacity to identify pathogens & their antimicrobial susceptibility.

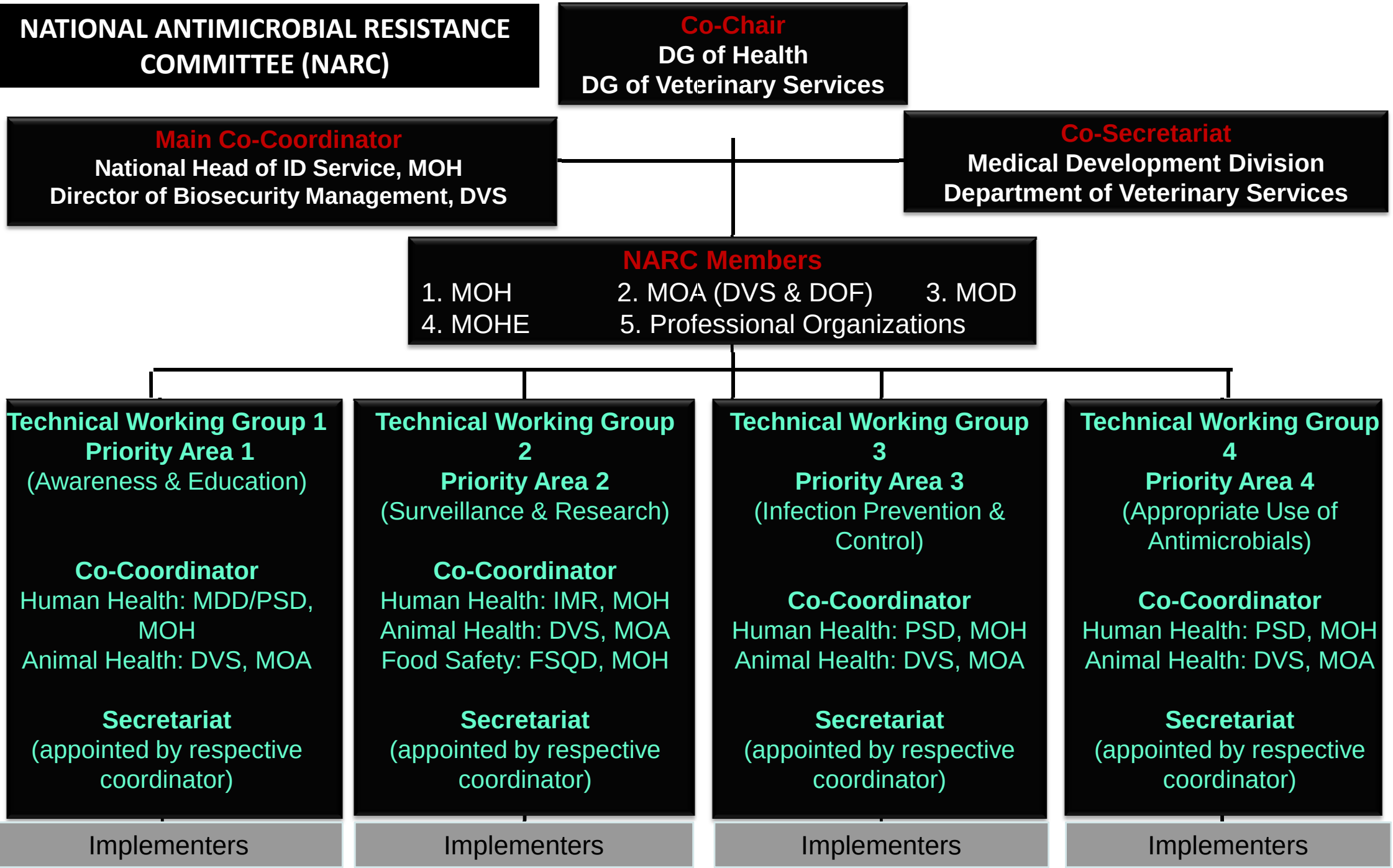
## Objective 4: Optimize the use of antimicrobial medicines in human and animal health

**Strategy 5:** Provision of stewardship programmes.

**Strategy 6:** Identification & elimination of economic incentives in all sectors that encourage inappropriate use of antimicrobial agents & introduction of incentives to optimize use.

**Strategy 7:** Develop policies on use of antimicrobial agents in terrestrial & aquatic animals including implementation of Codex Alimentarius & OIE international standards & guidelines as well as WHO/OIE guidance on the use of critically important antibiotics & reduction in nontherapeutic use of antimicrobial medicines in animal health.

# National Antimicrobial Resistance Committee (NARC)


NATIONAL ANTIMICROBIAL RESISTANCE COMMITTEE (NARC)
Co-Chair
DG of Health
DG of Veterinary Services
Main Co-Coordinator
National Head of ID Service, MOH
Director of Biosecurity Management, DVS
Co-Secretariat
Medical Development Division
Department of Veterinary Services
NARC Members
1. MOH
2. MOA (DVS & DOF)
3. MOD
4. MOHE
5. Professional Organizations
Technical Working Group 1
Priority Area 1
(Awareness & Education)
Co-Coordinator
Human Health: MDD/PSD, MOH
Animal Health: DVS, MOA
Secretariat
(appointed by respective coordinator)
Technical Working Group 2
Priority Area 2
(Surveillance & Research)
Co-Coordinator
Human Health: IMR, MOH
Animal Health: DVS, MOA
Food Safety: FSQD, MOH
Secretariat
(appointed by respective coordinator)
Technical Working Group 3
Priority Area 3
(Infection Prevention & Control)
Co-Coordinator
Human Health: PSD, MOH
Animal Health: DVS, MOA
Secretariat
(appointed by respective coordinator)
Technical Working Group 4
Priority Area 4
(Appropriate Use of Antimicrobials)
Co-Coordinator
Human Health: PSD, MOH
Animal Health: DVS, MOA
Secretariat
(appointed by respective coordinator)
Implementers
Implementers
Implementers
Implementers

# Members of NARC

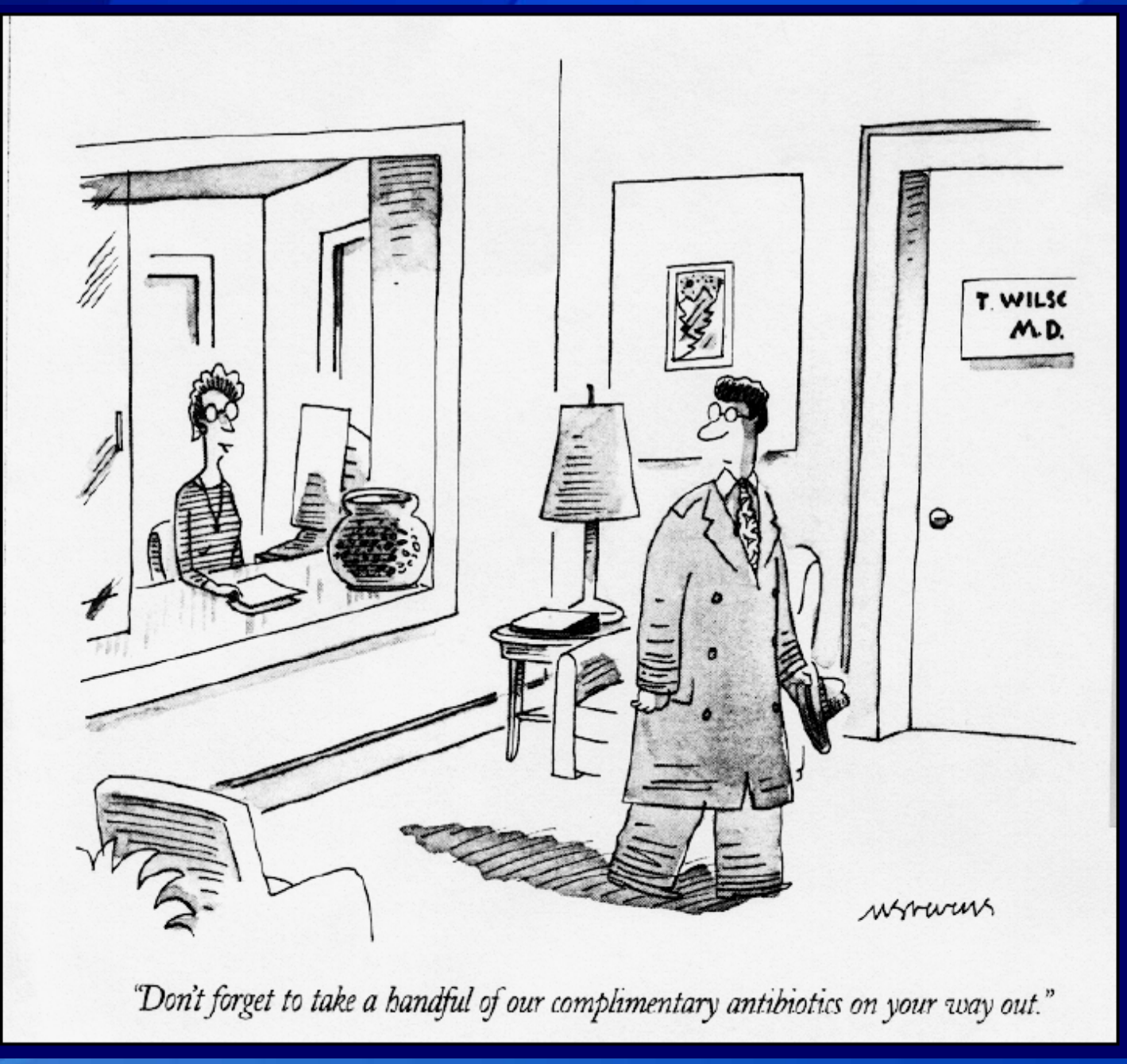
DG of Department of Fisheries
DG of Ministry of Defense (Medical)
Deputy DG of Health (Public Health)
Deputy DG of Health (Medical)
Deputy DG of Health (Research and Technical Support)
Deputy DG of Department of Veterinary Services (Veterinary Health)
Deputy DG of Department of Veterinary Services (Development)
Principal Director of Oral Health
Senior Director of Pharmaceutical Services
Senior Director of Food Safety and Quality
Senior Director of Commodity Development Division, Department of Veterinary Services
Senior Director of

- Senior Director of Biosecurity Managem & SPS Division **(Main Co-coordinator f Animal Health)**
- Director of Medical Development Divisio
- Director of Disease Control Division
- Director of Institute of Medical Research
- Director of Veterinary Research Institute
- Director of Department of Veterinary Services and Animal Industry, Sabah
- Director of Veterinary Division, Sarawak Agriculture Department
- National Head of Infectious Disease Ser **(Main Co-coordinator for Human Heal**

# Members of NARC

Dean of Medical Faculty, University Malaya
Dean of Medical Faculty, Universiti Kebangsaan Malaysia
Dean of Medical Faculty, Universiti Sains Malaysia
Dean of Veterinary Medicine Faculty, Universiti Putra Malaysia
Master of Academy of Medicine
President of Malaysian Medical Associations (MMA)
President of Association of Private Hospitals Malaysia (APHM)
President of Malaysian Society of Infectious Disease & Chemotherapy (MSIDC)
President of Malaysian Pharmaceutical Society (MPS)
President of Malaysian Community Pharmacy Guild (MCPG)
President of Islamic Medical Association Malaysia (IMAM)
President of Malaysian Dental Association (MDA)
President of Veterinary Association Malaysia (VAM)
President of Malaysian Society of Animal Production (MSAP)
President of Federation of Livestock Farmers

- President of Malaysian Association of Food Animal Veterinarian (MAFAV)
- President of Ruminant Farmers Association Malaysia
- President Malaysian Animal Health & Nutrition Industry Association (MAHIA)
- President of Malaysian Shrimp Industry Association
- Head of Infection Control Unit, MOH **(NARC Secretary of Human Health)**
- Head of Zoonosis and Public Health Unit**,** DVS **(NARC Secretary of Animal Health)**
- Co-coordinators - human health TWG 1 (Awareness and Education)
- Co-coordinators - animal health TWG 1 (Awareness and Education)
- Co-coordinators - human health TWG 2 (Surveillance and Research)
- Co-coordinators - animal health TWG 2 (Surveillance and Research)
- Co-coordinators - food safety TWG 2 (Surveillance and Research)
- Co-coordinators - human health TWG 3 (Infection Preventio and Control)
- Co-coordinators - animal health TWG 3 (Infection Preventio and Control)
- Co-coordinators - human health TWG 4 (Appropriate Use o




"Don't forget to take a handful of our complimentary antibiotics on your way out."

# THANK YOU

No Action Today,
No Cure Tomorrow