How to prevent the development of catastrophic antibiotic resistance in developing countries?

Or is it already catastrophic...?

Oxford University Clinical Research Unit

Vietnam

Heiman Wertheim MD PhD

ECCMID 2013


WELCOMES HRH THE PRINCE ANDREW
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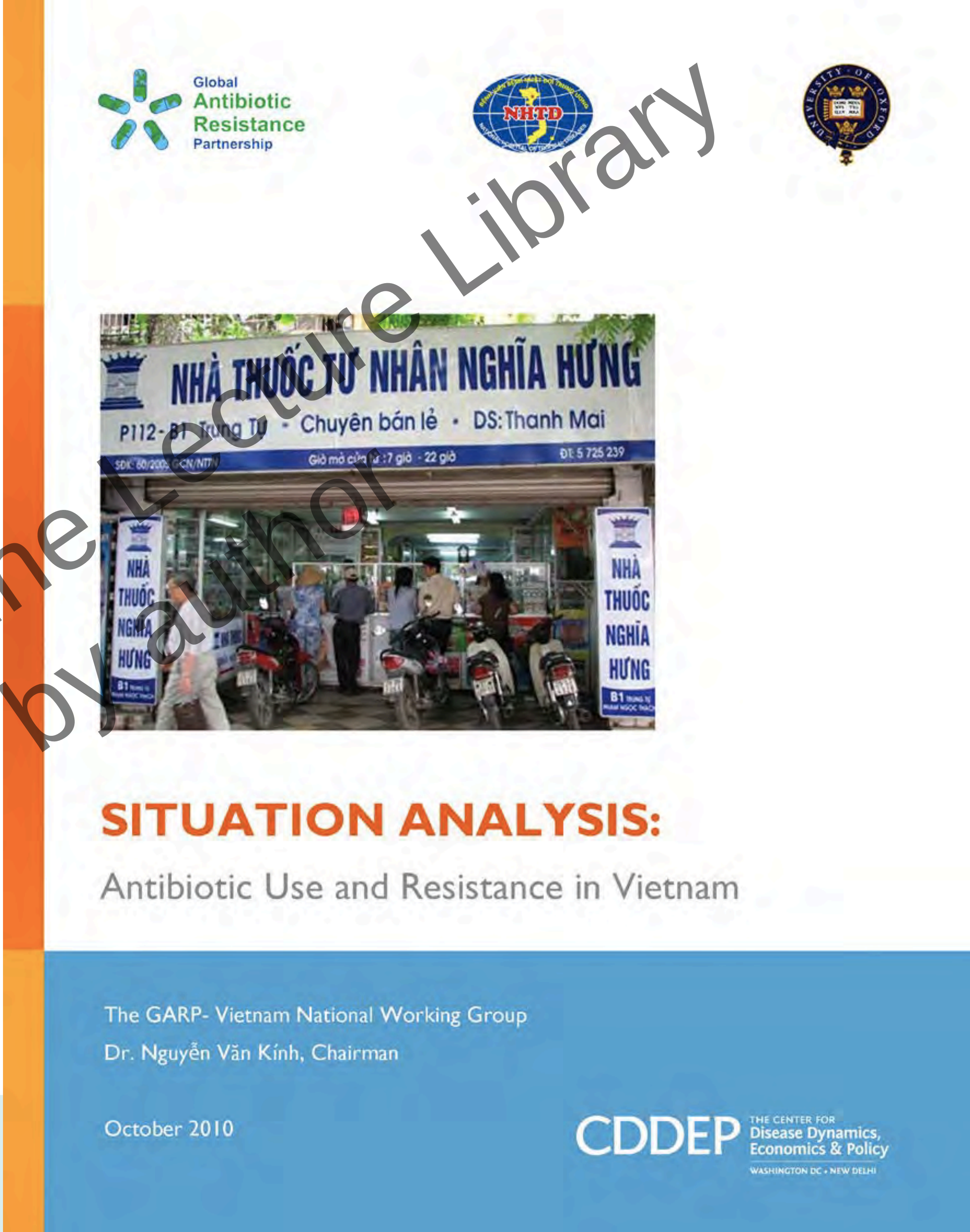
BỆNH VIỆN
ĐỚI TRUNG ƯƠNG
TROPICAL DISEASES

Vietnam:
Situation analysis report released in January 2011

Available at:
www.cddep.org/publications/



This talk

- What is catastrophic antibiotic resistance?

- Are we there yet?
  - If so, can we reverse or improve the situation?

- Note:
  - The issue is global and not just in developing countries
  - I cover only bacterial antibiotic resistance (not TB)

Even developed countries are still developing

Catastrophic (Oxford dictionary)

- *Adj.*
  - –Involving or causing sudden great damage or suffering (*a catastrophic earthquake*)
  - –Extremely unfortunate or unsuccessful (*catastrophic mismanagement of the economy*)
  - –Involving a sudden and large-scale alteration in state

A catastrophic ICU patient in Asia

- Hospital-acquired pneumonia with multi-resistant GNB
- Treatment would be colistin
- Colistin not always readily available for human use in Asia
- Patient died
- Colistin available for agricultural use

A good mix for a catastrophe…

ANTIBIOTICS

+

RESISTANCE GENES

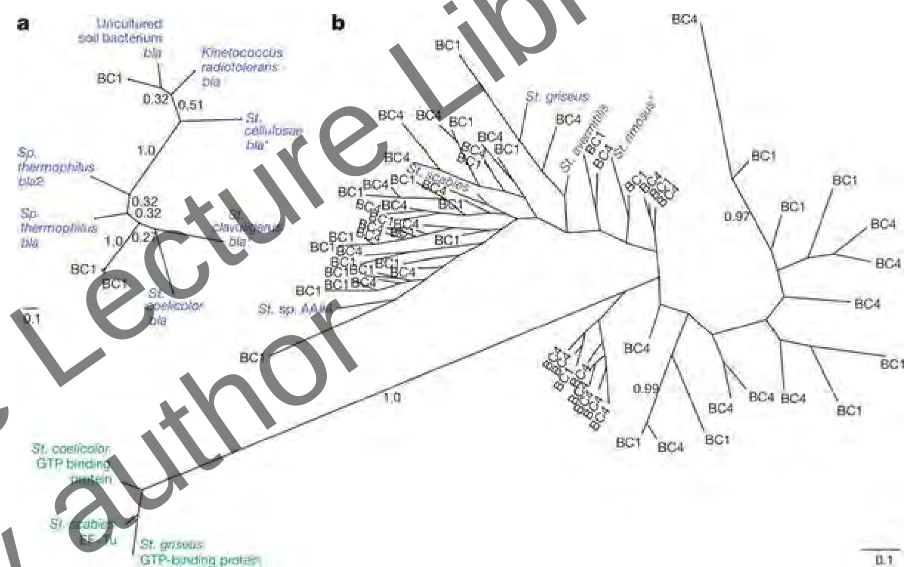
+

MOBILE GENETIC ELEMENTS

+

BACTERIAL PATHOGENS

Resistance is old and abound



DaCosta, Nature 2011

Antibiotic Resistance Is Prevalent in an Isolated Cave Microbiome

Kirandeep Bhullar[1], Nicholas Waglechner[1], Andrew Pawlowski[1], Kalinka Koteva[1], Eric D. Banks[2], Michael D. Johnston[2], Hazel A. Barton[2], Gerard D. Wright[1]*

1 M.G. DeGroote Institute for Infectious Disease Research, Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada, 2 Department of Biology, University of Akron, Akron, Ohio, United States of America

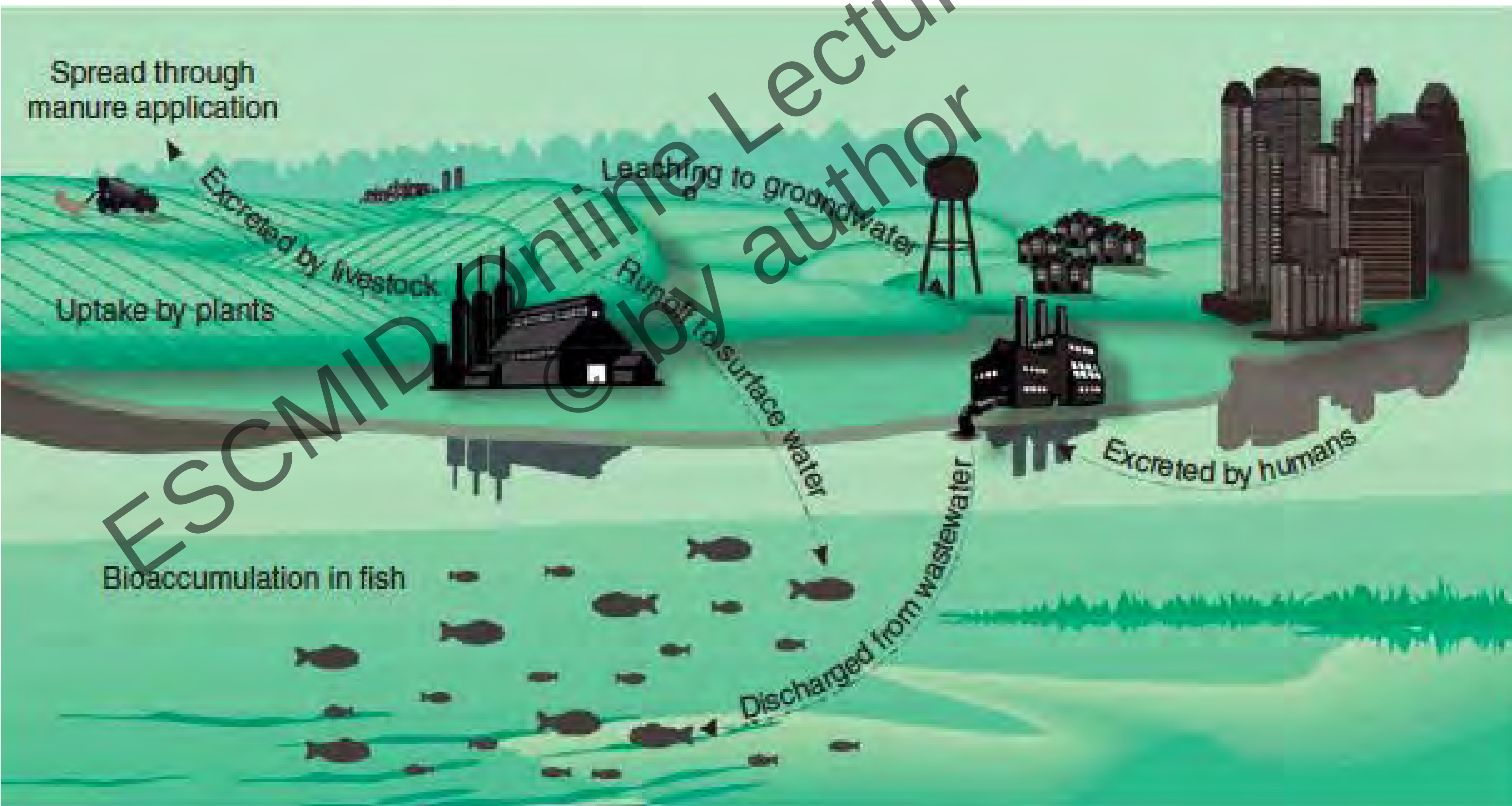
Abstract

Antibiotic resistance is a global challenge that impacts all pharmaceutically used antibiotics. The origin of the genes associated with this resistance is of significant importance to our understanding of the evolution and dissemination of antibiotic resistance in pathogens. A growing body of evidence implicates environmental organisms as reservoirs of these resistance genes; however, the role of anthropogenic use of antibiotics in the emergence of these genes is controversial. We report a screen of a sample of the culturable microbiome of Lechuguilla Cave, New Mexico, in a region of the cave that has been isolated for over 4 million years. We report that, like surface microbes, these bacteria were highly resistant to antibiotics; some strains were resistant to 14 different commercially available antibiotics. Resistance was detected to a wide range of structurally different antibiotics including daptomycin, an antibiotic of last resort in the treatment of drug resistant Gram-positive pathogens. Enzyme-mediated mechanisms of resistance were also discovered for natural and semi-synthetic macrolide antibiotics via glycosylation and through a kinase-mediated phosphorylation mechanism. Sequencing of the genome of one of the resistant bacteria identified a macrolide kinase encoding gene and characterization of its product revealed it to be related to a known family of kinases circulating in modern drug resistant pathogens. The implications of this study are significant to our understanding of the prevalence of resistance, even in microbiomes isolated from human use of antibiotics. This supports a growing understanding that antibiotic resistance is natural, ancient, and hard wired in the microbial pangenome.

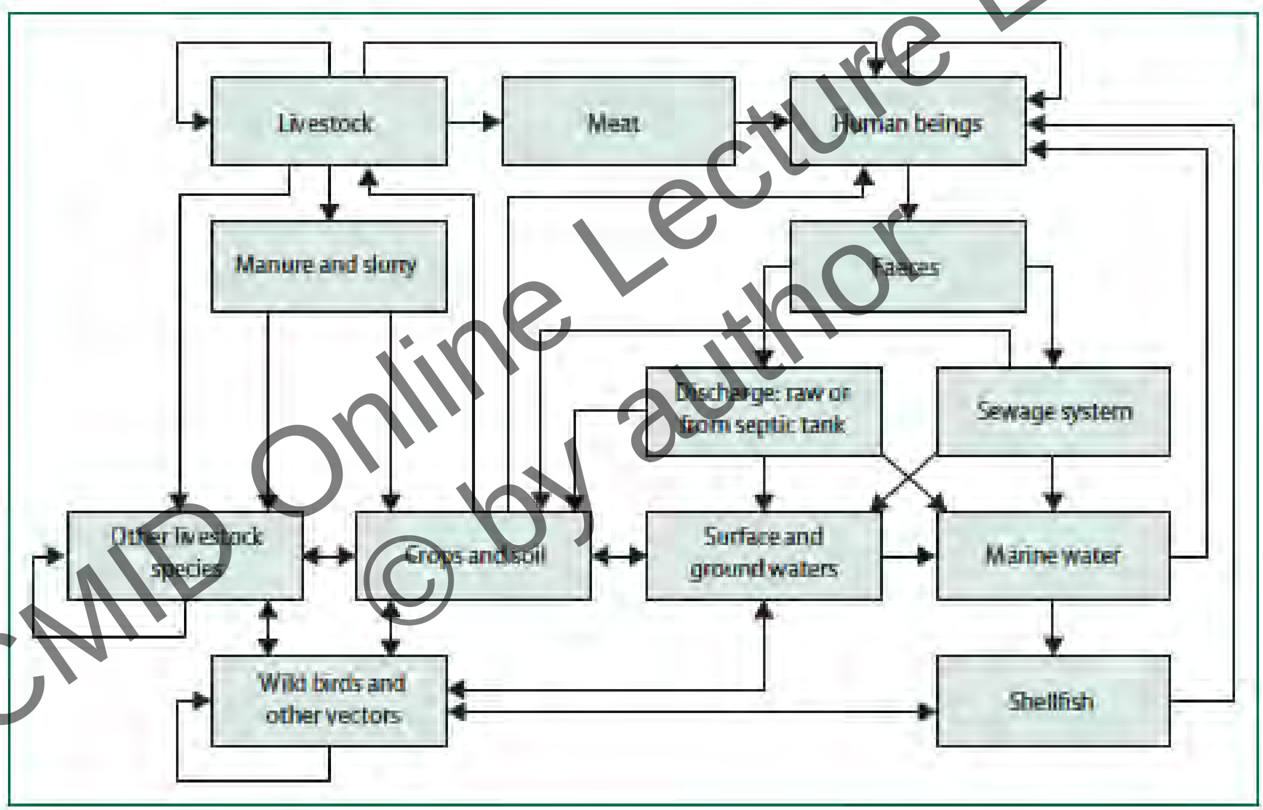
And resistance genes are easily shared

Smillie, Nature 2011

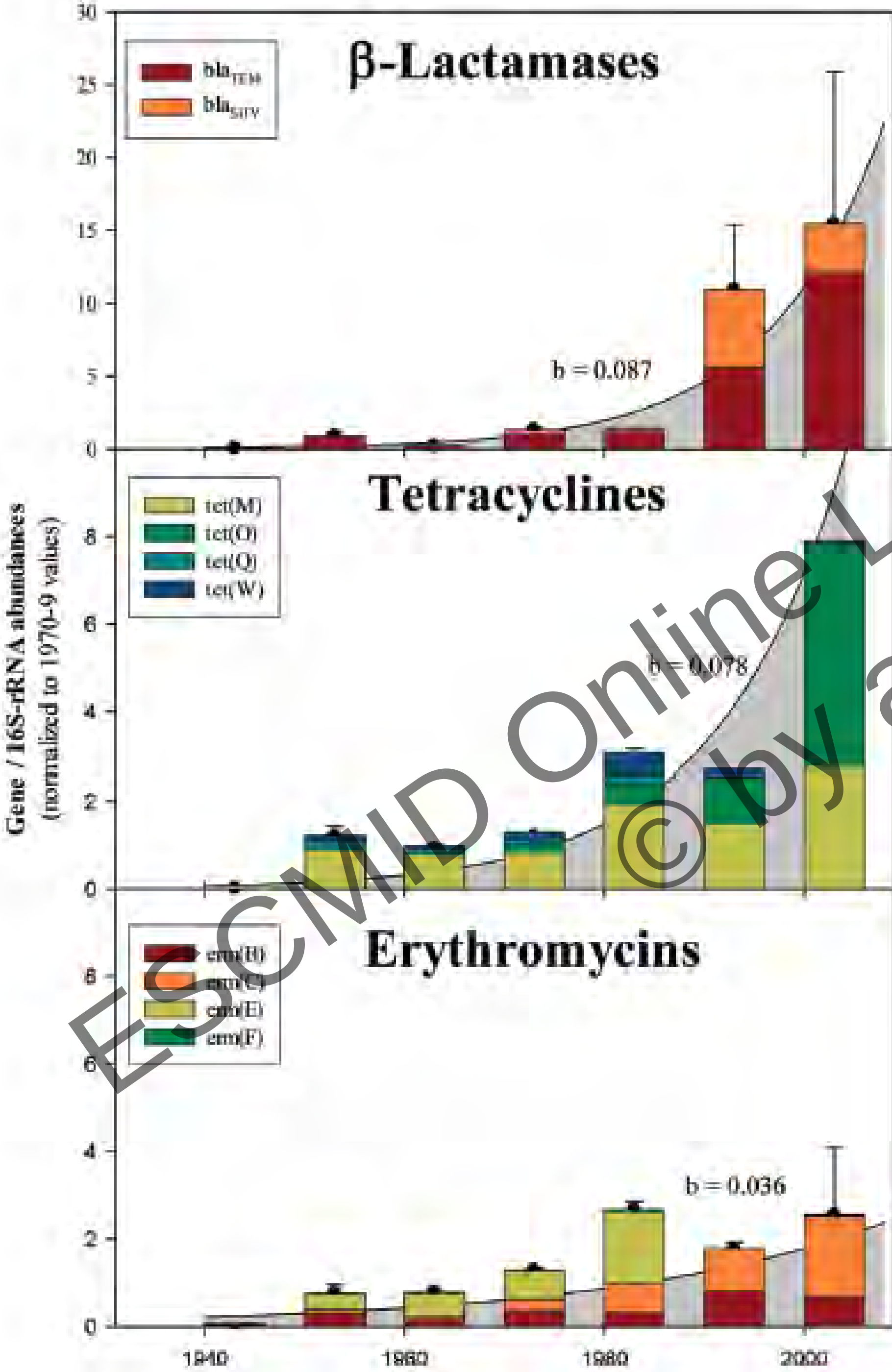
Resistance genes are shared in various environments with(out) AB pressure



Places of resistance gene exchange



Wellington, Lancet Inf Dis 2013



Increase in soil resistance genes since 1940

FIGURE 2. Relative increase of antibiotic resistance genes among soils collected at five sites in The Netherlands from 1940 to 2008. All values have been normalized to 16S rRNA gene abundances. Normalized values were then grouped according to decade and unitized relative to mean observed values from 1970 to 1979 for each site. Normalization and unitization were required to account for differences in bacterial abundances among sites and place data from each site into a common unit of measure. Each time series represents the unbiased sum of standardized values from all five sites. Table S2 provides detailed data for each site. *mecA*, *bla*$_{OXA-1}$, *vanA* and *ampC* were analyzed, but were below detection limits. Shaded areas are the best-fit curves for each class of detected antibiotics assuming a first-order model, which represents the basal level of resistance genes within the soils. Inset rate coefficients are for each class of antibiotic. Rate coefficients for each individual detected gene are provided in Table S3.

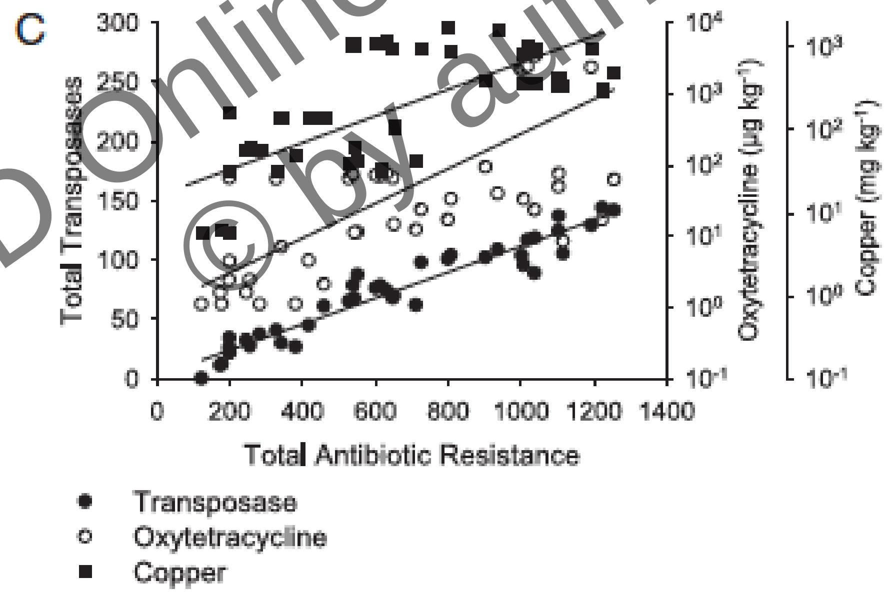
Environ. Sci. Technol. **2010**, *44*, 580–587

Diverse and abundant antibiotic resistance genes in Chinese swine farms

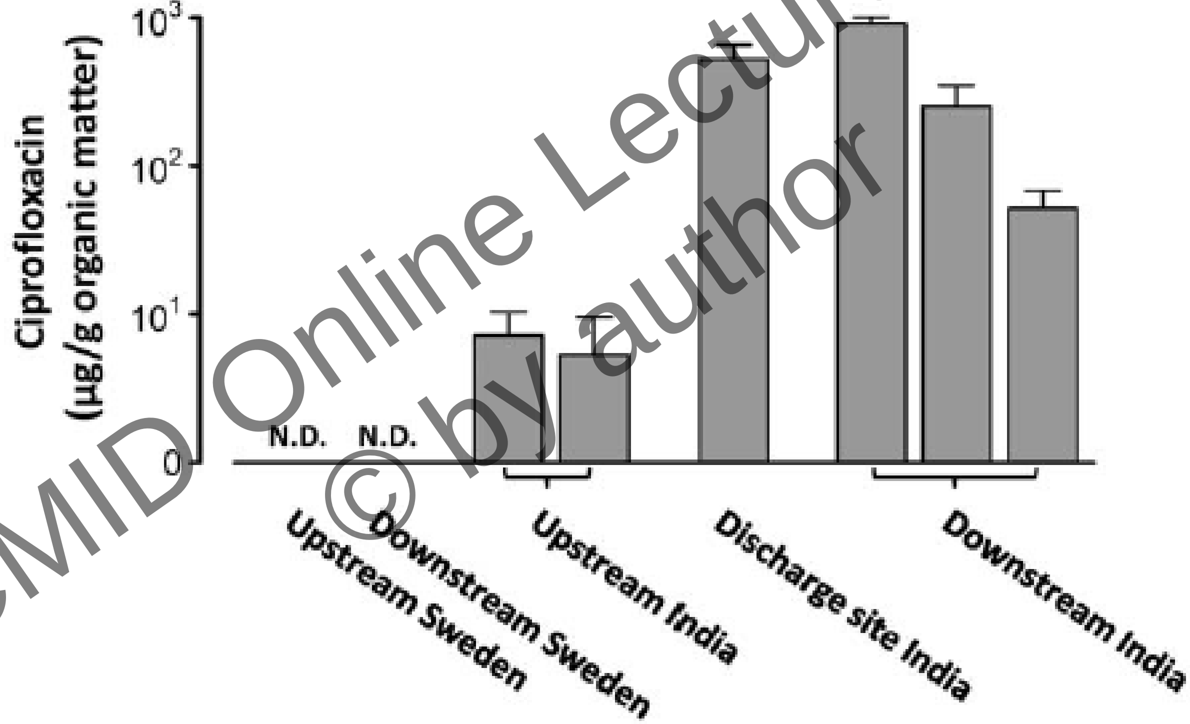
Yong-Guan Zhu[a,b,1,2], Timothy A. Johnson[c,d,1], Jian-Qiang Su[a], Min Qiao[b], Guang-Xia Guo[b], Robert D. Stedtfeld[c,e], Syed A. Hashsham[c,e], and James M. Tiedje[c,d,2]

[a]Key Lab of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen 361021, China; [b]Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing 100085, China; and [c]Center for Microbial Ecology, Departments of [d]Plant, Soil and Microbial Sciences, and [e]Civil and Environmental Engineering, Michigan State University, East Lansing, MI 48824

Contributed by James M. Tiedje, December 31, 2012 (sent for review October 31, 2012)



Antibiotic environmental contamination India



Kristiansson, PLOS ONE 2011

Resistance gene abundance ~ antibiotic

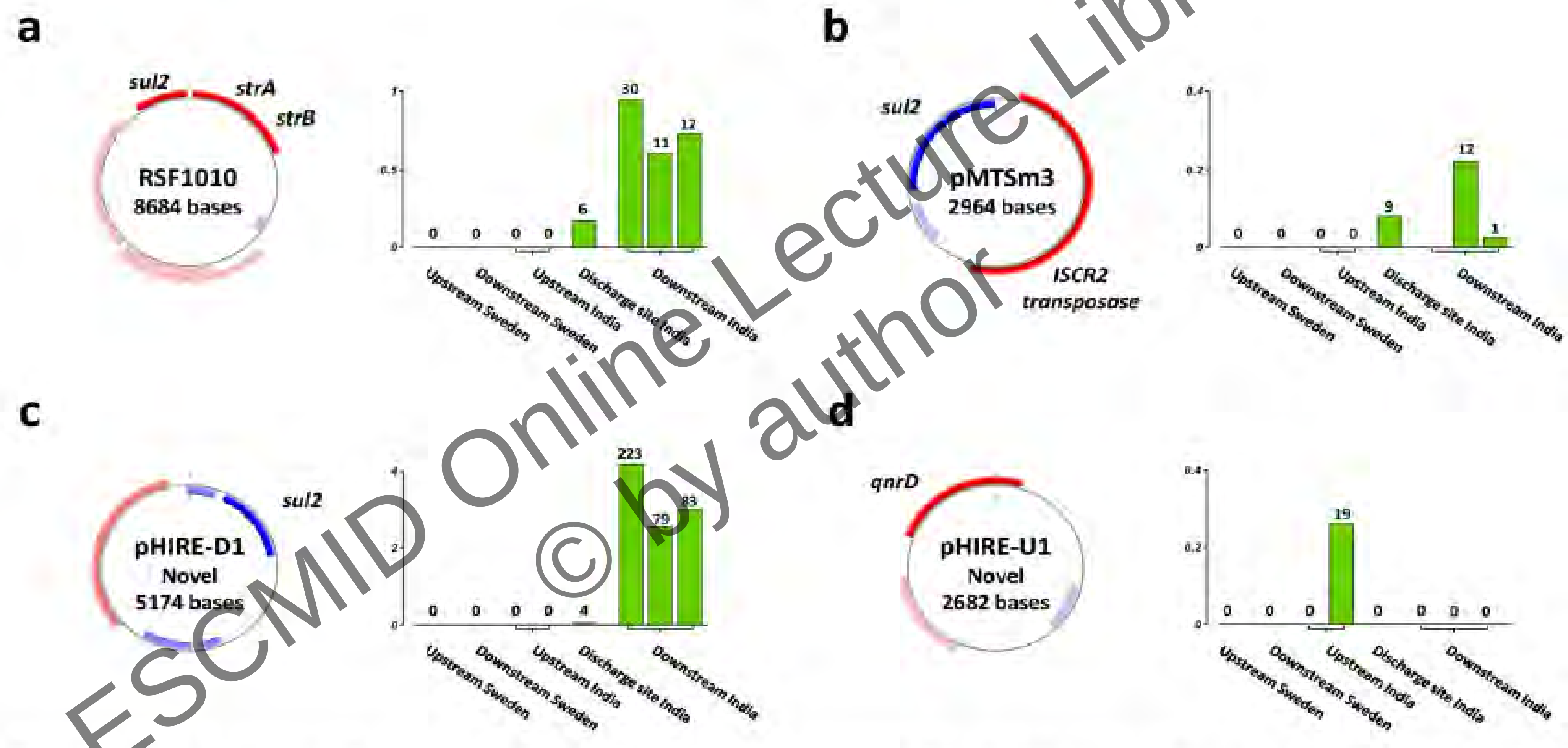


Figure 4. The abundance of resistance-carrying plasmids in environmental bacterial communities exposed to antibiotics. Four plasmids were detected at high levels, two already described (a–b) and two previously not characterized (c–d). Their relative abundance is given in relation to the total amount of sequenced DNA and the numbers above the bars show the estimated plasmid coverage in each metagenome.
doi:10.1371/journal.pone.0017038.g004

A call for other types of surveillance: genes and antibiotics

- Antibiotics should be considered to be a pollutant and monitored
- Mobile antimicrobial resistance genes should be considered as unwanted invasive genetic material
- A need for standardized resistance gene surveillance and their mobile genetic elements
- However we still need to learn how resistance gene dynamics translate into public health measures
  - E.g. When should we remove resistance genes form environment? Where? How? At what cost?
- Important role for modelers

Techniques for gene removal are being investigated

WATER RESEARCH 47 (2013) 130–140

Available online at www.sciencedirect.com

SciVerse ScienceDirect

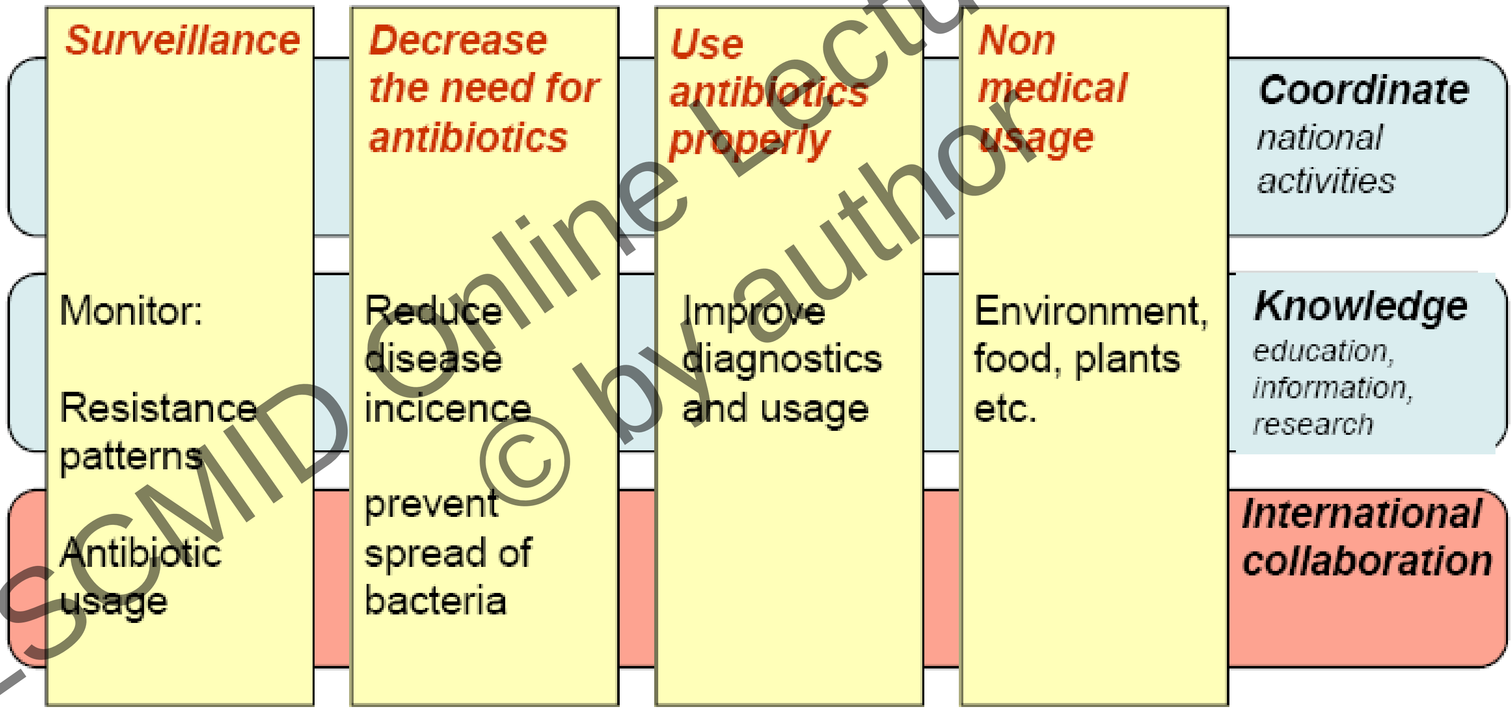
journal homepage: www.elsevier.com/locate/watres

Effect of wastewater colloids on membrane removal of antibiotic resistance genes

*Maria V. Riquelme Breazeal, John T. Novak, Peter J. Vikesland, Amy Pruden**

Via Department of Civil and Environmental Engineering, Virginia Tech, Blacksburg, VA 24061, USA

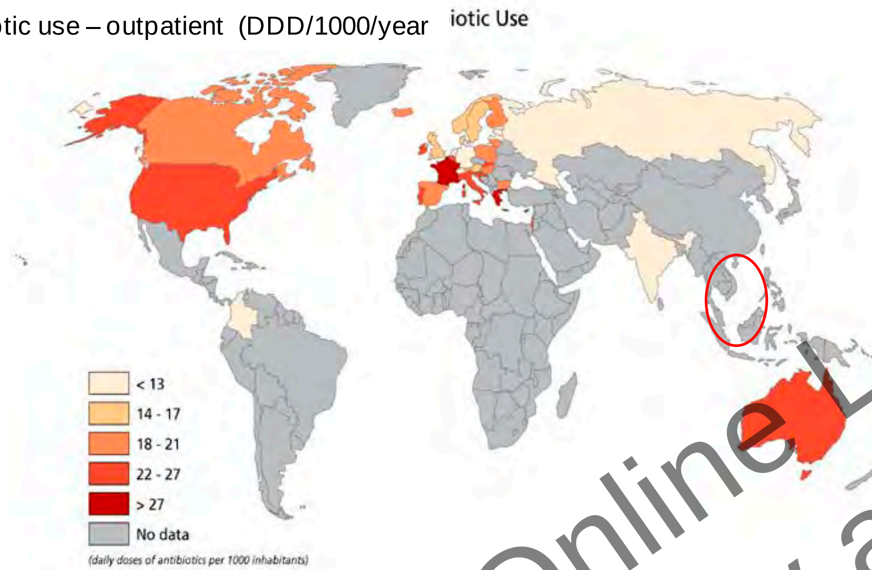
Addressing resistance



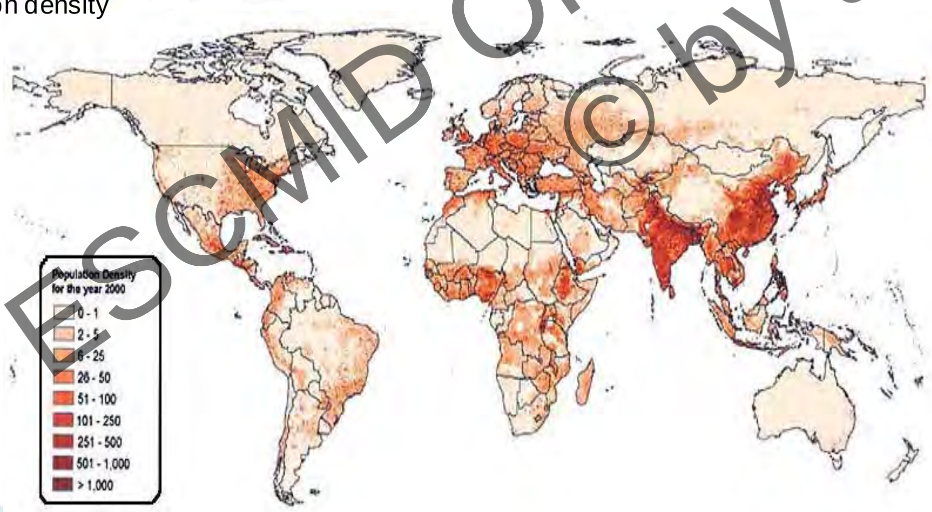
Source: ReAct

Antibiotic use in Asia?

Antibiotic use – outpatient (DDD/1000/year



Population density



- What is the current AB use for Asia?
- And what would be acceptable?

- High populations density in Asia will result in high environmental AB pressure.
- Same is true for livestock

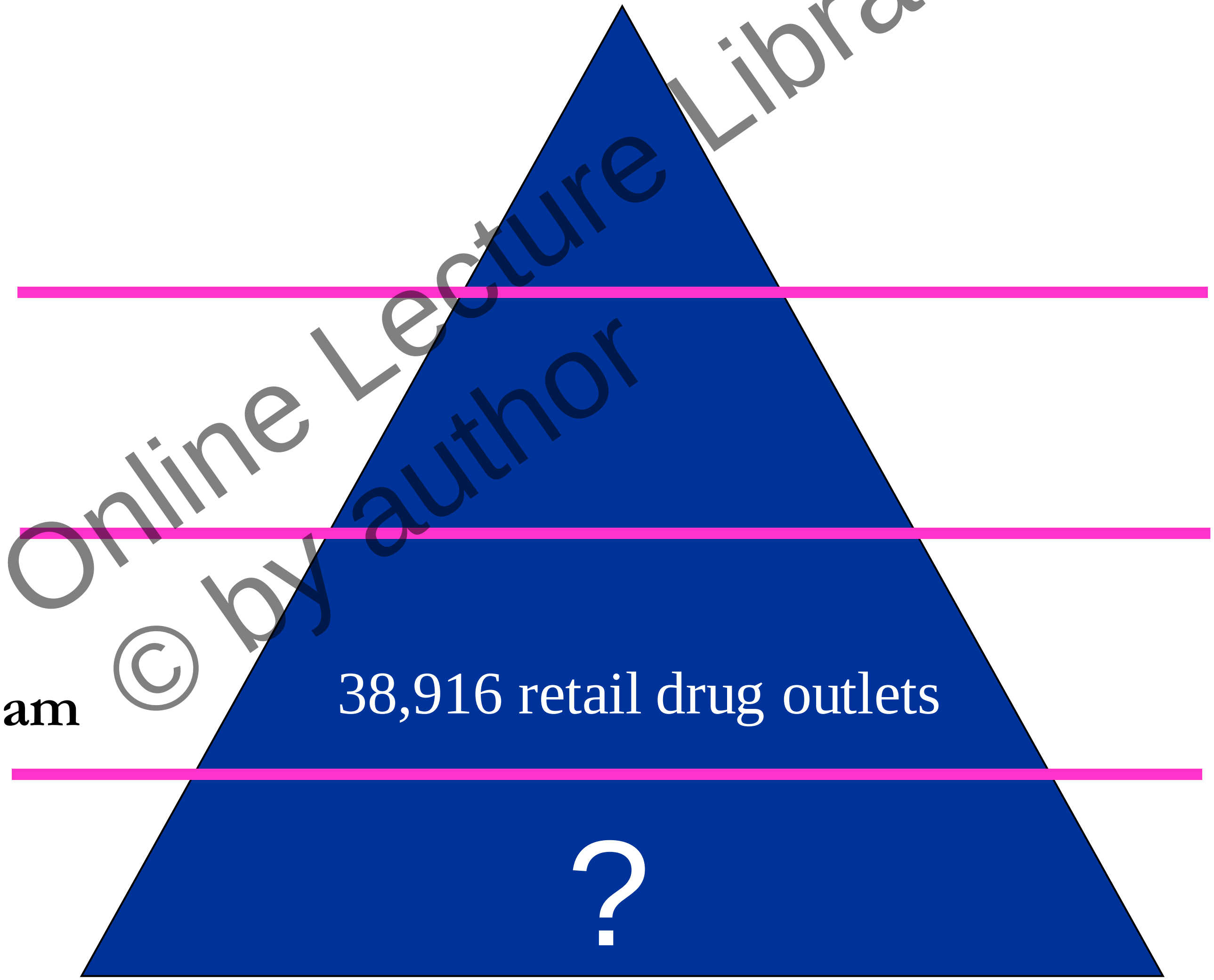
Community: key source of antibiotic use

Hospitals

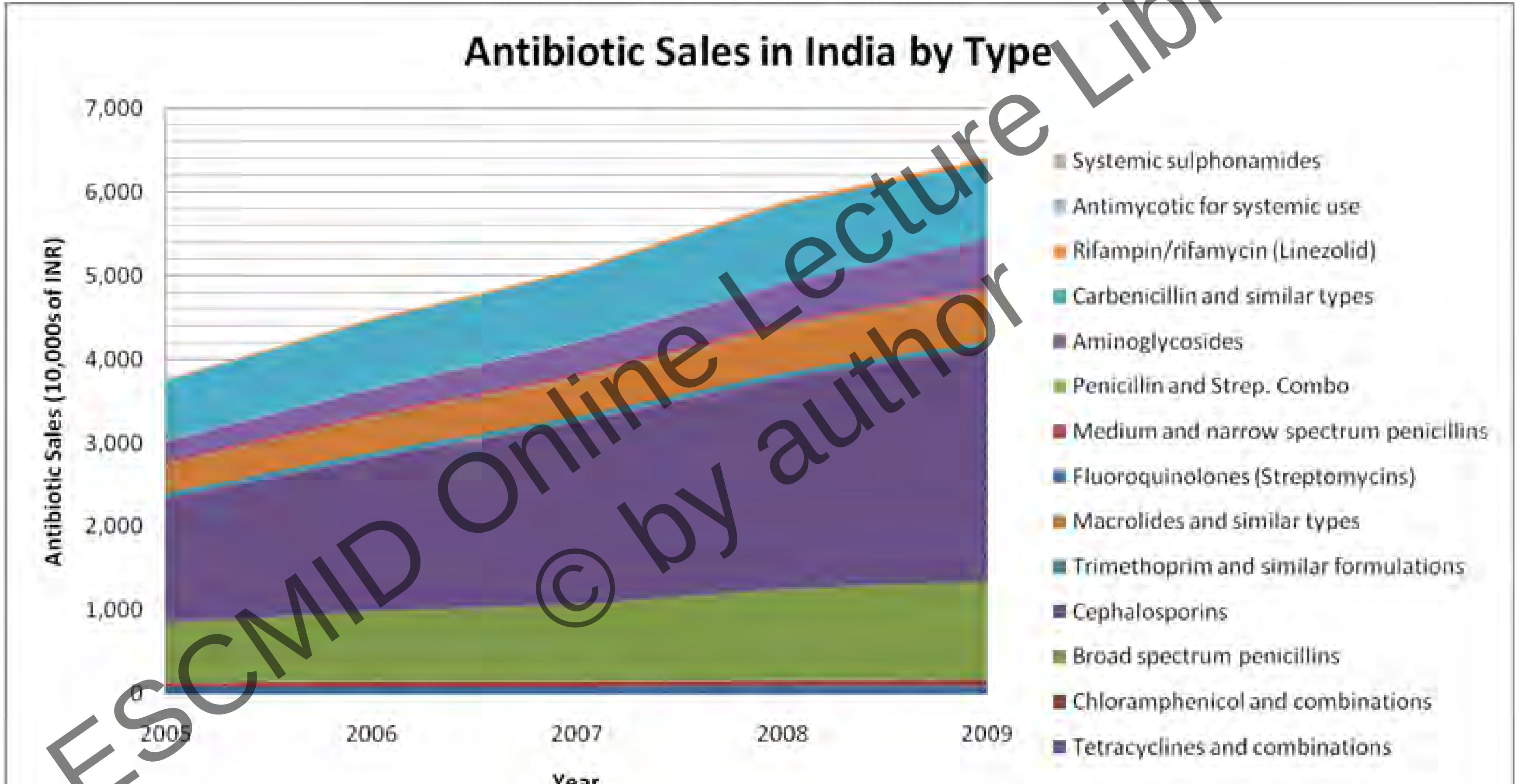
Health stations

Pharmacies in Community Vietnam

Agriculture

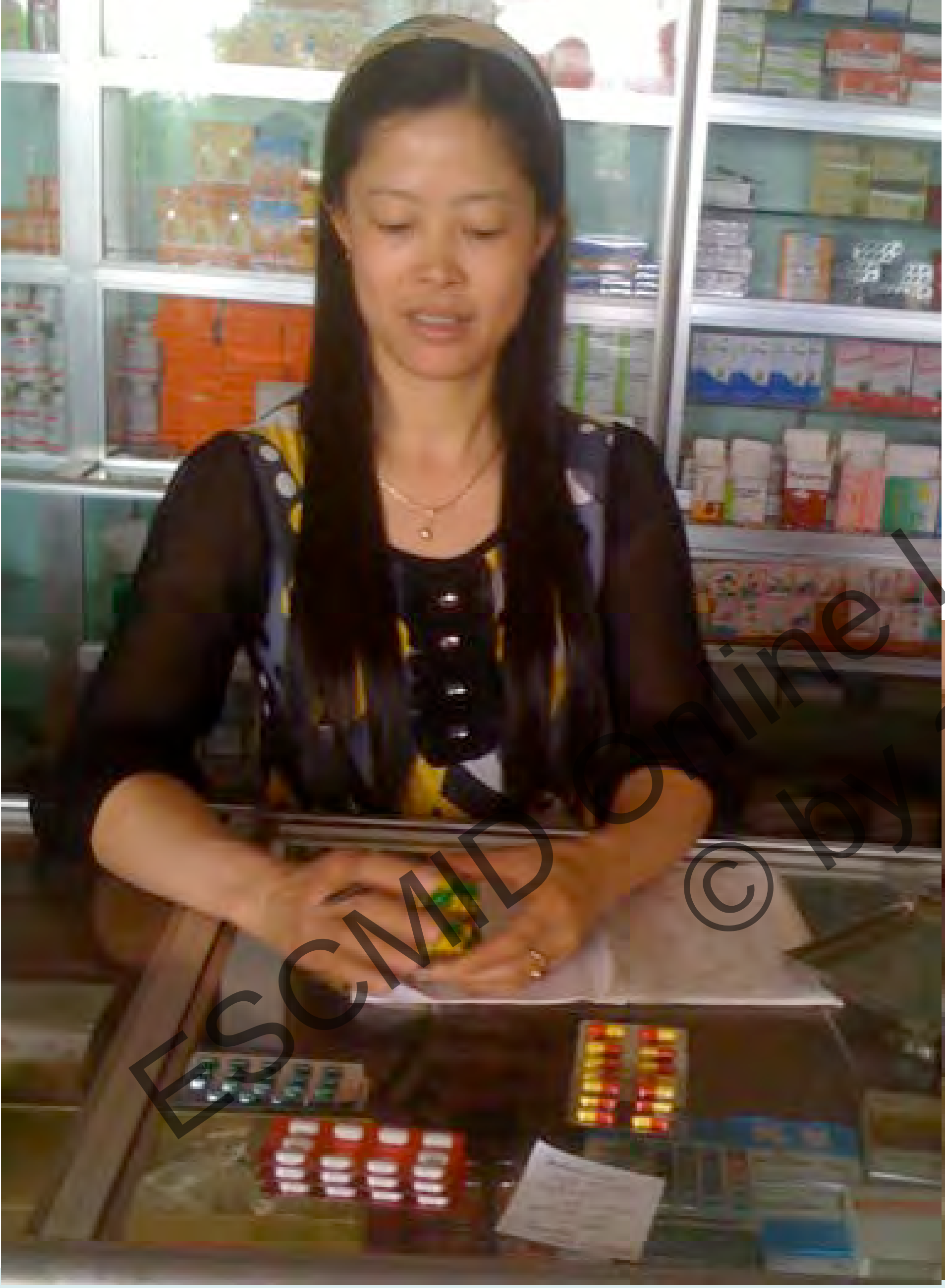


Increase wealth ~ increase antibiotic use



Source: GARP

But uncontrolled

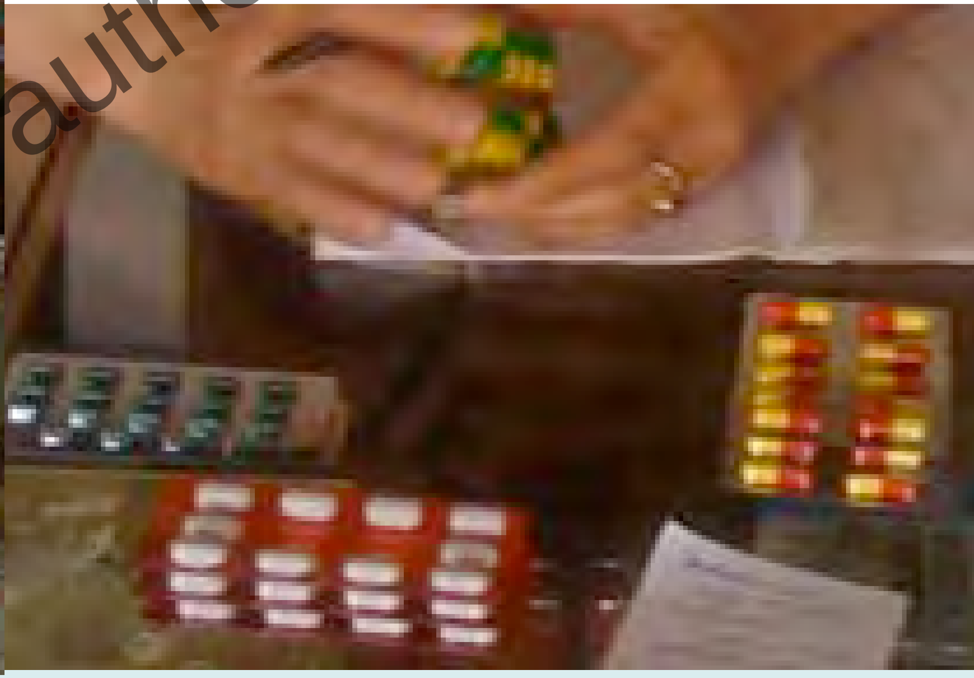


High inappropriate usage in communities for ARI

I had a cough and received 3 types of drugs, including antibiotics…

No prescription (despite law)

I did not take any drug and got better!



Important drivers of AB use resource constrained settings

- High out-of-pocket health expenditure – up to 60%
  - Self-medication is cheaper and quick
- Despite regulation, AB dispensed without prescription
  - No enforcement
- Financial incentives
- Lack of knowledge
- Lack of time doctor
- Lack of good (rapid) diagnostics

Treatment guidelines

- Most treatment guidelines outdated
- Recommendations for AB do not match current resistance data
- Guidelines use 'Western' data, not other regions
- Need to take in account local epidemiology
  - –*S. suis* common cause meningitis in SE Asia
  - –*K. pneumoniae* common in severe pneumonia

TIME

Thursday, Jan. 05, 2012

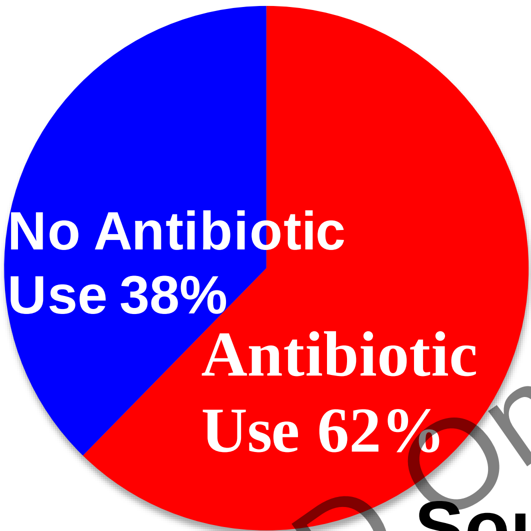
When Penicillin Pays: Why China Loves Antibiotics a Little *Too* Much

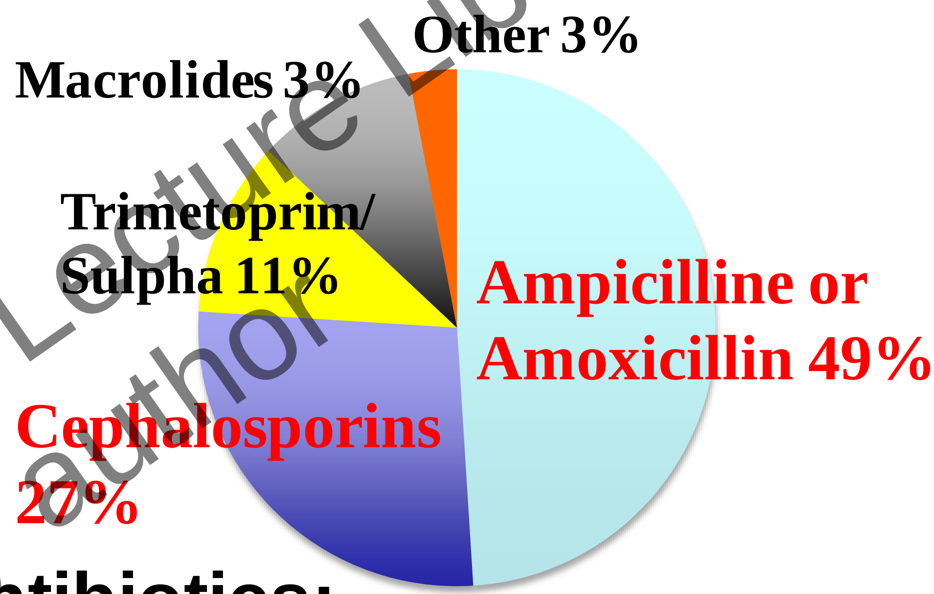
By Chengcheng Jiang / Beijing

Every year when the wet winter weather sweeps through southern Anhui province, Ling Cheng gets a niggling cough that she just can't shake. But instead of heading to the medicine cabinet, Ling, like millions of other Chinese, heads instead to her local hospital for a dose of IV antibiotics. "When the coughing gets annoying, I just go to the clinic two or three days in a row and take a drip," she says. "After that it usually clears up straight away — it's much more effective than taking pills."

Last month, the country's Ministry of Health revealed that on average each Chinese person consumes 138 g of antibiotics per year — 10 times the amount consumed per capita in the U.S. Meanwhile, three times as many Chinese people are prescribed penicillin compared with the international standard. The Ministry also pointed out that 70% of inpatients at Chinese hospitals received antibiotics; the World Health Organization (WHO) recommends a maximum of 30%. (Read about China's plan to reform its health care.)

AB use children during one month





Source antibiotics:

Self treatment	16%
Drug store	30%
Private clinic	24%
Public clinic	31%

Source:
QH Nguyen 2010

Antibiotic dispensing in private Vietnamese pharmacies

	Urban		Rural	
	n	**%**	**n**	**%**
Total transactions	2083	100	870	100
Buying antibiotics	499	24.0	257	29.5
With prescription	60	12.0	23	8.9
Comply with prescription	49	81.7	18	78.3
Not comply with prescription	11	18.3	5	21.7
Without prescription	439	88.0	234	91.1
Client made decision	218	49.7	66	28.2
Drug seller made decision	221	50.3	168	71.8

Conclusions pharmacy study

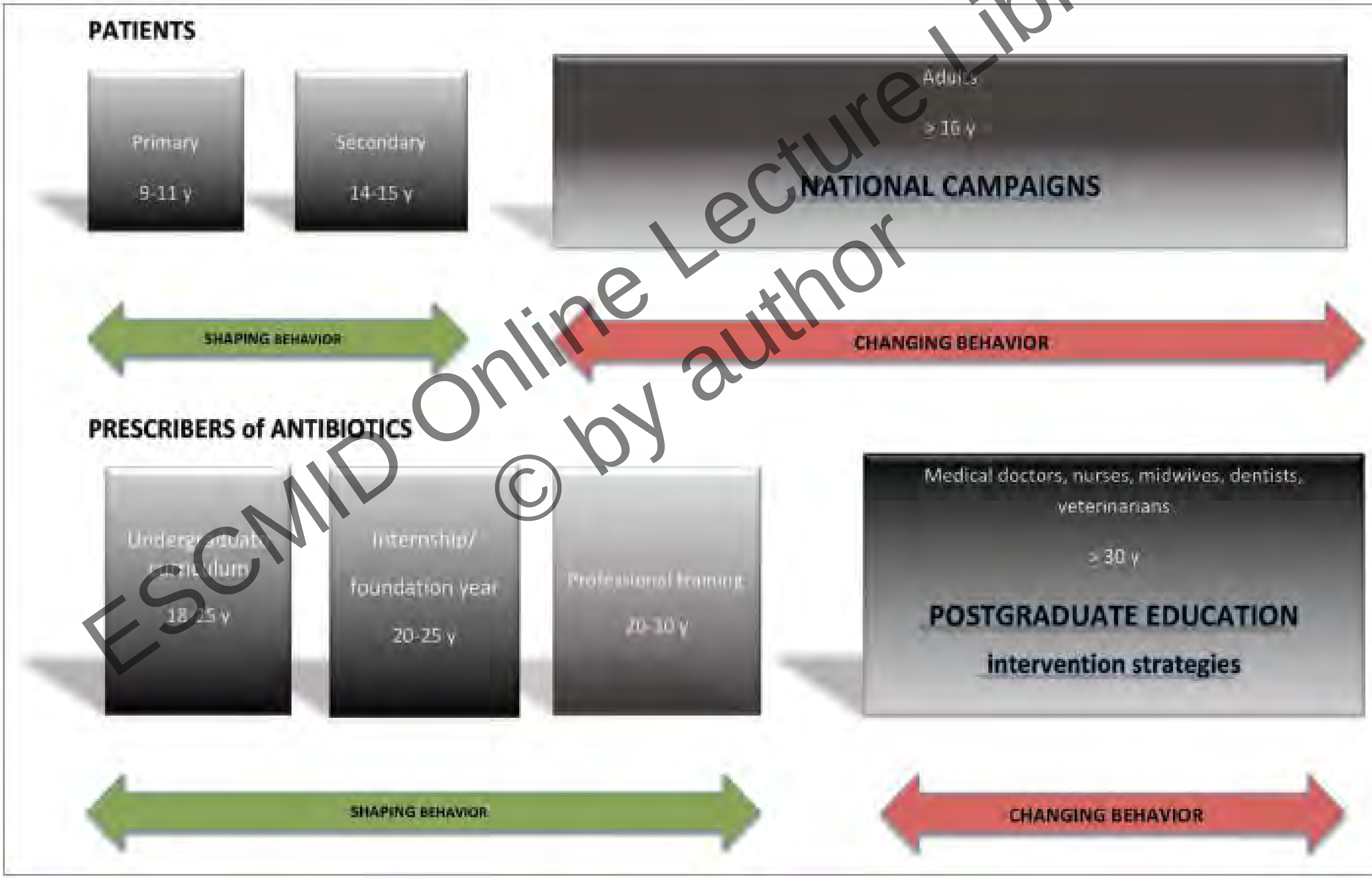
- 90% of antibiotics sold have no prescription
- Dispensed by inexperienced staff
- 25% of sales is AB sales
- Rural pharmacies sell more domestic drugs

- High AB demand from buyer -> community education
- Strong incentive for AB dispensing -> room for intervention

- Note: domestic antibiotics are often produced by companies in which the government is stakeholder.

Education - behaviour

Pulcini, Virulence 2013



Antibiotics Smart Use:
An initiative from Thailand

Objective:

- Reduce antibiotics prescriptions in three common diseases:
  - Upper respiratory tract infection (URI) e.g., common cold with/without sore throat
  - Acute diarrhea
  - Simple wound

PRECEDE-PROCEED Planning Model: ASU

Step 1 Social diagnosis

Step 2 Epidemiological assessment

Need assessment – To understand the situation on medication use problems in both national and local contexts. At the local context, participation with local team is crucial to understand the local situation/environment including possible causes of problems, stakeholders, etc..

Phase 3 Behavioral & environment assessment

Step 4 Educational and ecological assessment

- Cause prioritization by importance and changeability
- Selected causes:
(1)knowledge, belief, and self-efficacy of health professionals (on disease, treatment, and communication with patients)
(2)Patients' request of antibiotics

Step 5 Administrative and policy assessment

Analysis of resources, administrative procedures and organization

Planning (goal, intervention design, evaluation)

- **Tools for health professionals:** (to educate, to adjust attitudes, and to increase self-efficacy)
- **Tools for patients:** (to reduce expectation of receiving antibiotics)
- **Other measures:** Pay-for-service criteria, provincial policy, positive competition

Step 6 Implementation

Start with a training

Follow by stimulating & reminding to comply with the ASU plan as mentioned in step 5)

Predisposing factors: Knowledge, beliefs, attitudes, self-efficacy

Reinforcing factors: Patient's expectation, Peer pressure, drug promotion

Enabling factors: Hospital formulary, substitute drugs (e.g., herbal drug) and medical equipment

Prescribing behavior

Hospital context

Patient health

Quality of life

Step 7 Process evaluation

To evaluate if ASU was implemented
- whether tools were used
- whether target group expose to media/ messages

Step 8 Impact evaluation

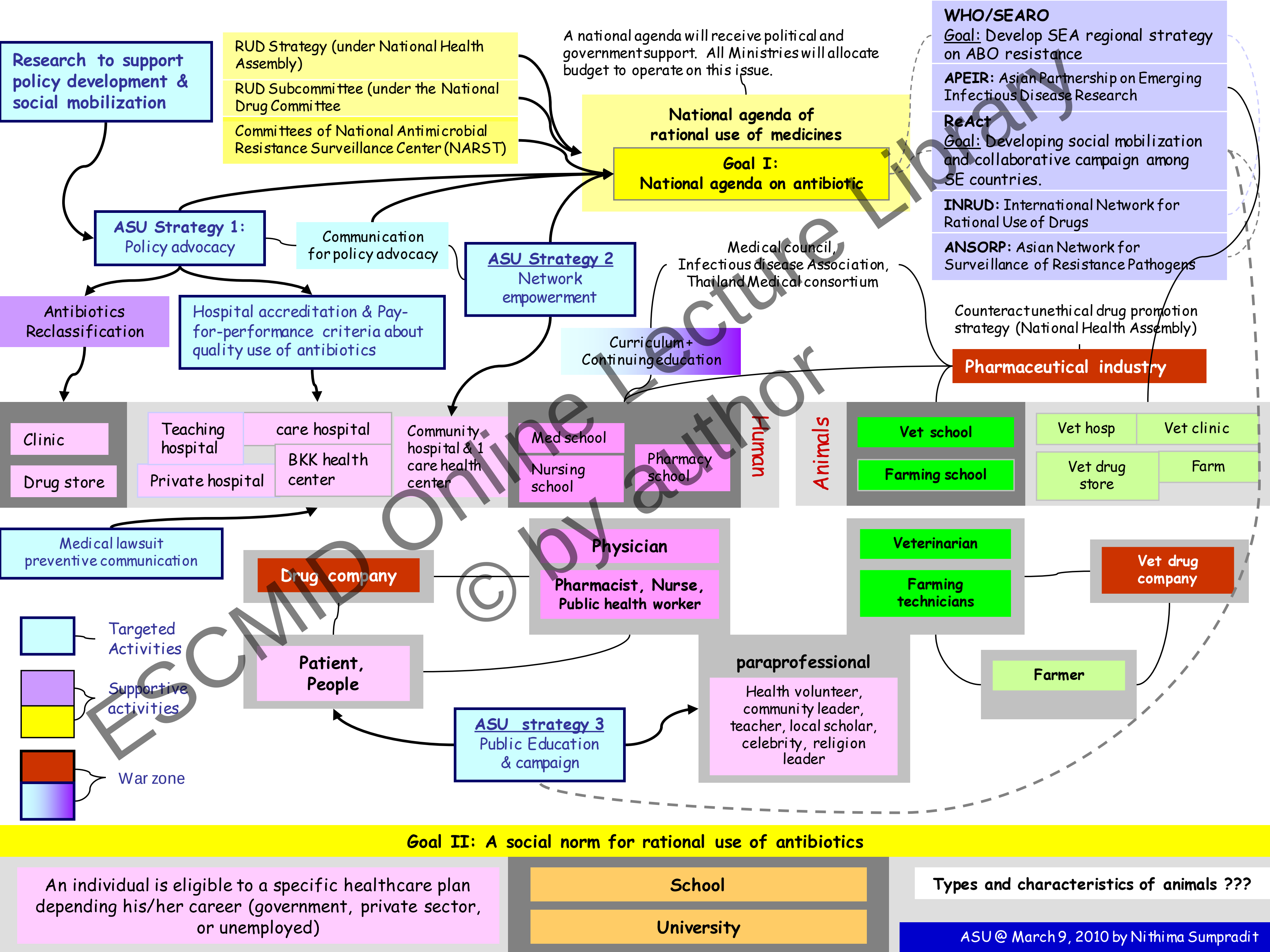
Indicator 1: Change in knowledge, attitude, self-efficacy, and intention

Indicator 2: Change in amount of antibiotics being prescribed

Indicator 3: Change in percent of targeted patients who were not prescribed with antibiotics

Step 9: Outcome evaluation

Indicator 4: Patients' perception of health and satisfaction (without antibiotics prescription)



Research to support policy development & social mobilization
RUD Strategy (under National Health Assembly)
RUD Subcommittee (under the National Drug Committee
Committees of National Antimicrobial Resistance Surveillance Center (NARST)
A national agenda will receive political and government support. All Ministries will allocate budget to operate on this issue.
National agenda of rational use of medicines
Goal I: National agenda on antibiotic
WHO/SEARO
Goal: Develop SEA regional strategy on ABO resistance
APEIR: Asian Partnership on Emerging Infectious Disease Research
ReAct
Goal: Developing social mobilization and collaborative campaign among SE countries.
INRUD: International Network for Rational Use of Drugs
ANSORP: Asian Network for Surveillance of Resistance Pathogens
ASU Strategy 1: Policy advocacy
Communication for policy advocacy
ASU Strategy 2
Network empowerment
Medical council, Infectious disease Association, Thailand Medical consortium
Antibiotics Reclassification
Hospital accreditation & Pay-for-performance criteria about quality use of antibiotics
Curriculum + Continuing education
Counteract unethical drug promotion strategy (National Health Assembly)
Pharmaceutical industry
Clinic
Drug store
Teaching hospital
care hospital
BKK health center
Private hospital
Community hospital & 1 care health center
Med school
Nursing school
Pharmacy school
Human
Animals
Vet school
Farming school
Vet hosp
Vet clinic
Vet drug store
Farm
Medical lawsuit preventive communication
Drug company
Physician
Pharmacist, Nurse, Public health worker
Veterinarian
Farming technicians
Vet drug company
Targeted Activities
Supportive activities
War zone
Patient, People
ASU strategy 3
Public Education & campaign
paraprofessional
Health volunteer, community leader, teacher, local scholar, celebrity, religion leader
Farmer
Goal II: A social norm for rational use of antibiotics
An individual is eligible to a specific healthcare plan depending his/her career (government, private sector, or unemployed)
School
University
Types and characteristics of animals ???
ASU @ March 9, 2010 by Nithima Sumpradit

Can CRP or other POC tests help?

Table 3. Effects of Intervention on Antibiotic Use After the Index Consultation (by CRP Category) and Within a 28-Day Follow-Up. Exploratory Data on Antibiotic Use Per Respiratory Tract Infection

Antibiotic Use	CRP Assistance % (n)	Control % (n)	RR[a]	95% CI
After index consultation	43.4 (56/129)	56.6 (73/129)	0.77	0.56-0.98
Rhinosinusitis	45.2 (33/73)	60.3 (47/78)		
LRTI	41.1 (23/56)	51.0 (26/51)		
Within 28-day follow-up	52.7 (68/129)	65.1 (84/129)	0.81	0.62-0.99
Rhinosinusitis	57.5 (42/73)	69.2 (54/78)		
LRTI	46.4 (26/56)	58.8 (30/51)		
By CRP category				
0-20 mg/L (n = 140)	26.0 (19/73)	49.3 (33/67)		
21-50 mg/L (n = 62)	56.5 (13/23)	59.0 (23/39)		
51-100 mg/L (n = 37)	68.2 (15/22)	66.7 (10/15)		
>100 mg/L (n = 19)	81.8 (9/11)	87.5 (7/8)		

CI = confidence interval; CRP = C-reactive protein; LRTI = lower respiratory tract infection; RR = relative risk.

Note: Statistical testing was not performed on the exploratory data on antibiotic use per respiratory tract infections, as this trial was designed to detect differences between the total group of patients per group.

[a] Relative risks corrected for clustering.

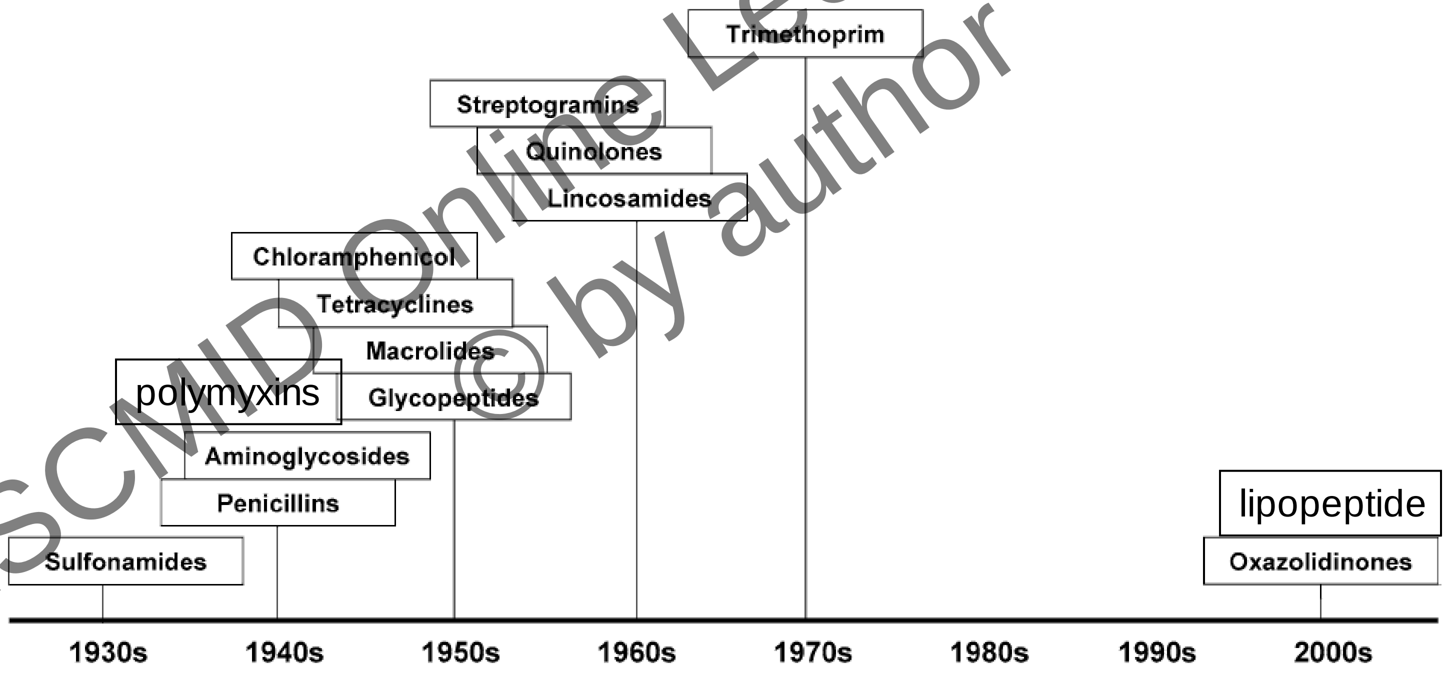
Cals, Ann Fam Med, 2010

CRP POC test trial Vietnam

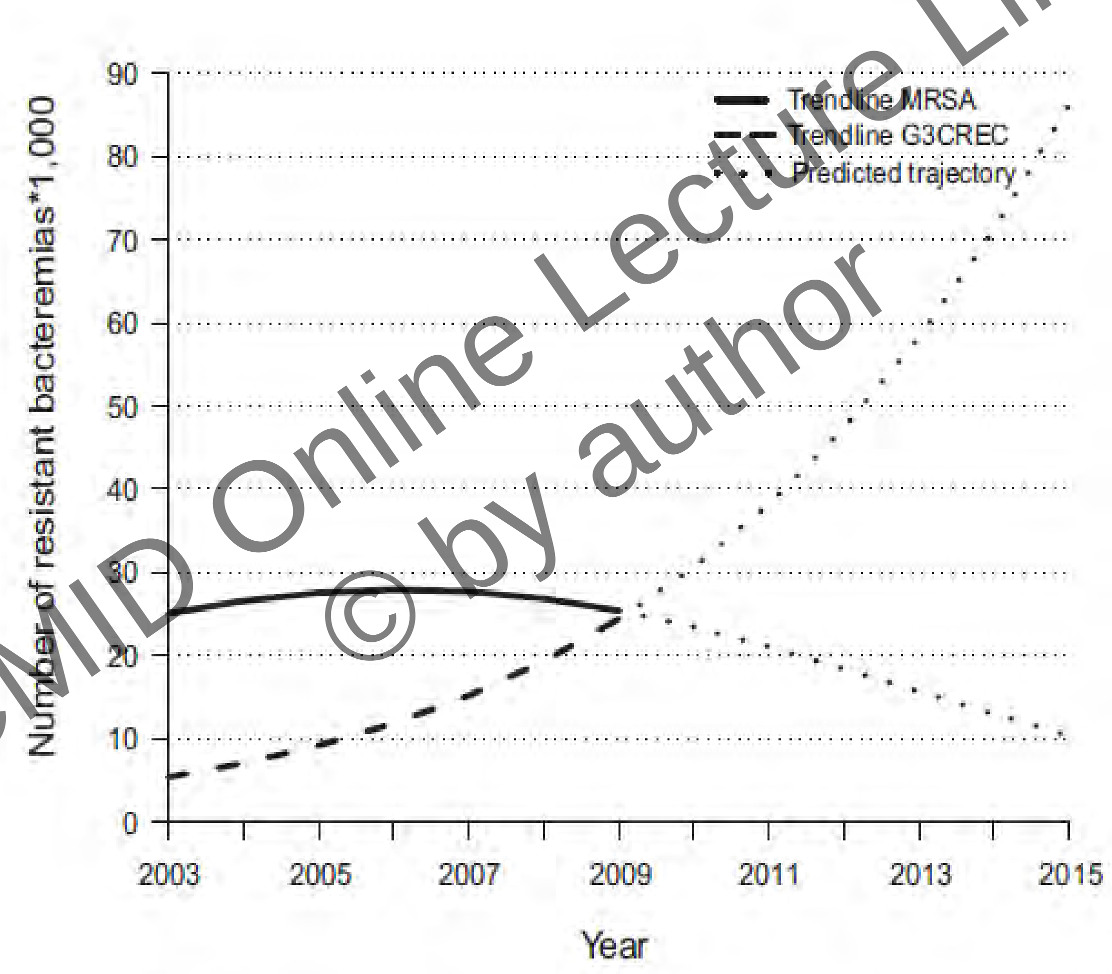
- RCT for non-severe acute respiratory infections
- Age > 5 years
- Sample size: 2000
- Ethical approval recently obtained
- Enrollment expected to start in 2 months

Antibiotic development mismatch

- Has been focused on gram- positive bacteria like MRSA and VRE
- The problem now is Gram-negative bacilli



Gram-negative resistance on the rise



Carbapenem resistant Gram-negative infections (NDM-1): a wake up call

Need to use more the 'old and forgotten'

REVIEWS OF ANTI-INFECTIVE AGENTS MAJOR ARTICLE

Louis D. Saravolatz, Section Editor

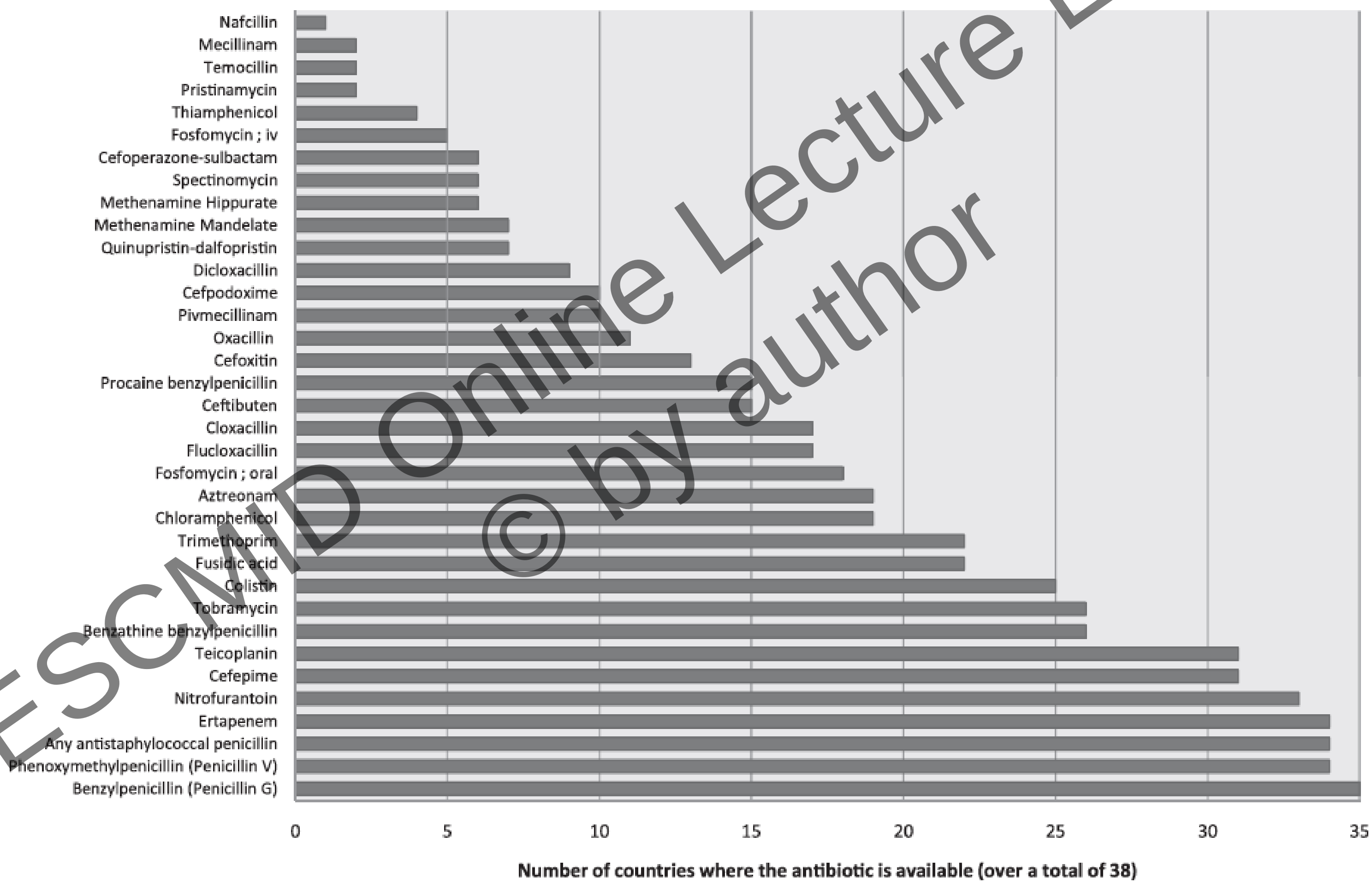
Forgotten Antibiotics: An Inventory in Europe, the United States, Canada, and Australia

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

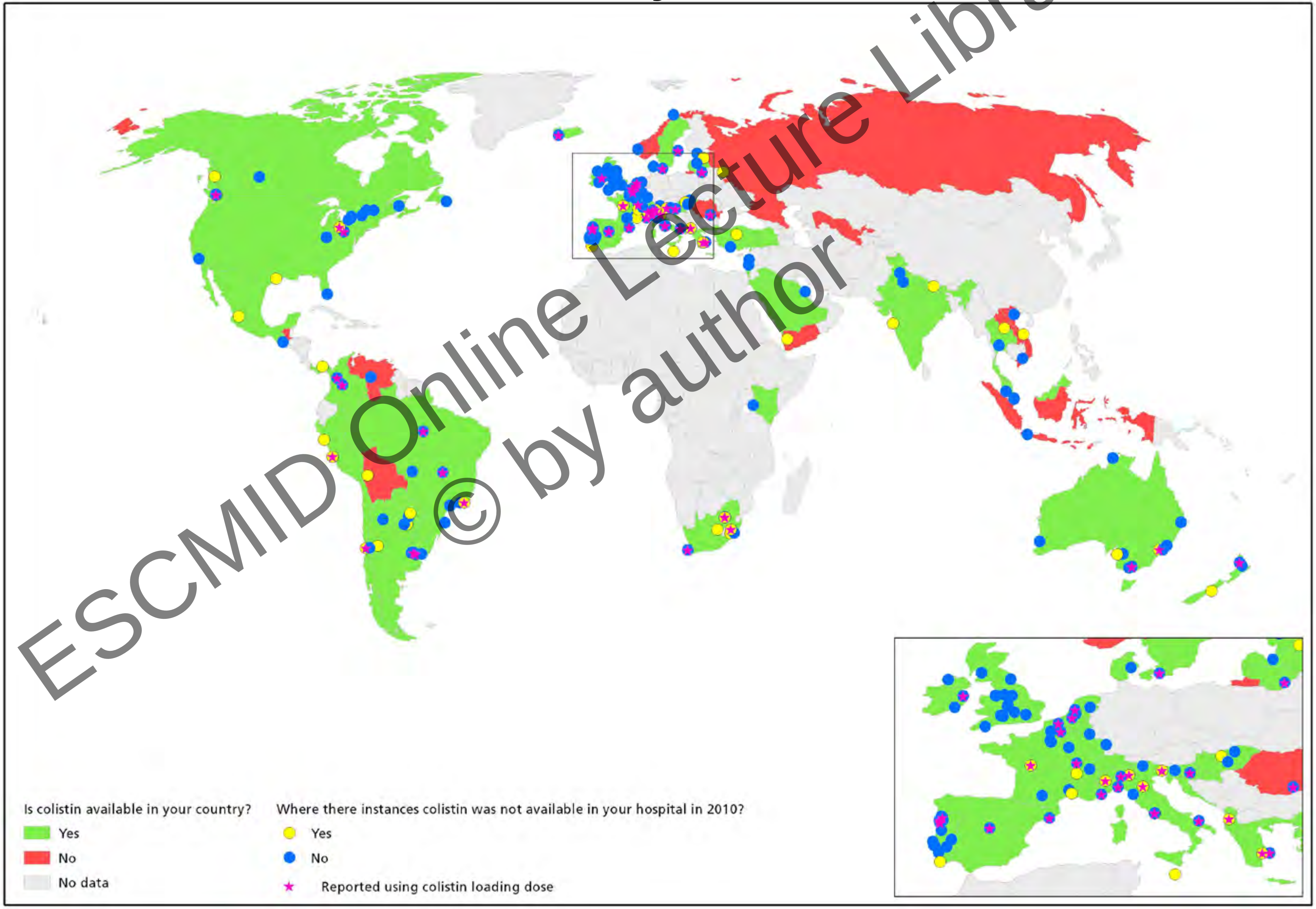
[1]Centre Hospitalier Universitaire de Nice, Service d'Infectiologie and Université de Nice Sophia-Antipolis, Faculté de Médecine, France; [2]Biology Department, Indiana University, Bloomington; [3]University of Wisconsin, School of Medicine and Public Health, Madison; [4]Department of Clinical Microbiology,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

268 • CID 2012:54 (15 January) • REVIEWS OF ANTI-INFECTIVE AGENTS

Need better access to 'old and forgotten' abx



If access: need to use well.
Results colistin survey



Antibiotic solutions

- Prudent use through education – incentives
- Drug development:
  - Gram-negative focus
  - New targets: eg plasmid replication
  - Biodegradable

- In mean time: make the old antibiotics available with clear guidance on when and how to use in multiple languages
- Open source treatment guidelines that can be easily adapted locally

Need for global ONE HEALTH stewardship

- So far very hospital focused and developed countries
- Antibiotic stewardship should be considered as standard of care and part of hospital accreditation
- Needs to include the world of animals, plants, water and so on…
- Need to prioritize and be pragmatic (eg Chennai declaration, India)

India needs "An implementable antibiotic policy" and NOT "A perfect policy"

"The Chennai Declaration"
Recommendations of "A roadmap- to tackle the challenge of antimicrobial resistance" - A joint meeting of medical societies of India

Ghafur A[1], Mathai D[2], Muruganathan A[3], Jayalal JA[4], Kant R[5], Chaudhary D[6], Prabhash K[7], Abraham OC[8], Gopalakrishnan R[9], Ramasubramanian V[10], Shah SN[11], Pardeshi R[12], Huilgol A[13], Kapil A[14], Gill JPS[15], Singh S[16], Rissam HS[17], Todi S[18], Hegde BM[19], Parikh P[20]

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FDA Cautions in Interpretation of Antimicrobial Resistance Data

April 22, 2013

Recently, the Environmental Working Group issued a report of its interpretation of the 2011 Retail Meat Annual Report of the National Antimicrobial Resistance Monitoring System (NARMS). While FDA is always concerned when we see antimicrobial resistance, we believe the EWG report oversimplifies the NARMS data and provides misleading conclusions. We do not believe that EWG fully considered important factors that put these results in context, including:

- whether the bacterium is a foodborne pathogen. The report highlights resistance to *Enterococcus*, but this is not considered a foodborne pathogen. Instead, we include it because its behavior is helpful in understanding how resistance occurs.
- which drug(s) the bacterium is naturally resistant to. For example, most *Enterococcus faecalis* is naturally resistant to the antibiotic class of lincosamides. Because we know and expect to see this resistance, we are not as concerned with resistance in this species the way we would be with resistance in true pathogens like *Salmonella* and *Campylobacter*.
- why NARMS includes certain drugs in its testing design. We include some antibiotics for epidemiology purposes– to track the spread of certain bacteria or certain genes. But resistance to these antibiotics doesn't reflect a danger to public health.
- whether the antibiotics that are commonly used to treat patients are still effective. NARMS data indicates that first-line treatments for all four bacteria that we track (*Salmonella*, *Enterococcus*, *Escherichia coli* and *Campylobacter*) are still effective.
- what the 2011 data indicate relative to similar data reported for prior years.

Additionally, we believe that it is inaccurate and alarmist to define bacteria resistant to one, or even a few, antimicrobials as "superbugs" if these same bacteria are still treatable by other commonly used antibiotics. This is especially misleading when speaking of bacteria that do not cause foodborne disease and have natural resistances, such as *Enterococcus*.

When taking such factors into account, FDA believes the notable findings in the 2011 NARMS Report include:

- In the critically important class of antimicrobials, the 2011 data showed no fluoroquinolone resistance in *Salmonella* from any source. This is the drug of choice for treating adults with *Salmonella*.
- Trimethoprim-sulfonamide is another drug used to treat *Salmonella* infections and resistance remains low (0% to 3.7%).
- Fluoroquinolone resistance in *Campylobacter* has stopped increasing and remained essentially unchanged since the FDA withdrew the use of this drug class in poultry in 2005.
- Macrolide antibiotic resistance in retail chicken isolates remains low, with 2011 results at 0.5% of *Campylobacter jejuni* and 4.3% of *Campylobacter coli*. The macrolide antibiotic erythromycin is the drug of choice for treating *Campylobacter* infections.
- Multidrug resistance is rare in *Campylobacter*. Only nine out of 634 *Campylobacter* isolates from poultry were resistant to 3 or more antimicrobial classes in 2011. However, gentamicin resistance in *Campylobacter coli* markedly increased from 0.7% in 2007 (when it first appeared in the NARMS retail meat report) to 18.1% in 2011. Gentamicin has been suggested as a possible second-line therapy for *Campylobacter* infections, although it is not commonly used.
- Resistance to third-generation cephalosporins, which are used to treat salmonellosis, has increased in *Salmonella* from chicken (10 to 33.5%) and turkey (8.1 to 22.4%) meats when comparing 2002 and 2011 percentages. FDA noted this development in previous years and has already taken action by prohibiting certain extra-label uses of

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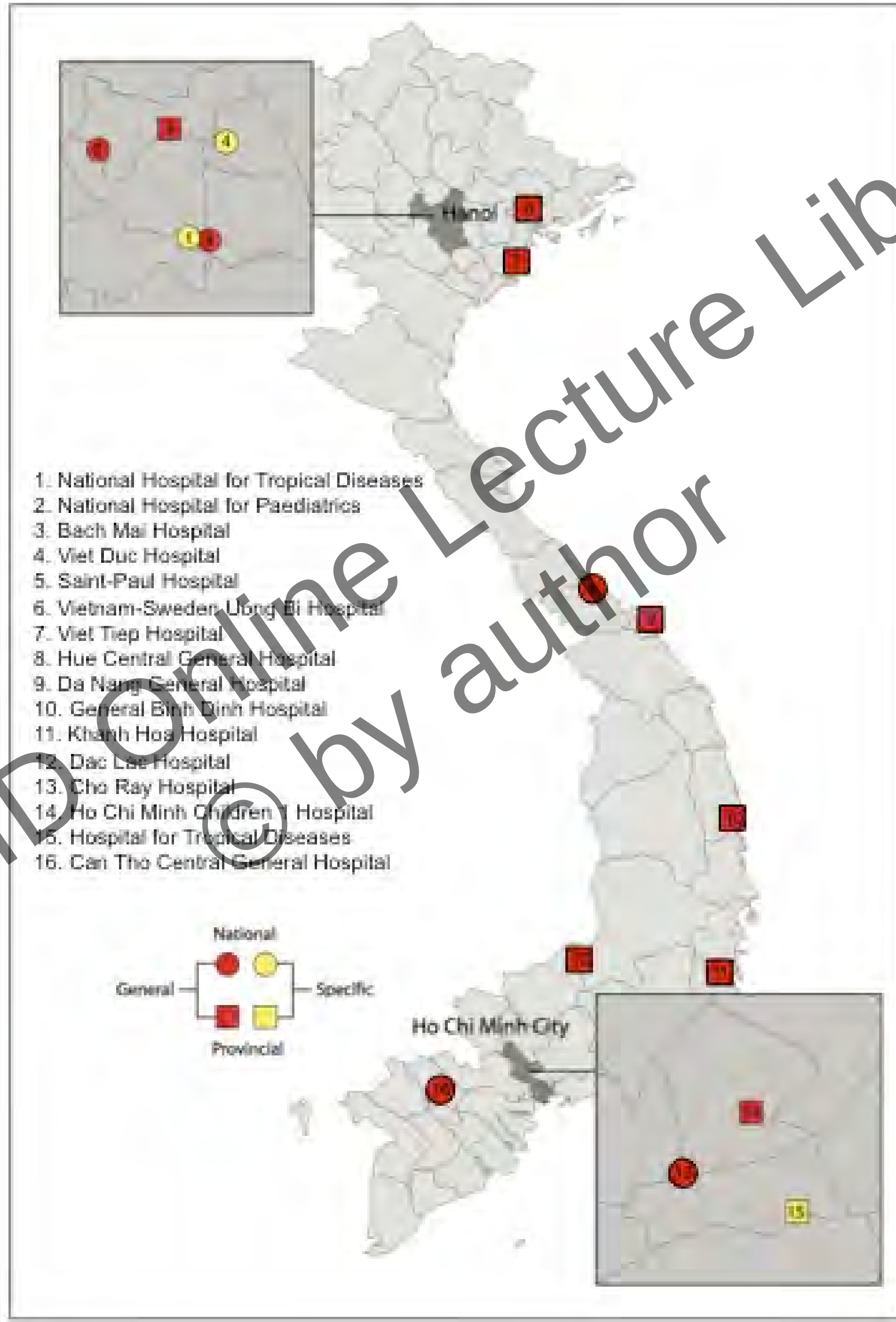
PLOS | MEDICINE

Health in Action

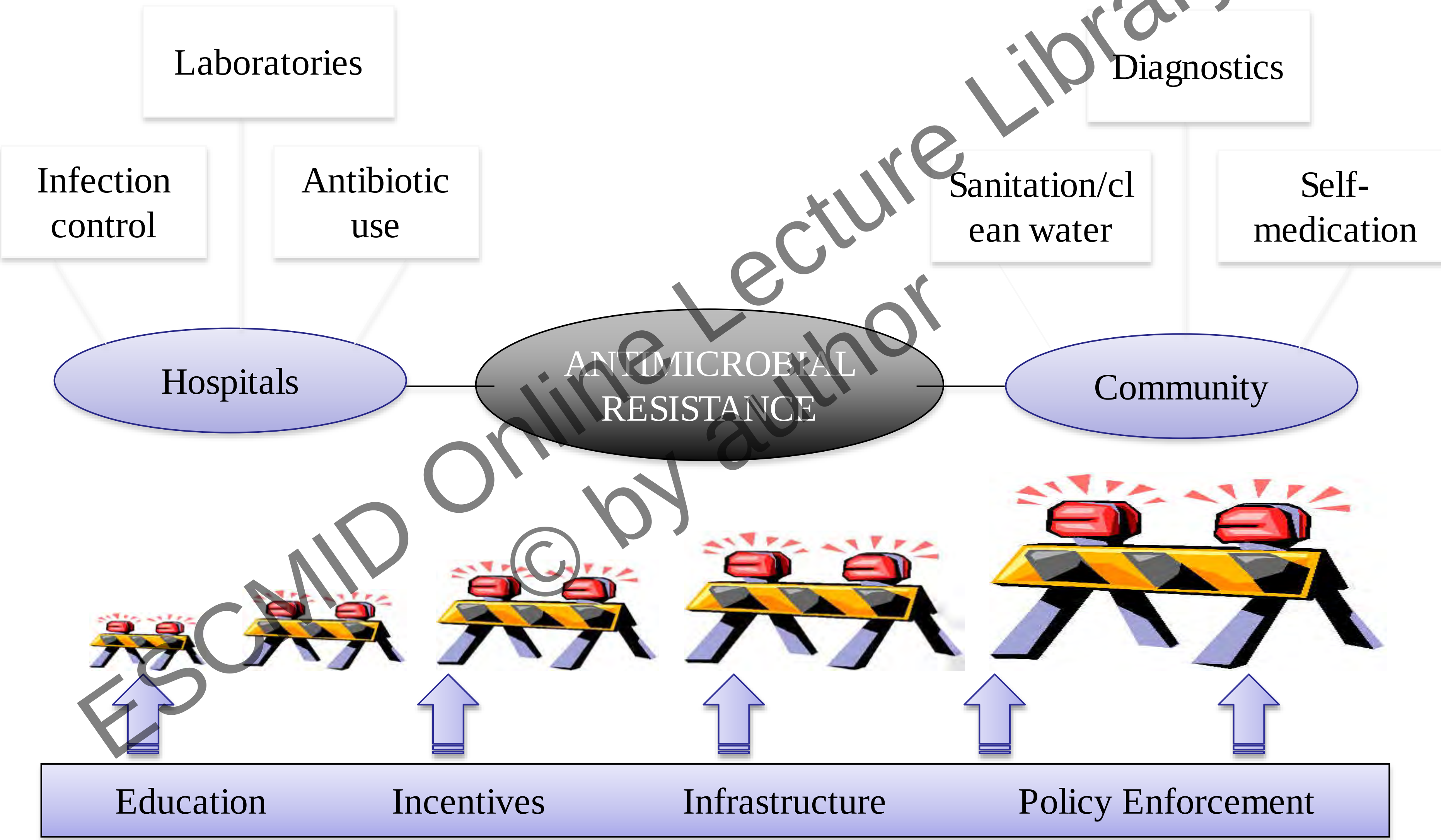
Providing Impetus, Tools, and Guidance to Strengthen National Capacity for Antimicrobial Stewardship in Viet Nam

Heiman F. L. Wertheim[1,2*¶], Arjun Chandna[1¶], Vu Dinh Phu[3], Pham Van Ca[3], Nguyen Thi Dai Phong[3], Lam Minh Yen[4], Nguyen Van Vinh Chau[2,4], Mattias Larsson[1], Ulf Rydell[5], Lennart E. Nilsson[5], Jeremy Farrar[1,2], Nguyen Van Kinh[2,3], Håkan Hanberger[5,6]

1 Oxford University Clinical Research Unit, Hanoi, Viet Nam, 2 South East Asia Infectious Disease Clinical Research Network, Ho Chi Minh City, Viet Nam, 3 National Hospital for Tropical Diseases, Hanoi, Viet Nam, 4 Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam, 5 Linköping University, Linköping, Sweden, 6 Department of Infectious Diseases, Östergöland, County Council of Östergöland, Linköping, Sweden


Hanoi
1. National Hospital for Tropical Diseases
2. National Hospital for Paediatrics
3. Bach Mai Hospital
4. Viet Duc Hospital
5. Saint-Paul Hospital
6. Vietnam-Sweden Uong Bi Hospital
7. Viet Tiep Hospital
8. Hue Central General Hospital
9. Da Nang General Hospital
10. General Binh Dinh Hospital
11. Khanh Hoa Hospital
12. Dac Lac Hospital
13. Cho Ray Hospital
14. Ho Chi Minh Children 1 Hospital
15. Hospital for Tropical Diseases
16. Can Tho Central General Hospital
National
General
Specific
Provincial
Ho Chi Minh City

Solutions and Barriers



VINARES objectives:

- To improve antibiotic stewardship by:
  - –Surveillance of hospital acquired infections
  - –Surveillance of antibiotic resistance
  - –Surveillance of antibiotic use
  - –Develop antibiotic stewardship program
  - –Develop treatment guidelines
  - –Share information and best practices through website, guidelines, meetings, workshops

VINA RES

UNIVERSITY OF OXFORD
wellcome trust

BỆNH VIỆN BỆNH NHIỆT ĐỚI TRUNG ƯƠNG
NHTD
NATIONAL HOSPITAL OF TROPICAL DISEASES

LINKÖPINGS UNIVERSITET

Sida

Challenges in Infection Control

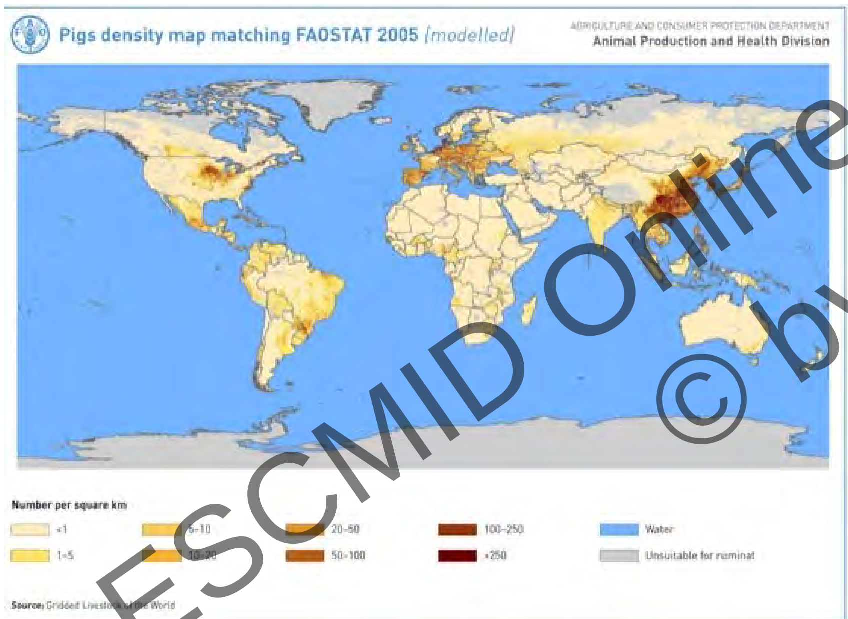
This bed is empty but in Asia often >1 patient per bed

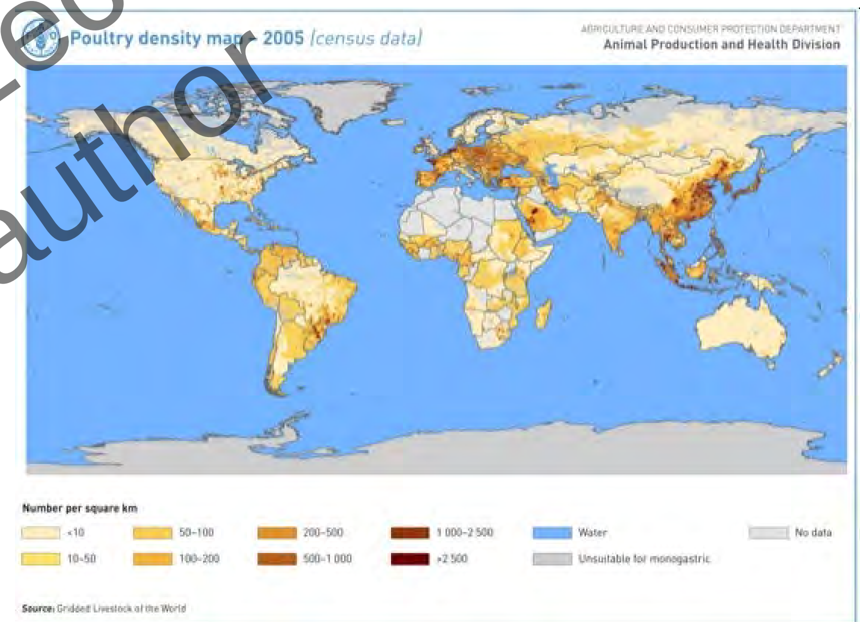
Resistance generally unknown

Foto by Erika Vlieghe

Control antibiotic use in animals…

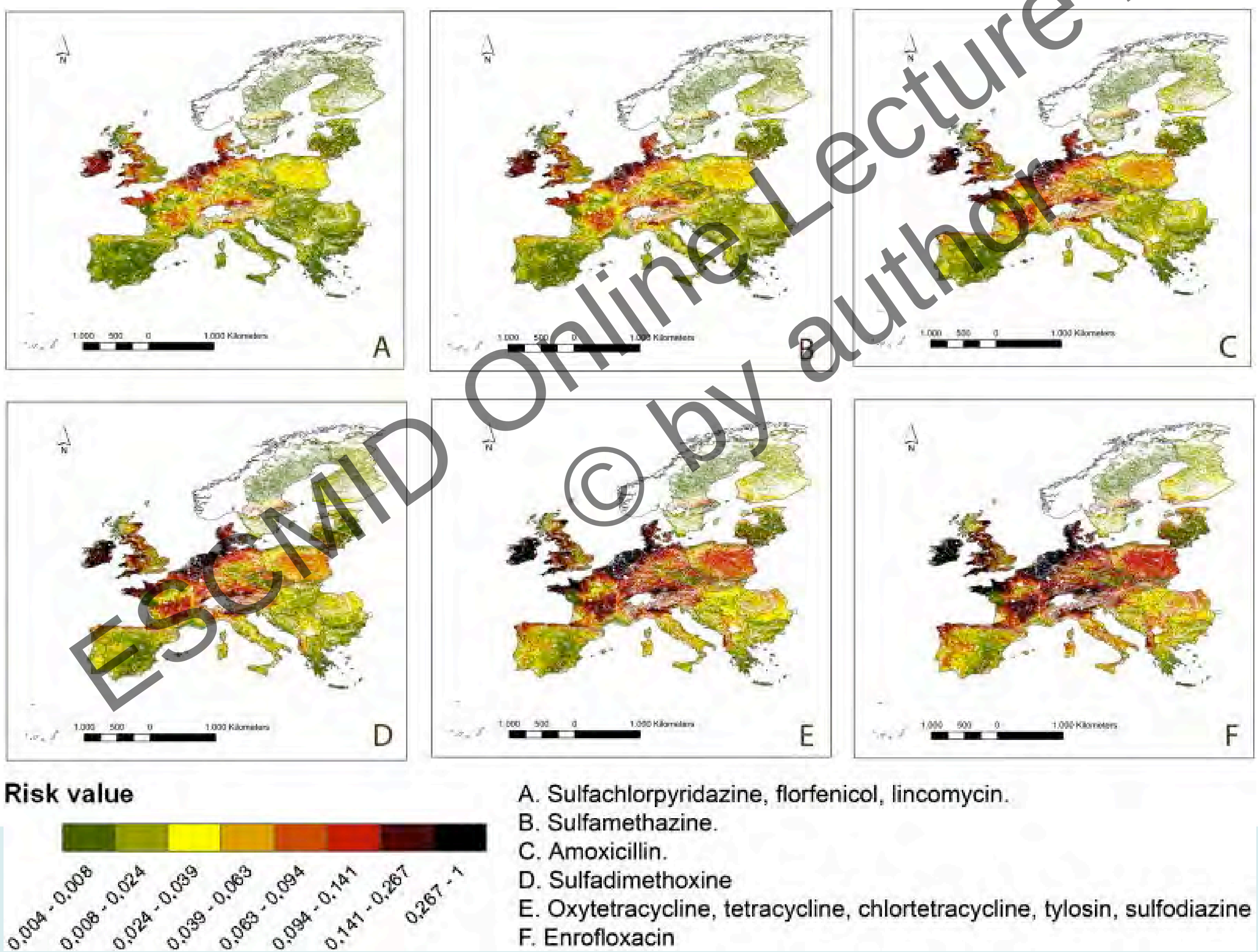
Most antibiotic use is in agriculture: animal stewardship = ONE HEALTH





And not to forget fish/shrimp farms...

Countries that perform well for humans may not do well for animals



Torre, 2012
Sci Total Envir

Antibiotic residue in vegetables in China

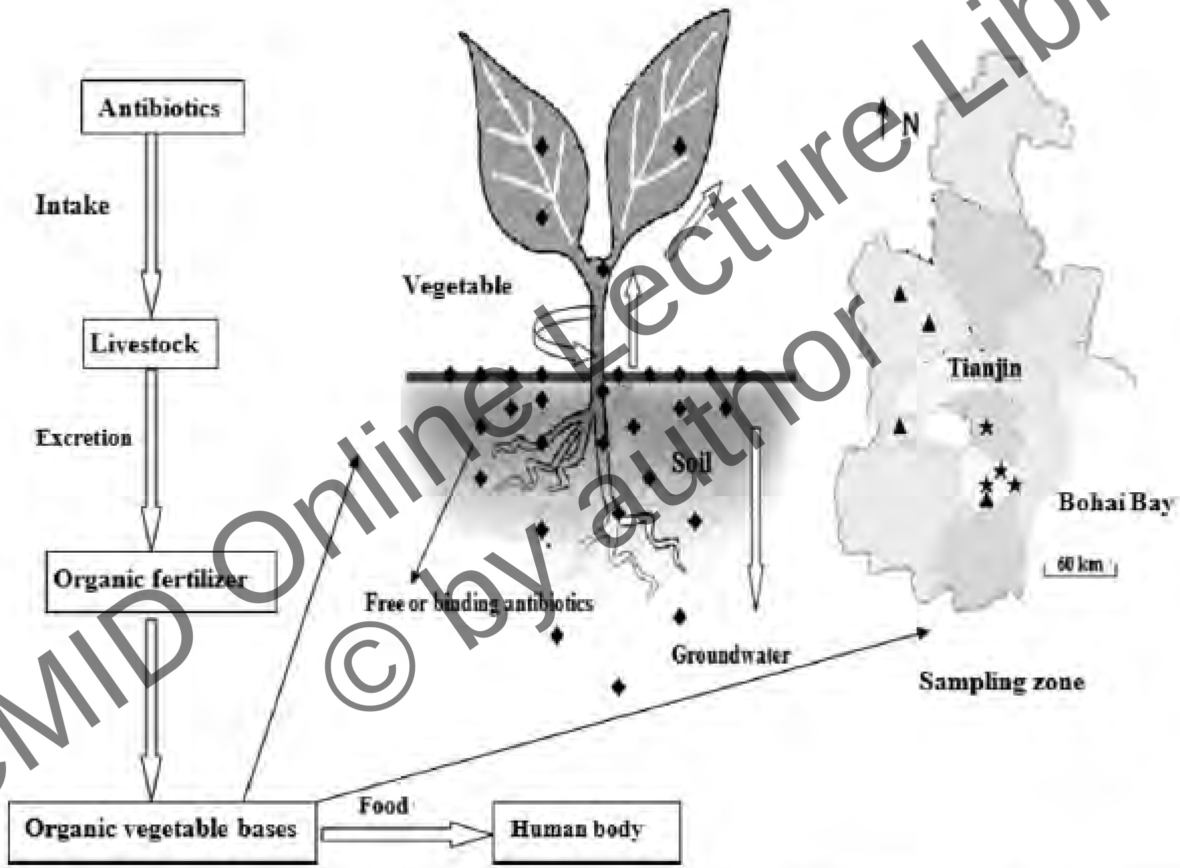


Fig. 1. The schematic of antibiotics in organic vegetable bases. ▲, location of four organic vegetable bases; ★, location of four livestock farms.

Hu, Environm Pollut 2010

Antibiotics should be considered pollutants and environmental levels need to be monitored and stay below a certain threshhold.

Make antibiotics biodegradable

WATER RESEARCH 42 (2008) 395–403

Available at www.sciencedirect.com

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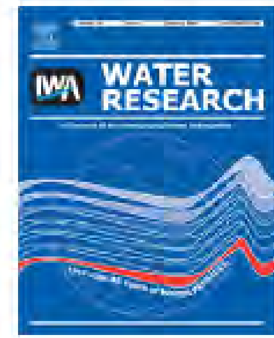
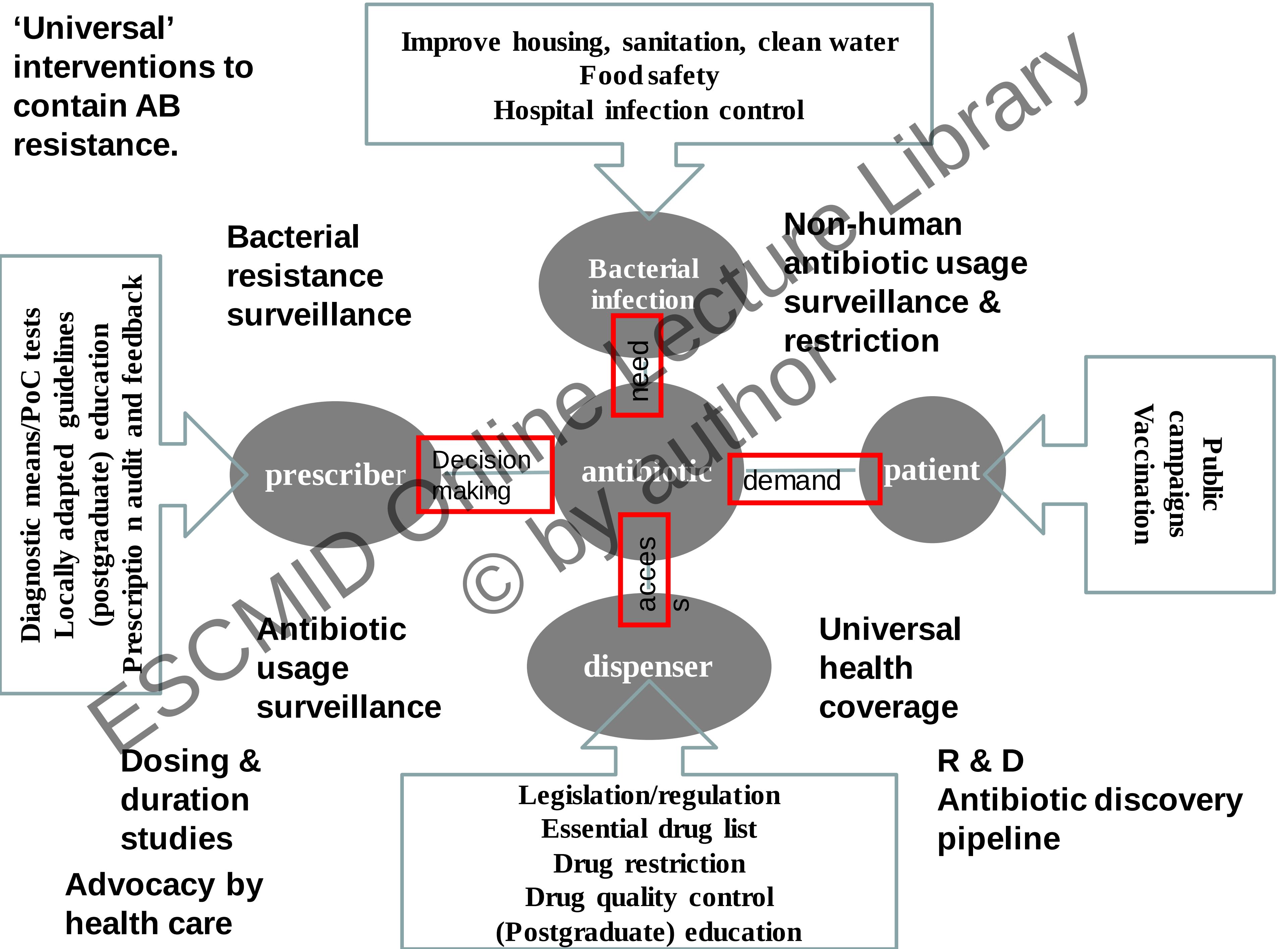


Removal of antibiotics from wastewater by sewage treatment facilities in Hong Kong and Shenzhen, China

A. Gulkowska[a], H.W. Leung[a], M.K. So[a], S. Taniyasu[b], N. Yamashita[b], Leo W.Y. Yeung[a], Bruce J. Richardson[a], A.P. Lei[c], J.P. Giesy[a,d,e], Paul K.S. Lam[a,*]


‘Universal’ interventions to contain AB resistance.
Improve housing, sanitation, clean water
Food safety
Hospital infection control
Bacterial resistance surveillance
Non-human antibiotic usage surveillance & restriction
Diagnostic means/PoC tests
Locally adapted guidelines
(postgraduate) education
Prescriptio n audit and feedback
Bacterial infection
need
prescriber
Decision making
antibiotic
demand
patient
Public
campaigns
Vaccination
acces s
dispenser
Antibiotic usage surveillance
Universal health coverage
Dosing & duration studies
Advocacy by health care
Legislation/regulation
Essential drug list
Drug restriction
Drug quality control
(Postgraduate) education
R & D
Antibiotic discovery pipeline

Go national is the right approach

MAJOR ARTICLE

Containment of a Country-wide Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* in Israeli Hospitals via a Nationally Implemented Intervention

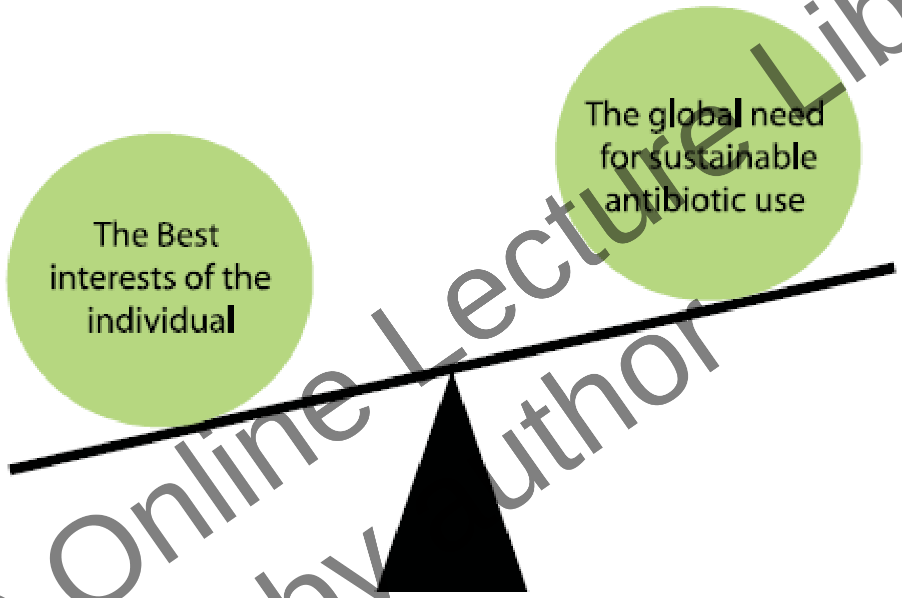
Mitchell J. Schwaber,[1] Boaz Lev,[2] Avi Israeli,[2] Ester Solter,[1] Gill Smollan,[1] Bina Rubinovitch,[1] Itamar Shalit,[1] Yehuda Carmeli,[1] and the Israel Carbapenem-Resistant Enterobacteriaceae Working Group[a]

[1]National Center for Infection Control, Israel Ministry of Health, Tel Aviv, and [2]Israel Ministry of Health, Jerusalem, Israel

Some thoughts

- Resistance is a given, but has not helped to attract proper attention: Start a resistance death registry?
- Communicating information on resistance to policymakers and lay public
  - Easier in case of HIV, TB and malaria when single pathogens are involved
- Besides bacterial surveillance also do standardized resistance gene and their mobile genetic elements surveillance for early warning
- Control and monitor antibiotic levels in environment
- Infection control needs an update
- Complex issue: analysis through modeling may help target interventions

A delicate balance



Antibiotic effectiveness is a valuable natural resource, like clean water or forests.

All antibiotic use, appropriate or not, 'uses up' some of the effectiveness.

But antibiotics are also lifesavers and we need access to them.

From carbon emissions trading to antibiotic emissions trading

- Resistance issue is similar to pollution.
- Solution possibly in environmental economics
- Fees/taxes/trading in antibiotic emissions into environment
- Revenue can be used to sponsor a global antibiotic resistance institute that supports worldwide initiatives

Time for bold ideas,

broad approach - ONE HEALTH,

leadership…

…and big funds

The future king of the Netherlands in Vietnam