The use and management of antibiotics: some proposals for Vietnam

Paul M. Tulkens, MD, PhD *
Prof. Françoise Van Bambeke, PharmD, PhD *
Prof. P. De Mol, MD, PhD **

* Louvain Drug Research Institute, *Université catholique de Louvain*, Brussels

** *Service de microbiologie*, *Université de Liège*, Liège

Presented at the Ministry of Health of the
Socialist Republic of Vietnam
Hanoi, Vietnam – 31 October 2013

With the support of *Wallonie-Bruxelles-International*

Objectives

Objectives:

- Examine the necessity of developing a policy on rational use of antibiotics in Vietnam due to the resistance threats (in both hospitals and community).
- Sharing experiences learned from the results Belgium has gained in the past 10 years in promoting the rational use of antibiotics
- Suggesting potentially useful approaches for Vietnam

Programme

- Presentation #1:
  Resistance to antibiotics and risks for Vietnam

  Questions and Answers

- Presentation #2:
  Potential solutions...
  The Belgian experience

  Questions and Answers

- Presentation #3:
  Suggestions for Vietnam

  General discussion

Who is present (for Belgium)

Prof. Françoise VAN BAMBEKE, Pharm, PhD

Université catholique de Louvain

- Pharmacology & Pharmacotherapy
- Antibiotic research (activity and resistance)

Prof. Patrick DE MOL, MD, PhD

Université de Liège

- Microbiology & Infection Control
- Vice-president of the Belgian *Conseil Supérieur de la Santé*

Prof. Paul M. TULKENS, MD, PhD

Université catholique de Louvain

- Pharmacology & Clinical Pharmacy
- Member of the Belgian Antibiotic Policy Coordination Committee

Why have we come to Vietnam ?

- Official program supported by "*Wallonie-Bruxelles*" to help implementing "**Clinical Pharmacy**" and "**Optimized use of antibiotics**" in Hanoi through the University of Pharmacy
- Application made in 2009 by the Cellular and Molecular Group of the Louvain Drug Research Institute (UCL) and the University of Pharmacy (Hanoi) for execution in 2010-2013
- Program successfully terminated (with a a symposium held in Hanoi on 30 October 2013)
- New program started in 2013 for 3 additional years for strengthening the previous activities

On 15 October 2013, visit of The Minister of Health (Dr Nguyen) in Brussels with brief presentation of our activities and the Belgian system of antibiotic policy.

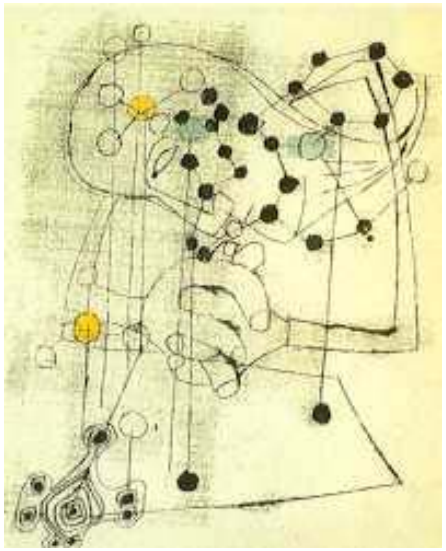
Antibiotics: what do we do ?

cellular pharmacokinetics

cellular pharmacodynamics

antibiotic toxicity

resistance

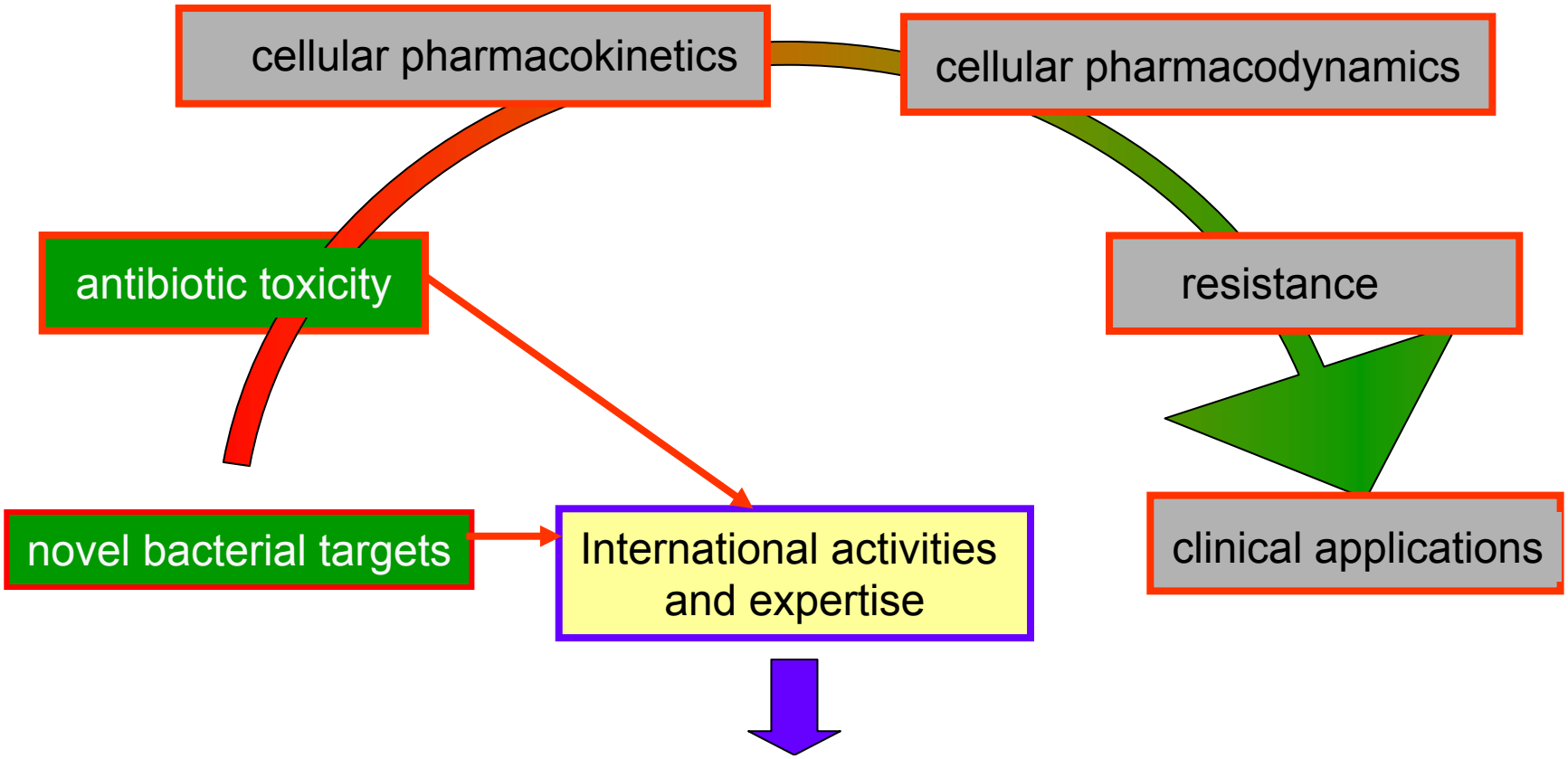


novel bacterial targets

clinical applications

antibiotics: from molecules to man

Antibiotics: what do we do ?



ID 214

Mailing address:
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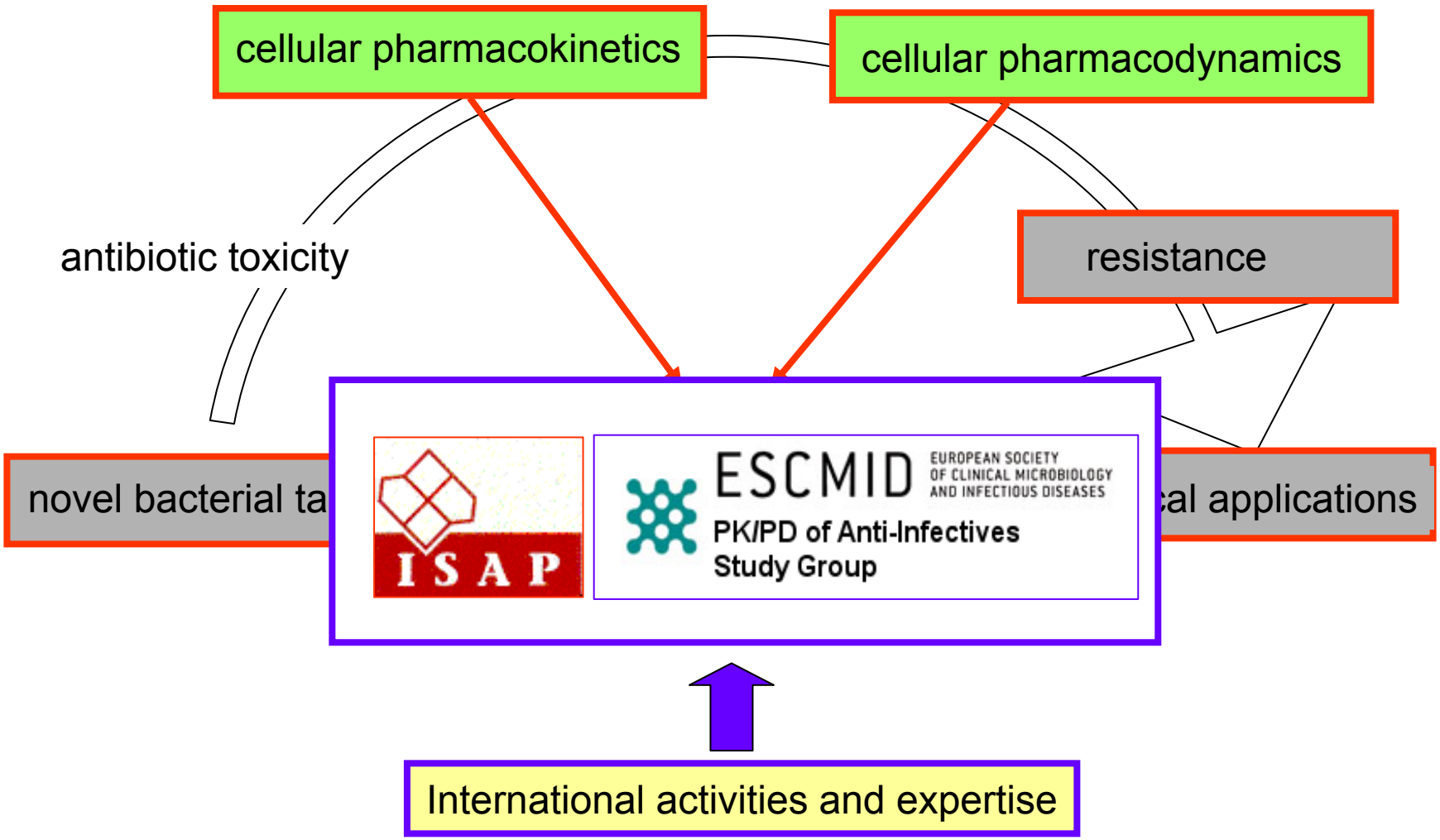
av. Mounier 73, B1.73.05
1200 Brussels – Belgium
francoise.vanbambeke@uclouvain.be

Type Three Secretion System (T3SS)-mediated internalisation and cytotoxicity of *Pseudomonas aeruginosa* by epithelial and phagocytic cells : does inflammasome make the difference?

A. Anantharajah[1], E. Faure[2,3], J.M. Buyck[1], PM.Tulkens[1], M.P. Mingeot-Leclercq[1], B. Guery[2,3] and F. Van Bambeke[1]

[1] Cellular and Molecular Pharmacology, Louvain Drug Research Institute, Université catholique de Louvain, Brussels, Belgium; [2] Lille-2 University hospital, Lille, France, [3]Host-Pathogen translational Research group Pseudomonas aeruginosa, Lille, France

Antibiotics: what do we do ?



Antibiotics: what do we do ?

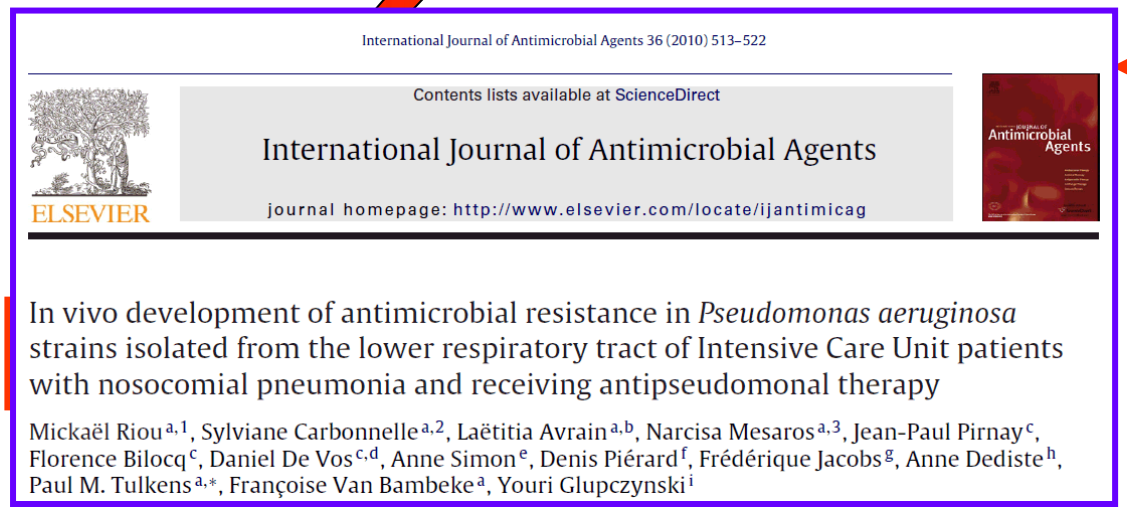
cellular pharmacokinetics

cellular pharmacodynamics

resistance

clinical applications

International activities and expertise



International Journal of Antimicrobial Agents 36 (2010) 513–522

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

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

ELSEVIER

In vivo development of antimicrobial resistance in *Pseudomonas aeruginosa* strains isolated from the lower respiratory tract of Intensive Care Unit patients with nosocomial pneumonia and receiving antipseudomonal therapy

Mickaël Riou[a,1], Sylviane Carbonnelle[a,2], Laëtitia Avrain[a,b], Narcisa Mesaros[a,3], Jean-Paul Pirnay[c], Florence Bilocq[c], Daniel De Vos[c,d], Anne Simon[e], Denis Piérard[f], Frédérique Jacobs[g], Anne Dediste[h], Paul M. Tulkens[a,*], Françoise Van Bambeke[a], Youri Glupczynski[i]

Antibiotics: what do we do ?

cellular pharmacokinetics

cellular pharmacodynamics

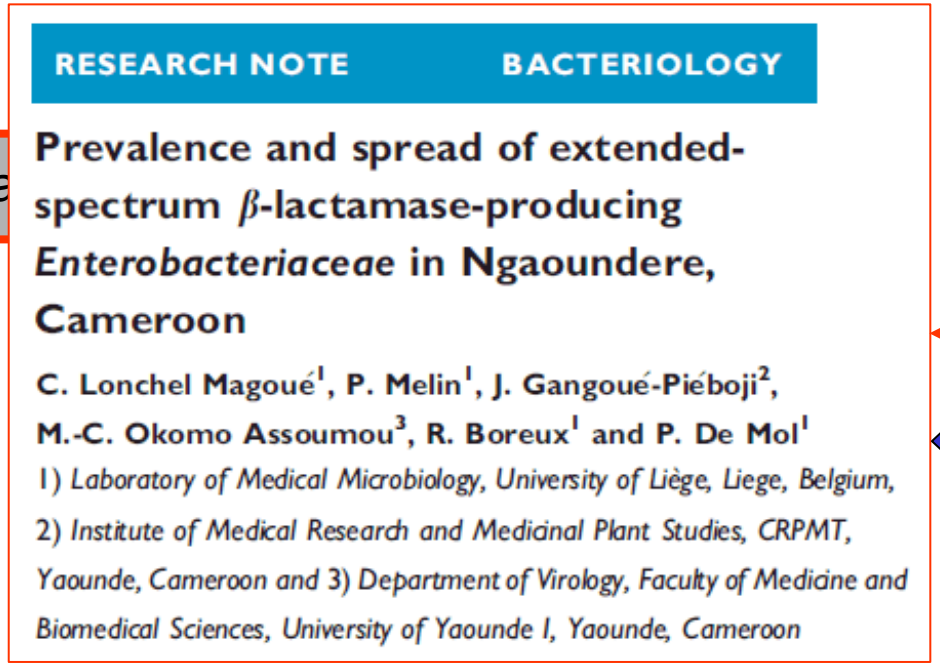
antibiotic toxicity

resistance

novel bacteria

clinical applications

International activities and expertise



RESEARCH NOTE BACTERIOLOGY

Prevalence and spread of extended-spectrum β-lactamase-producing *Enterobacteriaceae* in Ngaoundere, Cameroon

C. Lonchel Magoué[1], P. Melin[1], J. Gangoué-Piéboji[2], M.-C. Okomo Assoumou[3], R. Boreux[1] and P. De Mol[1]

1) *Laboratory of Medical Microbiology, University of Liège, Liege, Belgium,* 2) *Institute of Medical Research and Medicinal Plant Studies, CRPMT, Yaounde, Cameroon and* 3) *Department of Virology, Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaounde, Cameroon*

Programme

- Presentation #1:
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Are antibiotics following a path to madness ?

discovery in soil bacteria and fungi

1928 - …

Are antibiotics following a path to madness ?

1950 – 1980 …

and then we all saw the blooming tree of semi-synthetic and totally synthetic antibiotics

Are antibiotics following a path to madness ?

and the US General Surgeon told us that the fight was over

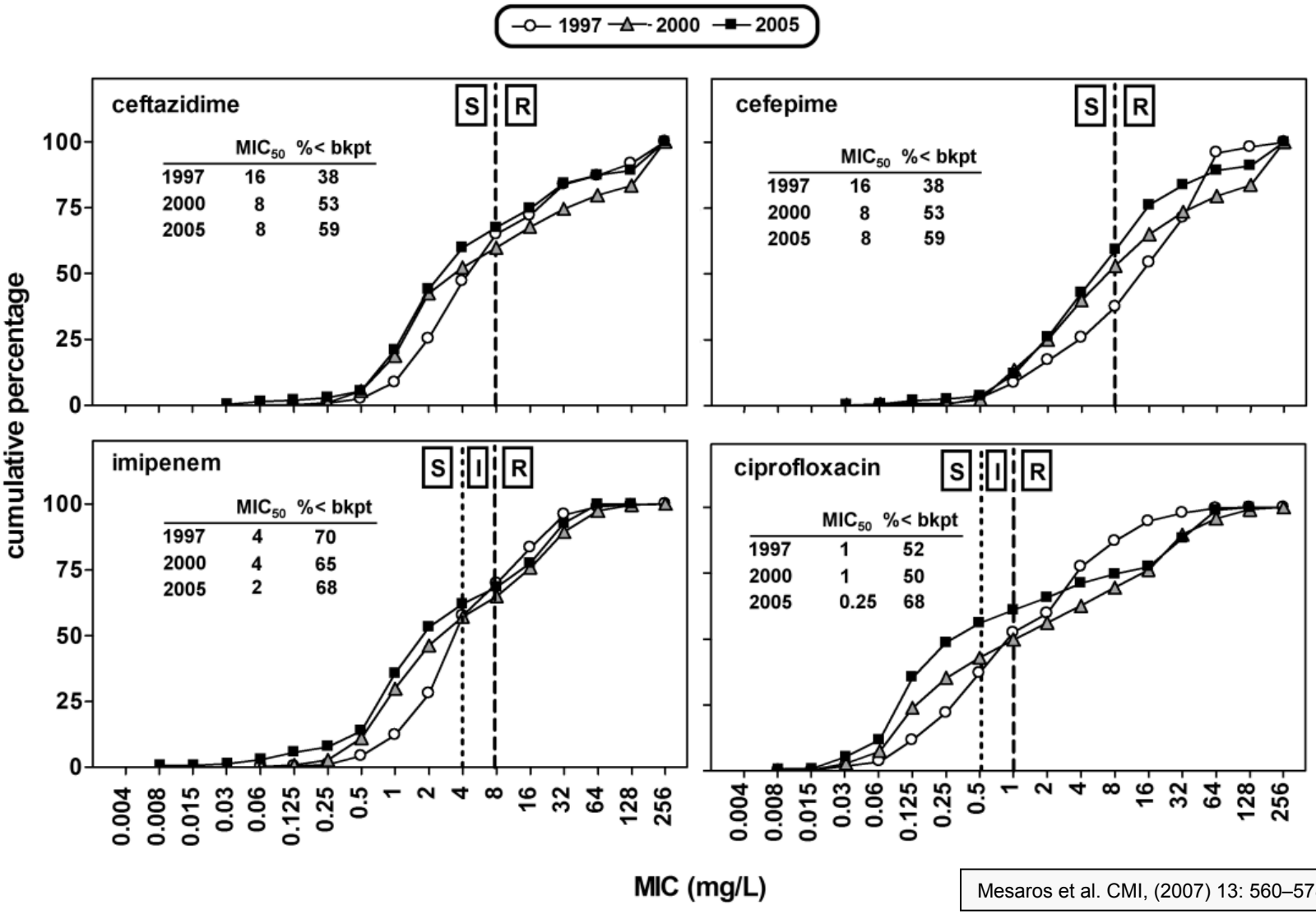
1970 …

Are antibiotics following a path to madness ?

But…

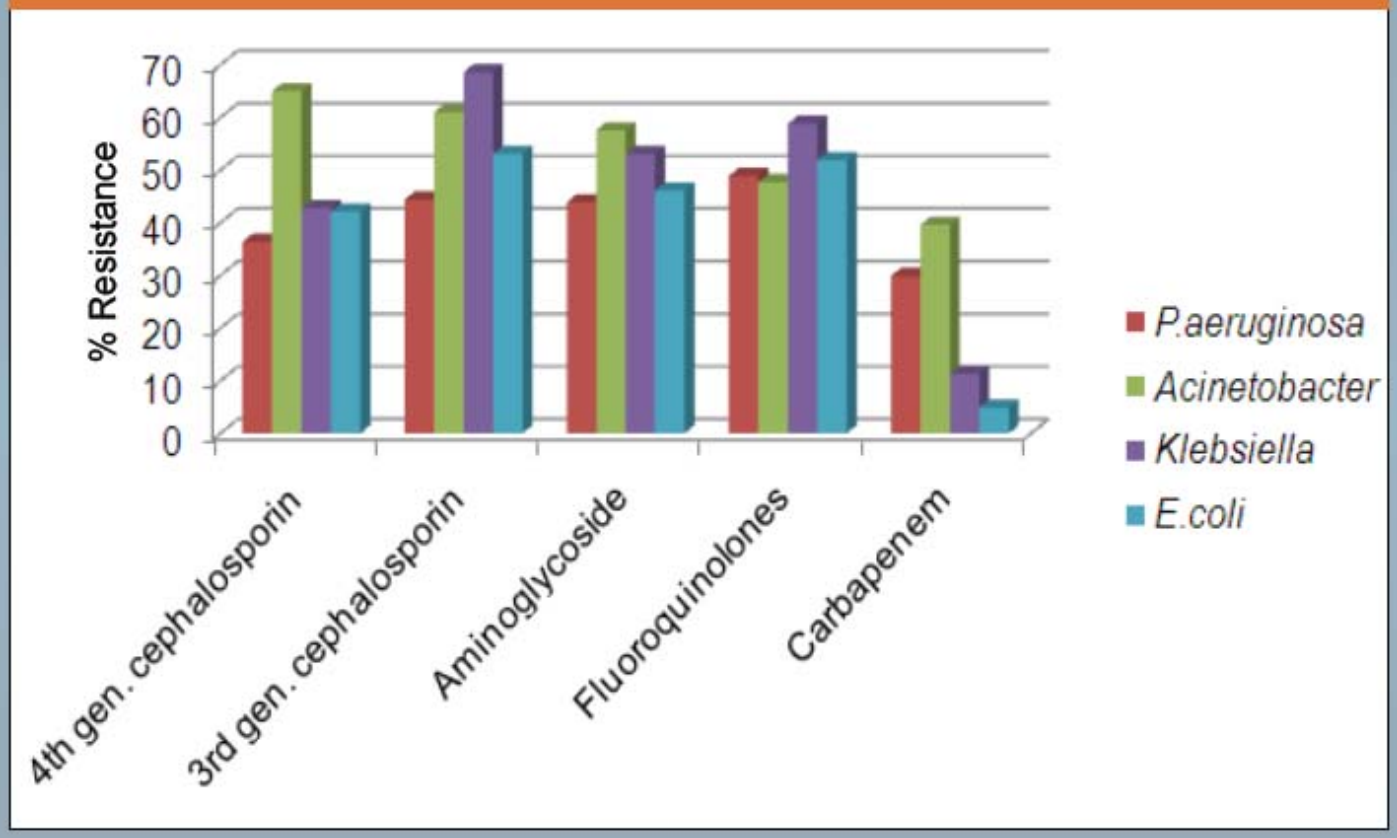
2012 …

Resistance of *P. aeruginosa in hospitals*
(International data – EUCAST breakpoints)

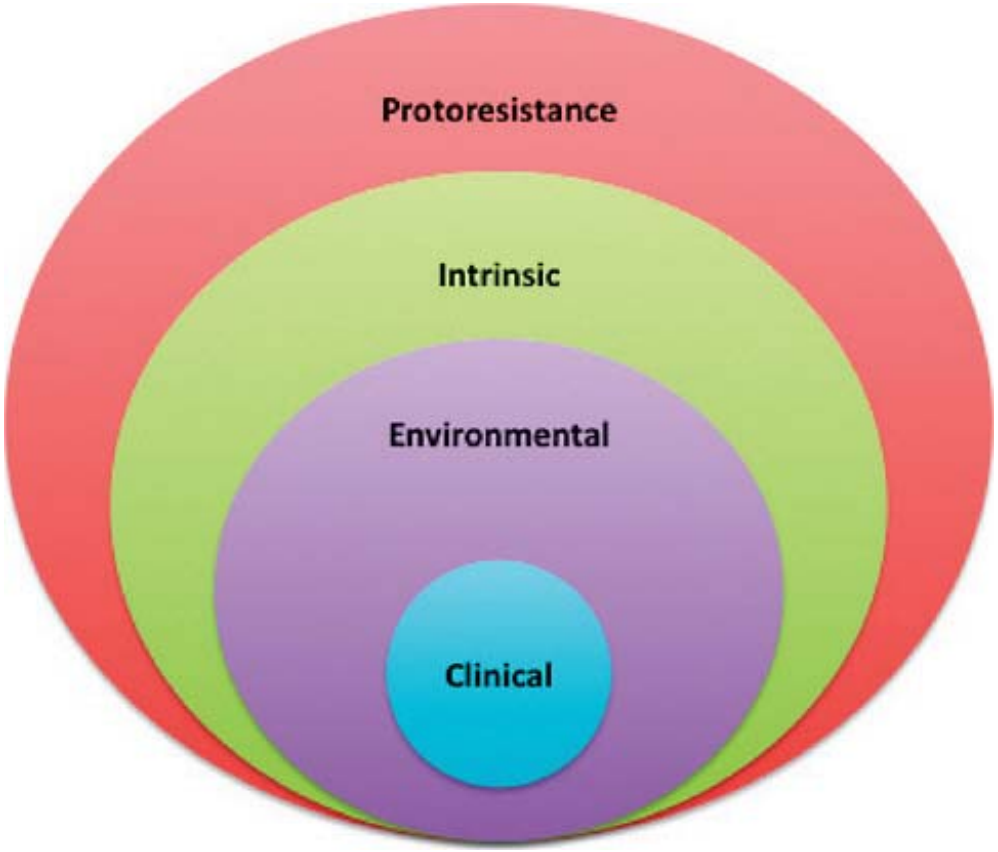


Mesaros et al. CMI, (2007) 13: 560–578

A major problem in Vietnam …



The resistome …



The antibiotic resistome.

- all the genes and their products that contribute to antibiotic resistance.
- highly redundant and interlocked system
- clinical resistance under represents the resistance capacity of bacteria.
- existing biochemical mechanisms (protoresistome) serve as a deep reservoir of precursors that can be co-opted and evolved to

Antibiotic Resistance:Implications for Global Health and Novel Intervention Strategies: Workshop Summary
http://www.nap.edu/openbook.php?record_id=12925

"Father resistance genes": an original example with aminoglycosides

Proc. Nat. Acad. Sci. USA
Vol. 70, No. 8, pp. 2276–2280, August 1973

Aminoglycoside Antibiotic-Inactivating Enzymes in Actinomycetes Similar to Those Present in Clinical Isolates of Antibiotic-Resistant Bacteria

(streptomyces/origin of R-factors/gentamicin-acetate)

RAOUL BENVENISTE* AND JULIAN DAVIES†

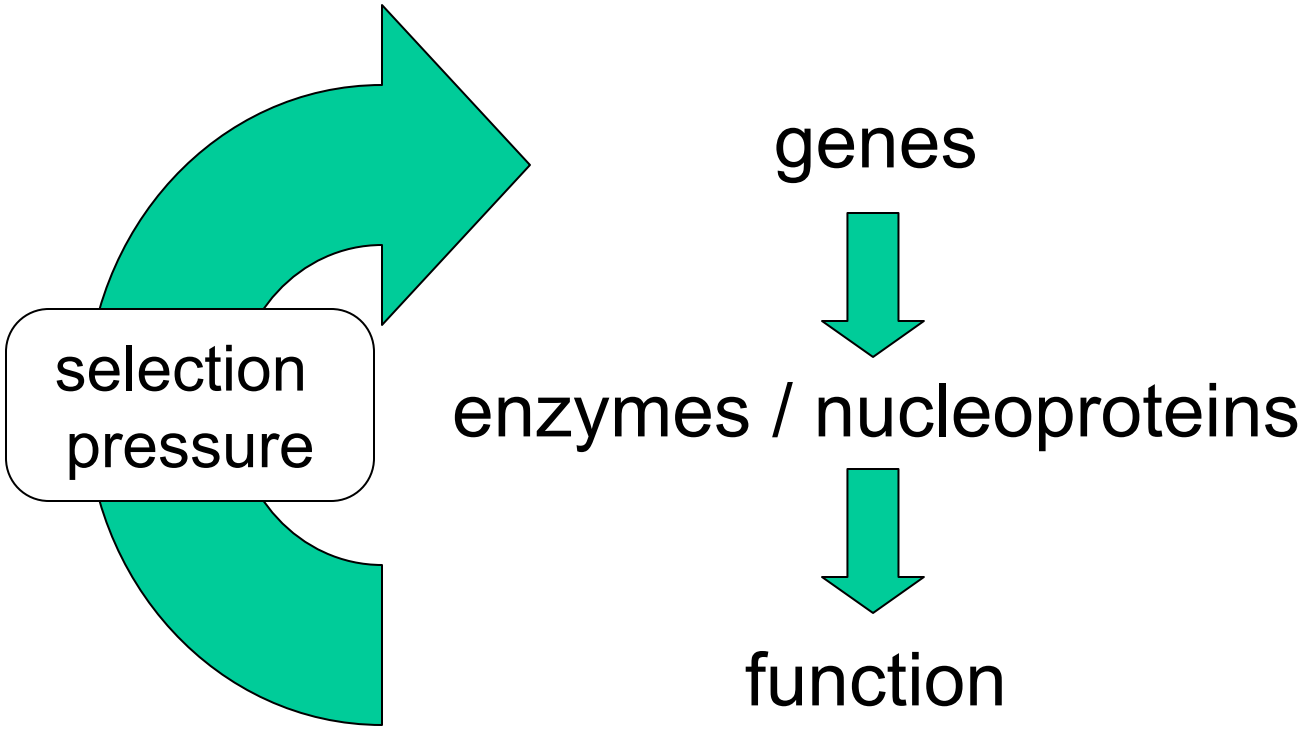
Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin—Madison, Madison, Wis. 53706

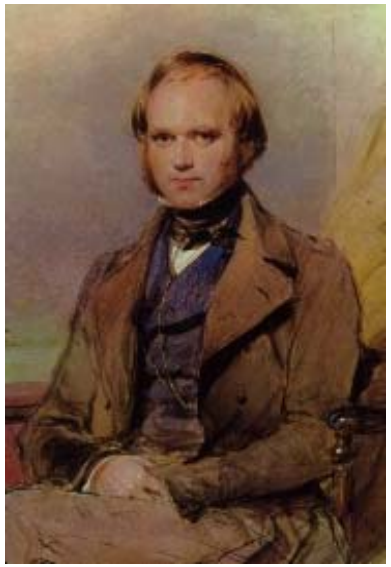
Communicated by Henry Lardy, May 11, 1973

- Actinomycetes produce aminoglycosides
- In order not to be killed by their production, they produce enzymes that degrade aminoglycosides
- The genes coding for these enzymes have been passed to clinically important pathogens

The selectome

A simple application of Darwin's principles ...



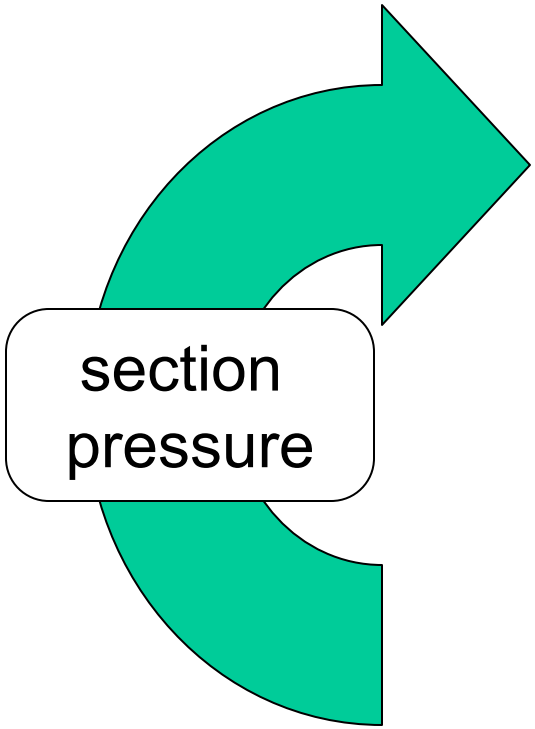


Detail of watercolor by
George Richmond, 1840.
Darwin Museum at Down House

How and why can you select so easily ?

A simple application of Darwin's principle…

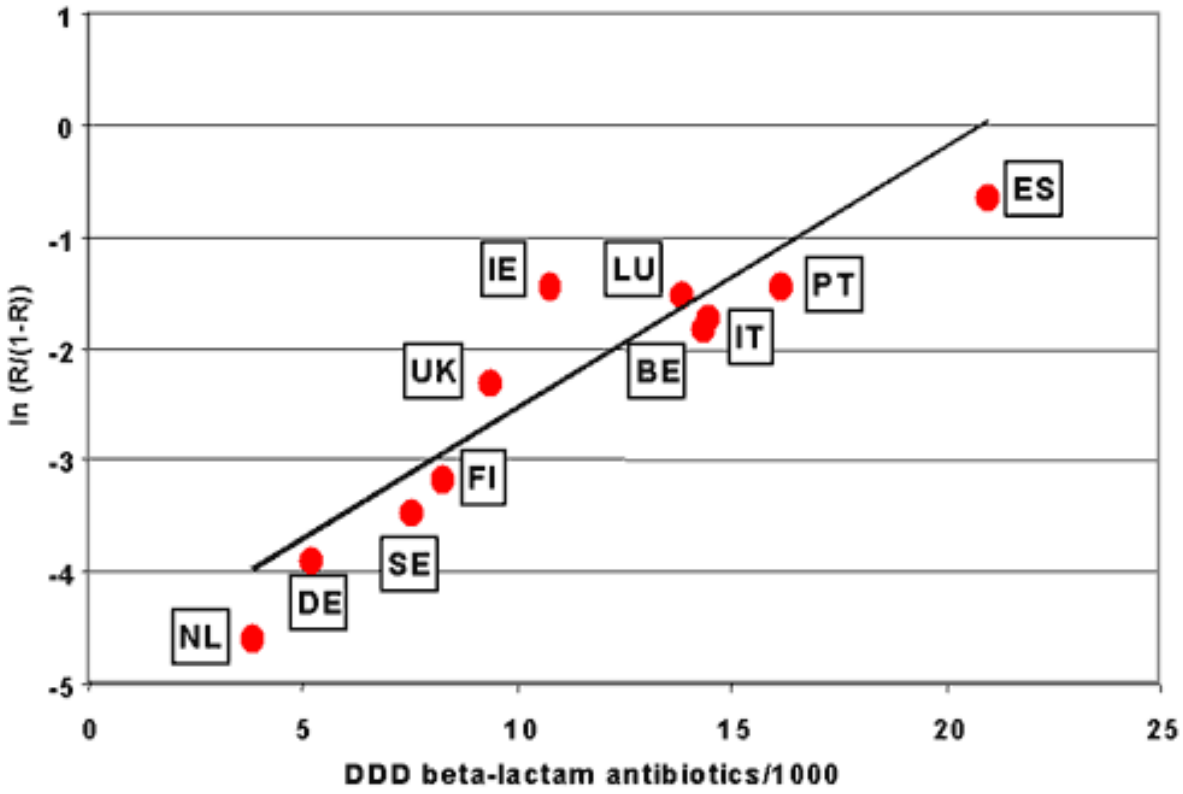
to a highly plastic material…



- an infectious focus typicaly contains more than 10^6 - 10^9 organisms
- most bacteria multiply VERY quickly (20 min…) and do mistake …
- they are not innocent or useless mistakes

fast selection of the fittest !

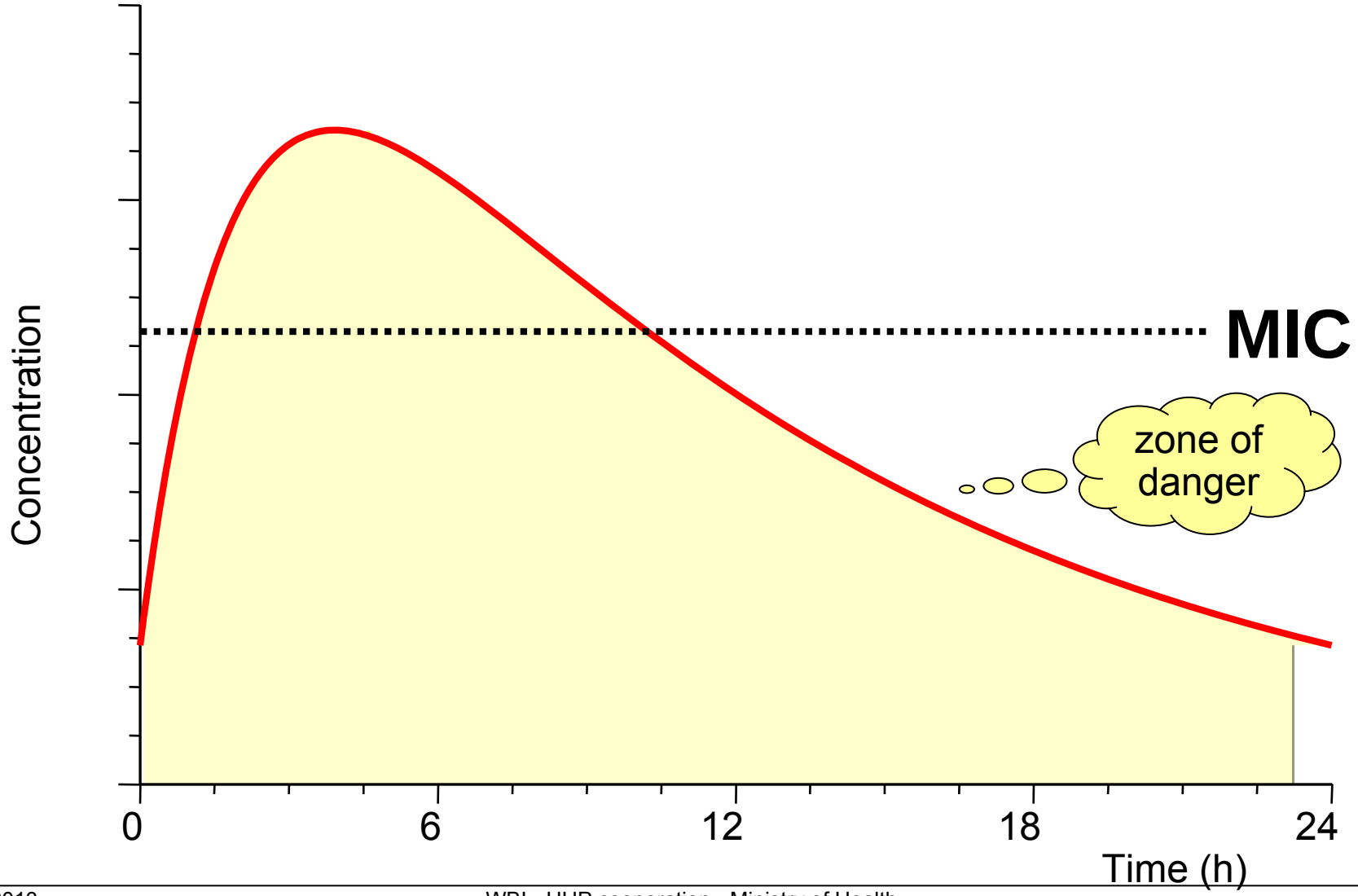
There is a clear association of resistance and the global use of antibiotics in EU contries



Logodds of resistance to penicillin among invasive isolates of Streptoccus pneumoniae regressed against outpatient sales of beta-lactam antibiotics in 11 European countries; (resistance data are from 1998 to 1999; antibiotic sales data 1997. DDD = defined daily dose)

Bronzwaer SL, Cars O, et al. Emerg Infect Dis 2002 Mar;8(3):278-82

There is also a fast emergence of resistance with the use of antibiotics at subtherapeutic doses



Actually, selecting for resistance is easy even in a closed system…

Exposure of *E. aerogenes* to anrti-Gram (-) β-lactams to 0.25 MIC for 14 days with daily readjustment of the concentration based on MIC determination

strains	Initial			TEM-exposed			Revertant		
	MIC (mg/L) [a]			MIC (mg/L)			MIC (mg/L)		
	TEM	FEP	MEM	TEM	FEP	MEM	TEM	FEP	MEM
2114/2 [c]	8	2	0.25	**2048**	**> 128**	**16**	**32**	4	0.5
2502/4 [c]	8	2	0.125	**8192**	4	0.25	**4096**	1	0.125
3511/1 [c]	**32**	2	0.125	**4096**	**32**	0.125	**4096**	**8**	0.5
7102/10 [d]	**512**	**32**	1	**16384**	**> 128**	4 [e]	**8192**	**64**	1

[a] figures in bold indicate values > the R breakpoint for Enterobacteriaceae (EUCAST for MEM [8] and FEP [4]; BSAC and Belgium for TEM [16])
[b] dotblot applied with antiOmp36 antibody; signal quantified for grey value after subtraction of the signal of a porin-negative strain (ImageJ software); negative values indicate a signal lower than the background
[c] ESBL TEM 24 (+) ; [d] ESBL (-) and AmpC (+) [high level] ; [e] Intermediate (I) according to EUCAST

Nguyen Thi Thu Hoai *et al*. (post-doc at LDRI)
presented at the 8th ISAAR, Seoul, Korea, 8 April 2011 and additional work in progress

A simple but very illustrative experiment …

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Nguyen Thi Thu Hoai *et al* (post-doc at IDRI) presented at the 8th ISAAR, Seoul, Korea, & [illegible] in progress

sub-MIC concentrations select for resistance !

What are the risks for Vietnam ?

1. Resistance seems to reach an alarming level in hospitals
   - ➢ increased use of "last resort" antibiotics (toxic and of dubious activity) or "makeshift" associations;
   - ➢ clinical experience of lack of efficacy of initial treatments...

Because there is no or very little progress in the discovery of new antibiotics against Gram-negative bacteria, failures in hospitals due to these organisms are likely to markedly increase

What are the risks for Vietnam ?

2. Resistance has also reached the community and moves from community to hospitals
   - ➢ patients enter hospitals with resistant strains;
   - ➢ failures in the community requiring hospitalizations
   - ➢ increased burden for hospitals

The global burden (hospital plus community) may become unbearable for the Health System leading to

major human and economic losses !

PDM

A few examples of antimicrobial resistance in Vietnam

Resistance to 11 antimicrobial drugs of *bla*$_{NDM-1}$–positive *Klebsiella pneumoniae* isolates from the Kim Nguu River, Hanoi, Vietnam

Antimicrobial drug	MIC, mg/L	
	Site X	Site Y
Piperacillin/tazobactam	64–>256	64–>256
Ceftazidime	>256	>256
Ceftriaxone	96–>256	128–>256
Meropenem	8–>32	12–>32
Imipenem	6–>32	>32
Fosfomycin	3–8	8
Gentamicin	>1,024	>1,024
Tobramycin	384–>1,024	256–384
Ciprofloxacin	0.064–1.5	0.064
Colistin	0.19–2	0.125–0.38
Tigecycline	1.5–3	0.5–1.5

Emerg Infect Dis. 2012 August; 18(8): 1383–1385

Resistance prevalence to tested antibiotics among 818 fecal isolates of *E.coli* from children aged 6-60 months in FilaBavi, Vietnam (BMC Infect Dis. 2012; 12: 92).

Antibiotic(s) tested	Prevalence of resistance % (n, total n = 818)
TET	74 (609)
SXT	68 (559)
AMP	65 (533)
CHL	40 (325)
NAL	27 (220)
CIP	< 1 (2)
TET + SXT + AMP	45 (368)
TET + SXT + AMP + CHL	25 (208)
TET + SXT + AMP + CHL + NAL	8 (68)

Abbreviations used: TET = tetracycline; SXT = co-trimoxazole; AMP = ampicillin; CHL = chloramphenicol; NAL = nalidixic acid; CIP = ciprofloxacin

Prevalence of multiresistant Gram-negative organisms in a surgical hospital in HCMC, Vietnam

Number of isolates of each bacterial species, with prevalence of ESBL detection amongst *Enterobacteriaceae*

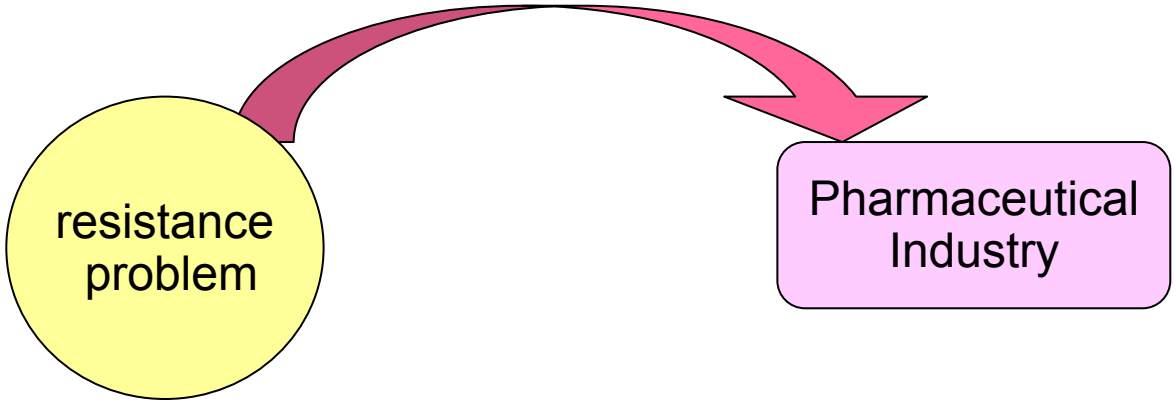
Organism	Number	ESBL (*n*)	ESBL (%)
Enterobacter spp.	71	4	5.5
Escherichia coli	150	29	19.3
Salmonella spp.	5	0	0.0
Klebsiella spp.	12	0	0.0
Citrobacter spp.	2	0	0.0
Proteus spp.	22	0	0.0
Edwardsiella spp.	10	7	70.0
Enterobacteriaceae	272	40	14.7

Tropical Medicine & International Health. 11, 11, p 1725–30, 2006

PMT

What are the risks for Vietnam ?

3. The system will NOT be self-healing because the current medico-economic system favors over-use (and mis-use) of antibiotics



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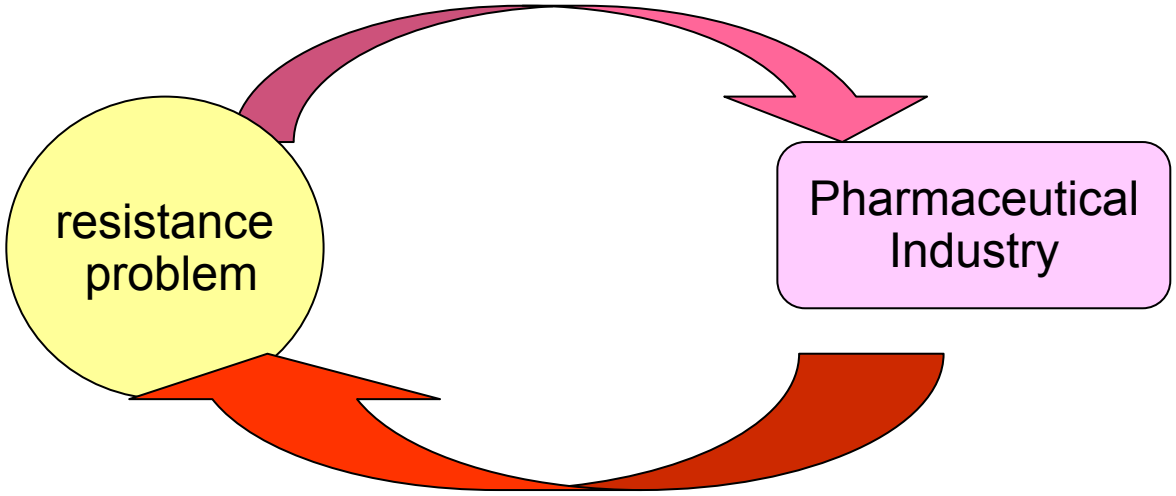

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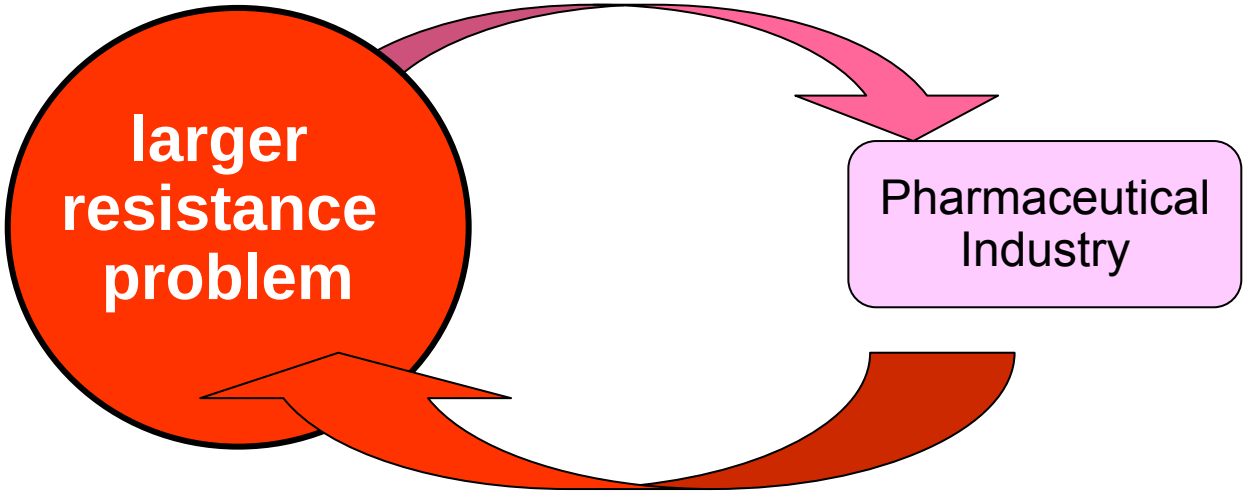


There is a clear need to change the rules in Vietnam

(as in many other countries)

High antibiotic consumption as a risk ?

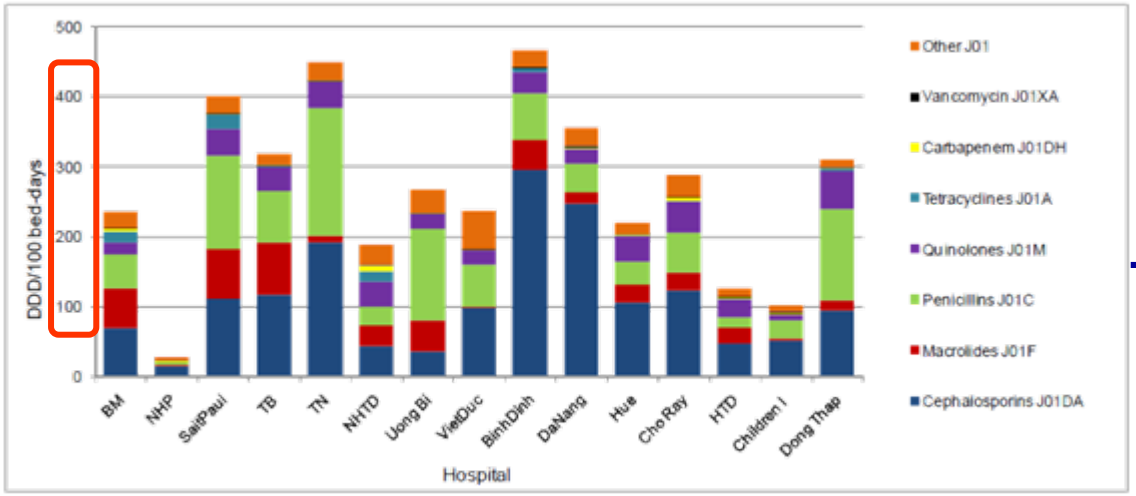
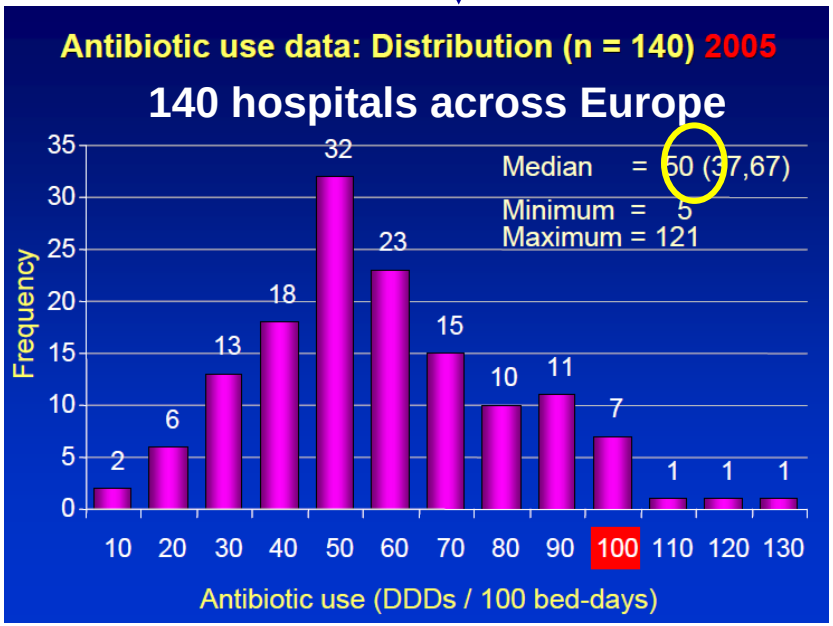


Figure 2. Total antibiotic consumption for systemic use (J01) by ATC class in 15 hospitals in Vietnam in 2008

Higher consumption than in Europe, e.g.

First report on antibiotic use and resistance in Vietnam hospitals



ARPAC
Antibiotic Resistance Prevention And Control

Conclusions (part #1)

- Resistance is a worldwide problem;
- Vietnam is not an exception, but levels of resistance seem to be very high;
- Resistance is, like in other countries, linked to overconsumption and/or wide distribution of antibiotics;
- In the absence of public coordinated action, no or little improvement is to be expected.

Time for questions and answers

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  Questions and Answers

- Presentation #2:
  Potential solutions...
  The Belgian experience

  Questions and Answers

- Presentation #3:
  Suggestions for Vietnam

  General discussion

Potential lines of action

ESSAY

Tackling antibiotic resistance

Karen Bush, Patrice Courvalin, Gautam Dantas, Julian Davies, Barry Eisenstein, Pentti Huovinen, George A. Jacoby, Roy Kishony, Barry N. Kreiswirth, Elizabeth Kutter, Stephen A. Lerner, Stuart Levy, Kim Lewis, Olga Lomovskaya, Jeffrey H. Miller, Shahriar Mobashery, Laura J. V. Piddock, Steven Projan, Christopher M. Thomas, Alexander Tomasz, Paul M. Tulkens, Timothy R. Walsh, James D. Watson, Jan Witkowski, Wolfgang Witte, Gerry Wright, Pamela Yeh and Helen I. Zgurskaya

Nature Reviews Microbiology 9, 894-896 (December 2011)

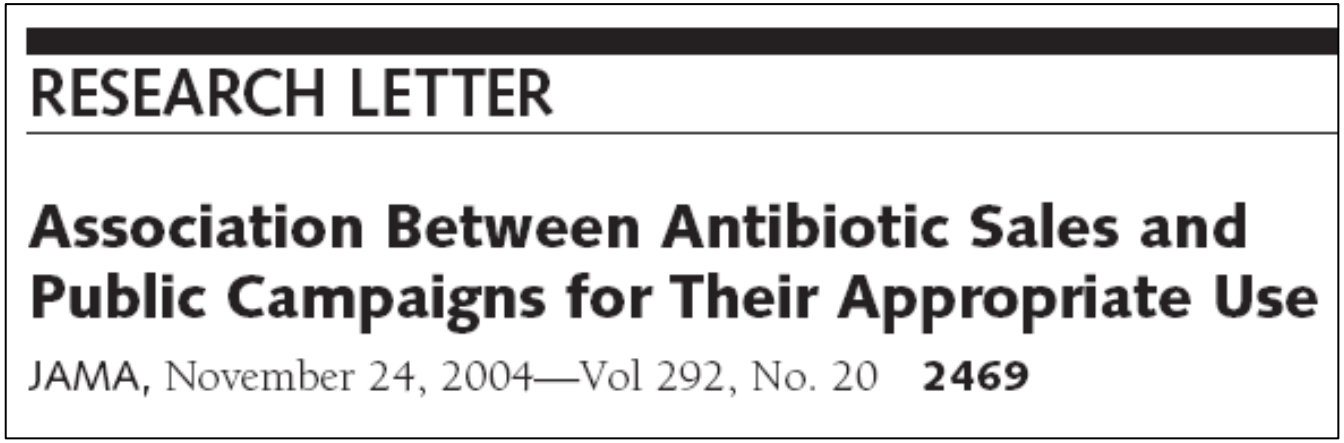
7 pillars of wisdom ?

1. **Public education**
2. **Public health, sanitation and quality of life**
3. New antibiotics → new / poorly exploited targets
4. Old antibiotics
5. **Better antibiotic use**
6. Alternatives to antibiotics
7. Collaborative approach and new Economics

Bush *et al*. Nature Reviews Microbiology 9, 894-896 (December 2011)

Public campaigns in Belgium

- Launched in 2000 (1st in Europe)
- Repeated (and evaluated) each year until now



RESEARCH LETTER

Association Between Antibiotic Sales and Public Campaigns for Their Appropriate Use

JAMA, November 24, 2004—Vol 292, No. 20 **2469**

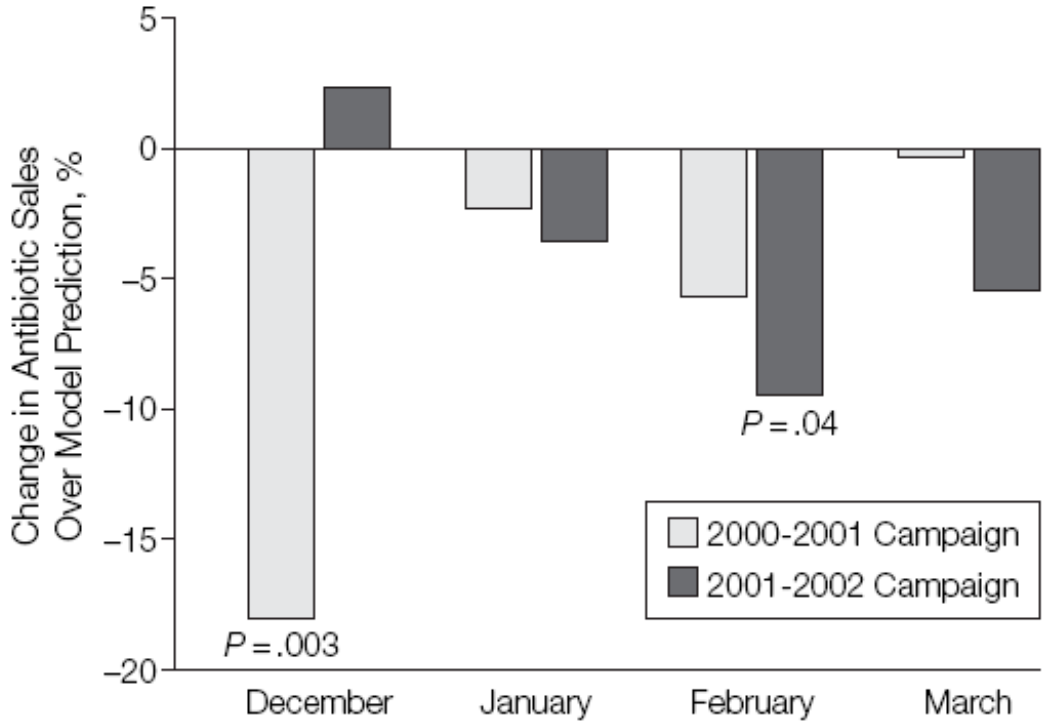
Bauraind I, Lopez-Lozano J-M, Beyaert A, Marchal J-L, Yane F, Goossens H, Tulkens PM, Verbist L

Public campaigns and decrease of antibiotic consumption in the community

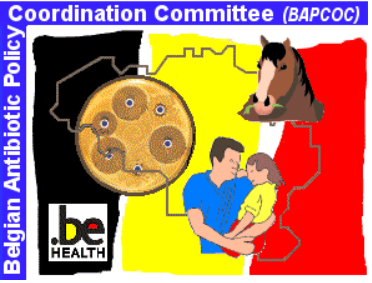
RESEARCH L

Association
Public Camp

JAMA, November 2

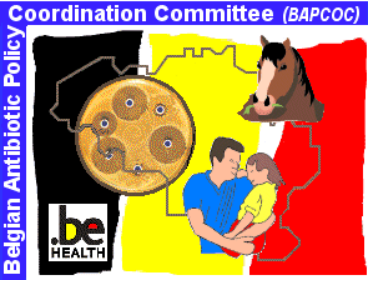


Residual seasonal autoregressive terms: lag period, 12 months; estimated coefficient: 0.83 [SE, 0.06]; constant: 7459075 (SD, 431387) defined daily doses/mo. The *P* values are indicated for the months and campaigns for which the changes were statistically significant.



Belgian Antibiotic Policy Coordination Committee

- Created by Royal Decree in 1999
- Multidisciplinary
- Scientific Experts and Representatives of the main Institutions
- With expertise in
  - microbiology,
  - resistance to antibiotics,
  - antibiotic management
  - assessment of antibiotic consuption
  - infection control and hygiene



Belgian Antibiotic Policy Coordination Committee

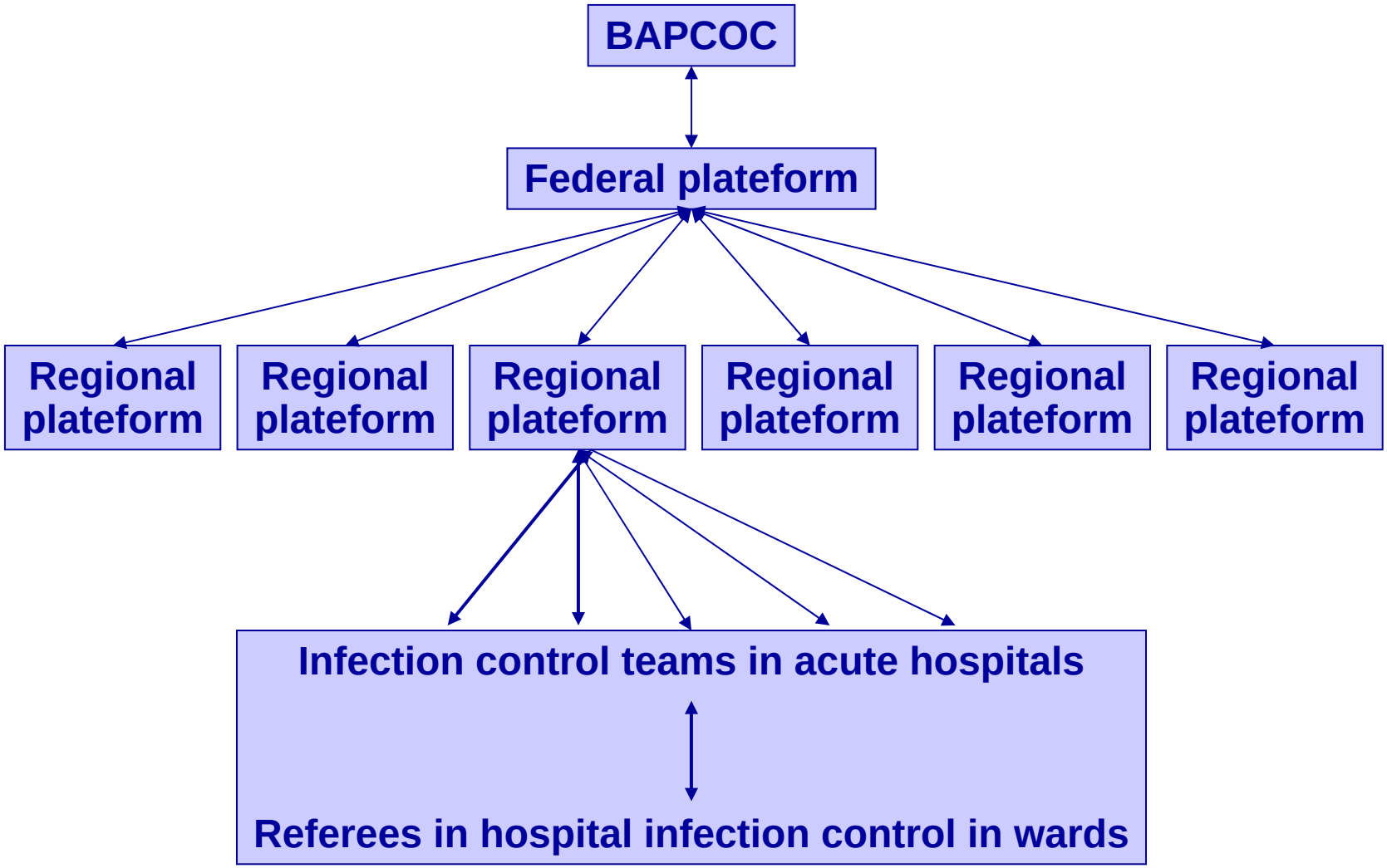
6 Working groups

- veterinary medicine
- public actions
- out-patients (community)
- hospital
- medical statistics
- Drug reimbursement committee

↔ **Scientific platforms**

PDM

Structure of infection control in hospitals



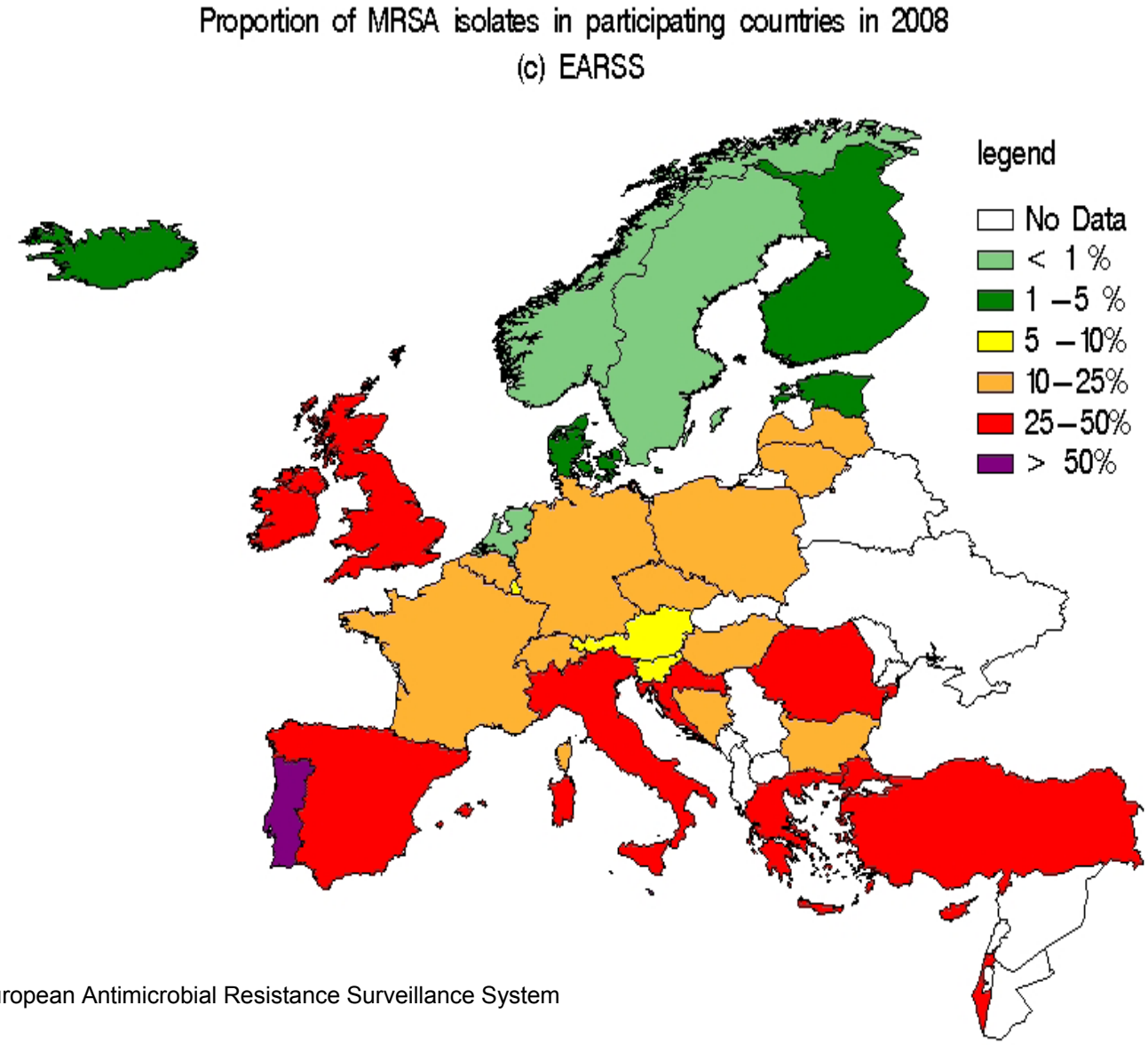
Non-antibiotic targeted prevention measures

- Developing nations
  - improving sanitation
  - cleaning up water supplies
  - relieving overcrowding
  - frequent hand washing

- Industrialized countries
  - frequent hand washing,
  - developing vaccines
  - Infection control programs in hospitals and in the community,

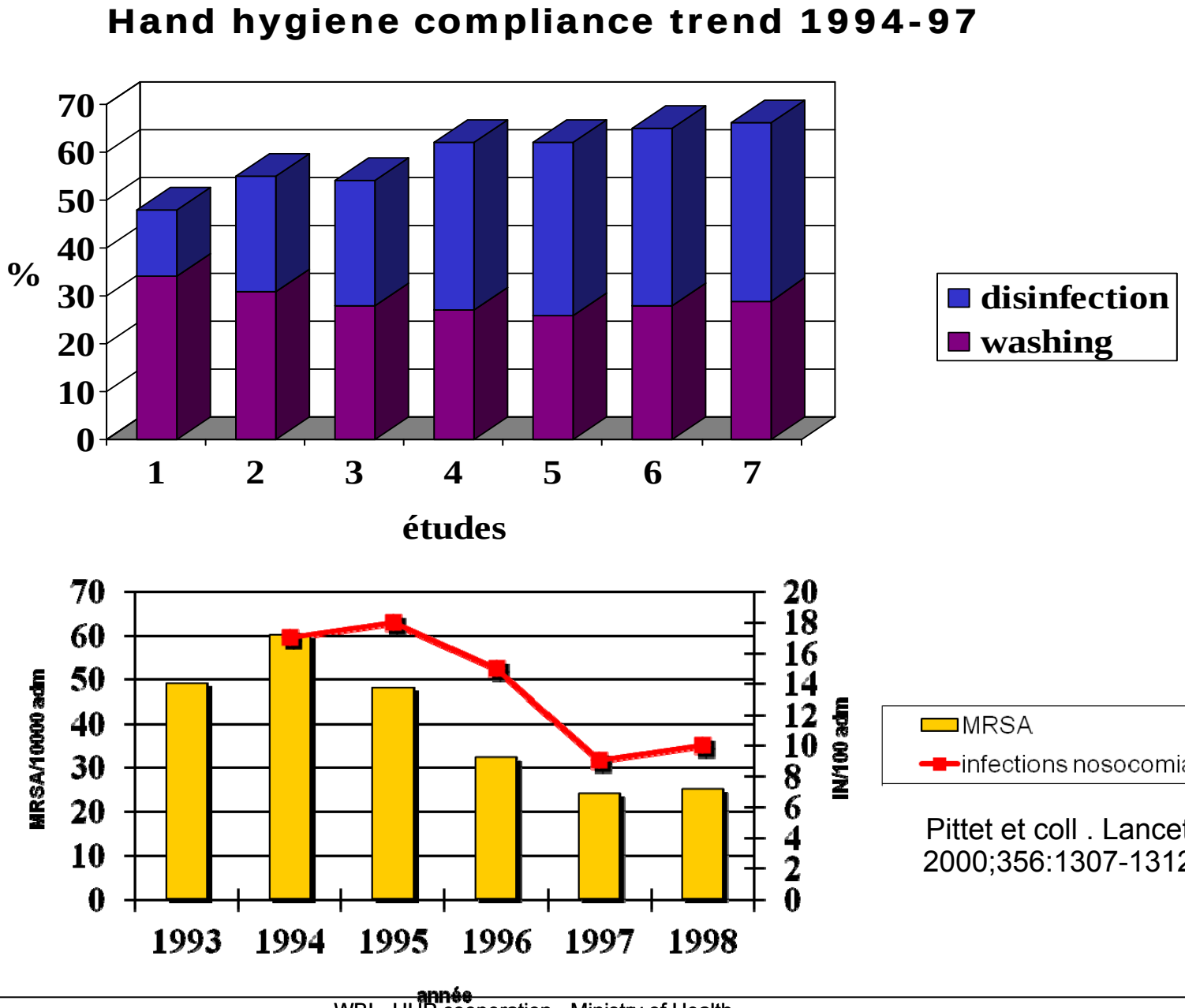
Global strategy for containment of antimicrobial resistance (WHO)

Trends of MRSA through Europe



EARSS: European Antimicrobial Resistance Surveillance System

Impact of Hand Hygiene on nosocomial infections



Pittet et coll . Lancet 2000;356:1307-1312

Epidemiological surveys in Belgium

- **National Institute for Public Health**: activities based on
  - **Sentinel laboratories** (associated with large hospitals)
    - Collection of specific strains (non-suscept. *S. pneumoniae*, MRSA, Carbapenemase-prodicing *Enterobacteriaceae*, *Legionella*…)
  - **National reference Centers** associated with University Hospitals or with NIH
    - characterization of the strains, epidemiology
  - **Sentinel general practitioners**
    - determination of the ongoing clinical situation of epidemic diseases (acute respiratory diseases, diarrhea,…)
    - Collection and analysis of the data at the NIH level

Epidemiological survey of *S. pneumoniae*

Pathologie Biologie 58 (2010) 147–151

ELSEVIER MASSON

Disponible en ligne sur ScienceDirect www.sciencedirect.com

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10th Survey of antimicrobial resistance in noninvasive clinical isolates of *Streptococcus pneumoniae* collected in Belgium during winter 2007–2008

Dixième surveillance de la résistance aux antibiotiques dans des souches non invasives de Streptococcus pneumoniae collectionnées en Belgique pendant l'hiver 2007 à 2008

R. Vanhoof [a,*], K. Camps [b], M. Carpentier [c], S. De Craeye [a], J. Frans [d], Y. Glupczynski [e], P. Goffinet [f], B. Gordts [g], D. Govaerts [h], L. Ide [i], P. Lefèvre [j], M. Lontie [k], R. Cartuyvels [l], F. Meunier [m], B. Mulongo [n], I. Philippart [o], I. Surmont [p], E. Van Bossuyt [a], J. Van Eldere [q], J. Verhaegen [q]

[a] *WIV/ISP, Unit of Antibiotic Research, Institute of Public Health, 642, Engelandstraat, 1180 Brussel, Belgium*
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[e] *Clinique universitaire de Mont-Godinne, 5530 Yvoir, Belgium*
[f] *Cliniques du Sud-Luxembourg, 6700 Arlon, Belgium*
[g] *AZ St. Jan, 8000 Brugge, Belgium*
[h] *CHU André-Vésale, 6110 Montignies-le-Tilleul, Belgium*
[i] *AZ Jan Palfijn, 9000 Gent, Belgium*
[j] *Hôpital Princesse-Paola, 6900 Marche-en-Famenne, Belgium*
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[l] *Virga-Jesseziekenhuis, 3500 Hasselt, Belgium*
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[p] *H.-Hartziekenhuis, 8800 Roeselare, Belgium*
[q] *National Reference Centre Pneumococci, UZ Gasthuisberg, 3000 Leuven, Belgium*

Epidemiological survey of *S. pneumoniae*

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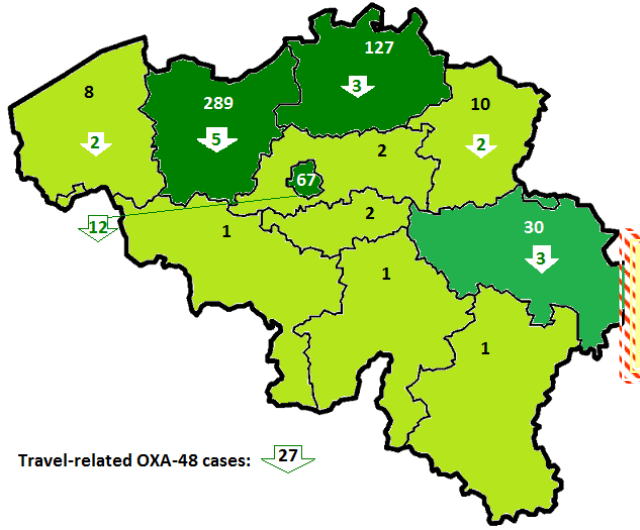
Regional distribution by carbapenemase type:

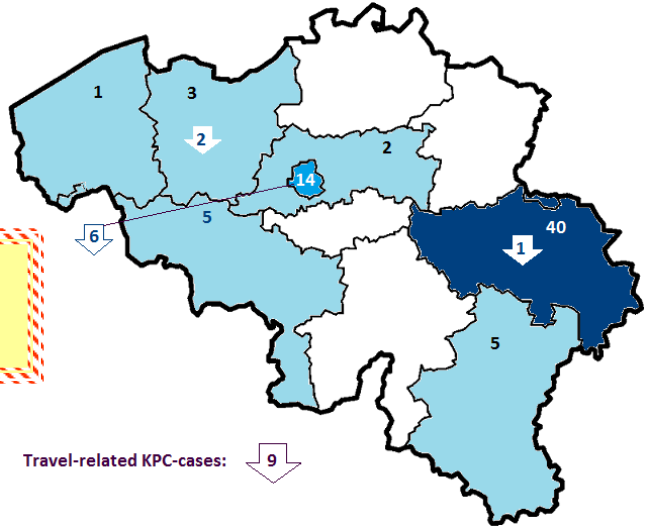
1/1/2012 - 30/06/2013

Belgian surveillance data: January 2012 - June 2013



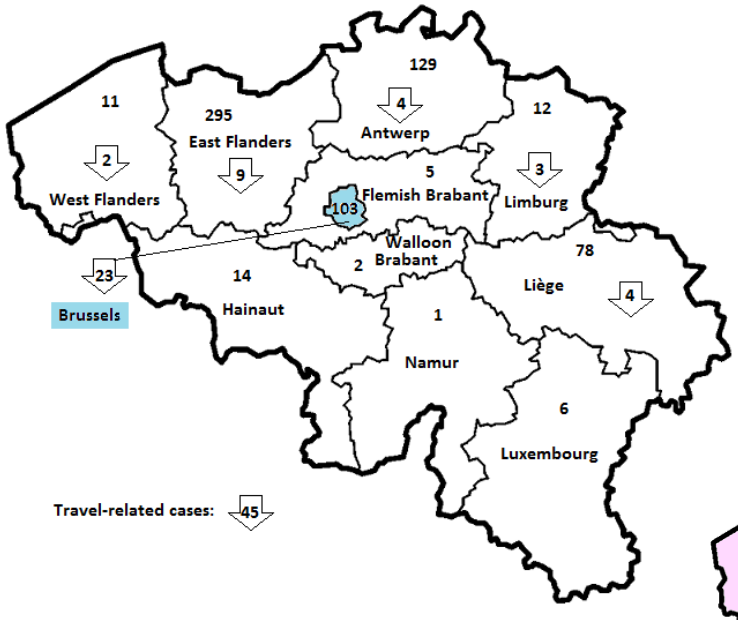
OXA-48: *538 cases*

Hospitals with OXA-48 clusters: 14



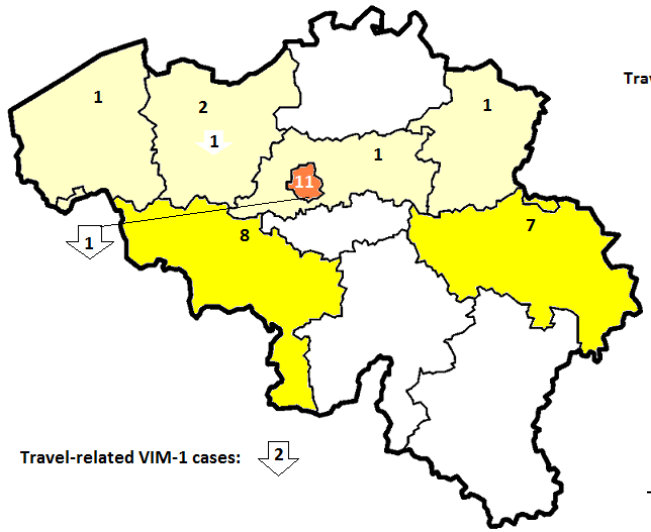
KPC-2: *70 cases*

Hospitals with KPC-clusters: 6



VIM-1: *31 cases*

Hospitals with VIM-clusters: 1



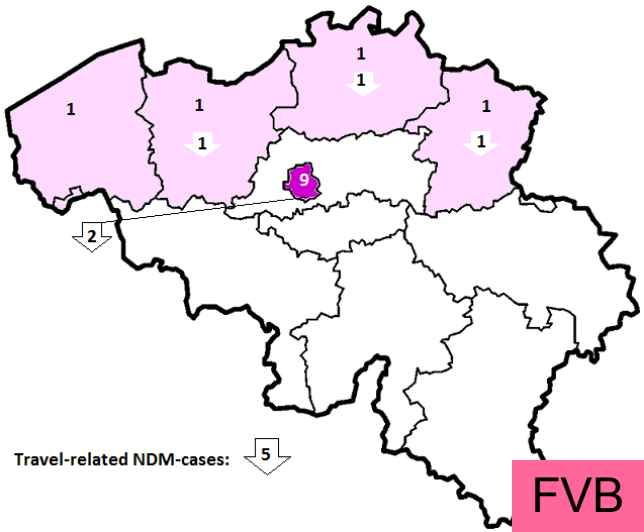
All carbapenemase types: 656 *cases*

Hospitals with ≥ 1 cluster: 20 (22 clusters)

ICAAC 2013, B. Jans, D. T-D Huang, P. Bogaerts, B. Catry, Y. Glupczynski

NDM: *13 cases*

Hospitals with NDM-clusters: 1



FVB

Guidelines to improve antibiotic use

service public fédéral
SANTE PUBLIQUE, SECURITE DE LA CHAINE ALIMENTAIRE ET ENVIRONNEMENT

Ma santé | Sécurité alimentaire | Soins de santé | Animaux et végétaux | Environnement

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- Hygiène hospitalière
- NOSO INFO
- E-Bug
- Pharmaciens
- MR/MRS/MRPA
- PPS HAI & Ab use

suivre cette page

Pratique ambulatoire

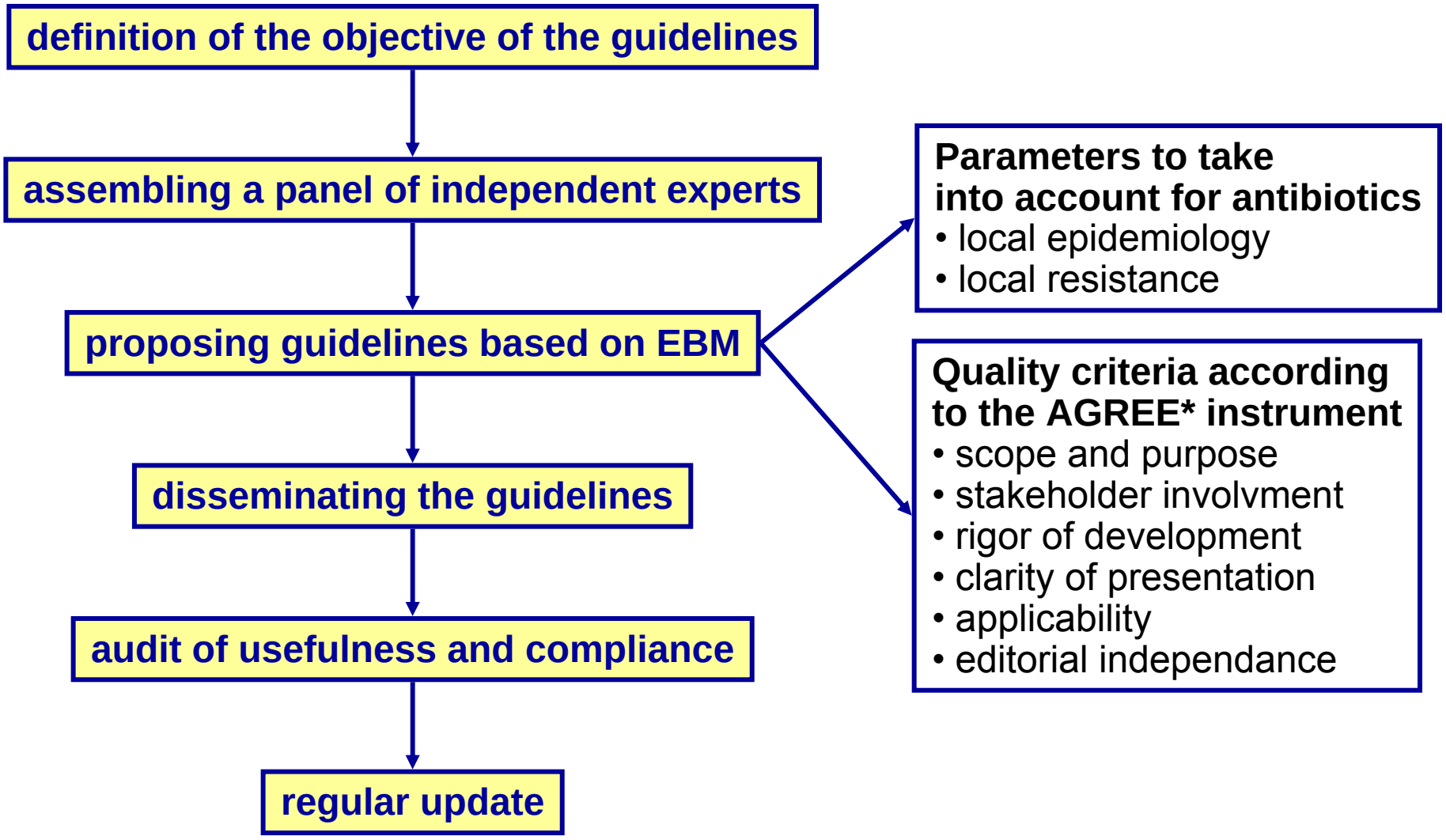
* NOUVEAU *

[PDF] Guide belge des traitements anti-infectieux en pratique ambulatoire - édition 2012

[PDF] Intercalaire antibiotiques pour médecins généraliste - édition 2012 (résumé du guide ci-dessus)

Recommandation - Prise en charge de la gastro-entérite aiguë en pratique ambulatoire

Setting-up guidelines to improve antibiotic use



***A**ppraisal of **G**uidelines **R**esearch and **E**valuation – developed through an EU-funded research project and available on http://www.agreetrust.org/

Guidelines in Vietnam: current issues

Based on reflections from GARP Phase 1 Vietnam
Nguyen Van Kinh, M.D, Ph.D
Chairman, GARP-Vietnam
Director of National Hospital for Tropical Diseases
On behalf of GARP-VN National Working Group

- Most treatment guidelines outdated
- Recommendations for antibiotics do not take into account current resistance profiles
- Guidelines use 'Western' data, not Asian
- Must take into account local epidemiology

→ improvement desirable

Antibiotic policy control group in Belgium

Multidisciplinary team …

manager

Infectious diseases MD

Clinical pharmacist trained in ID

informatician

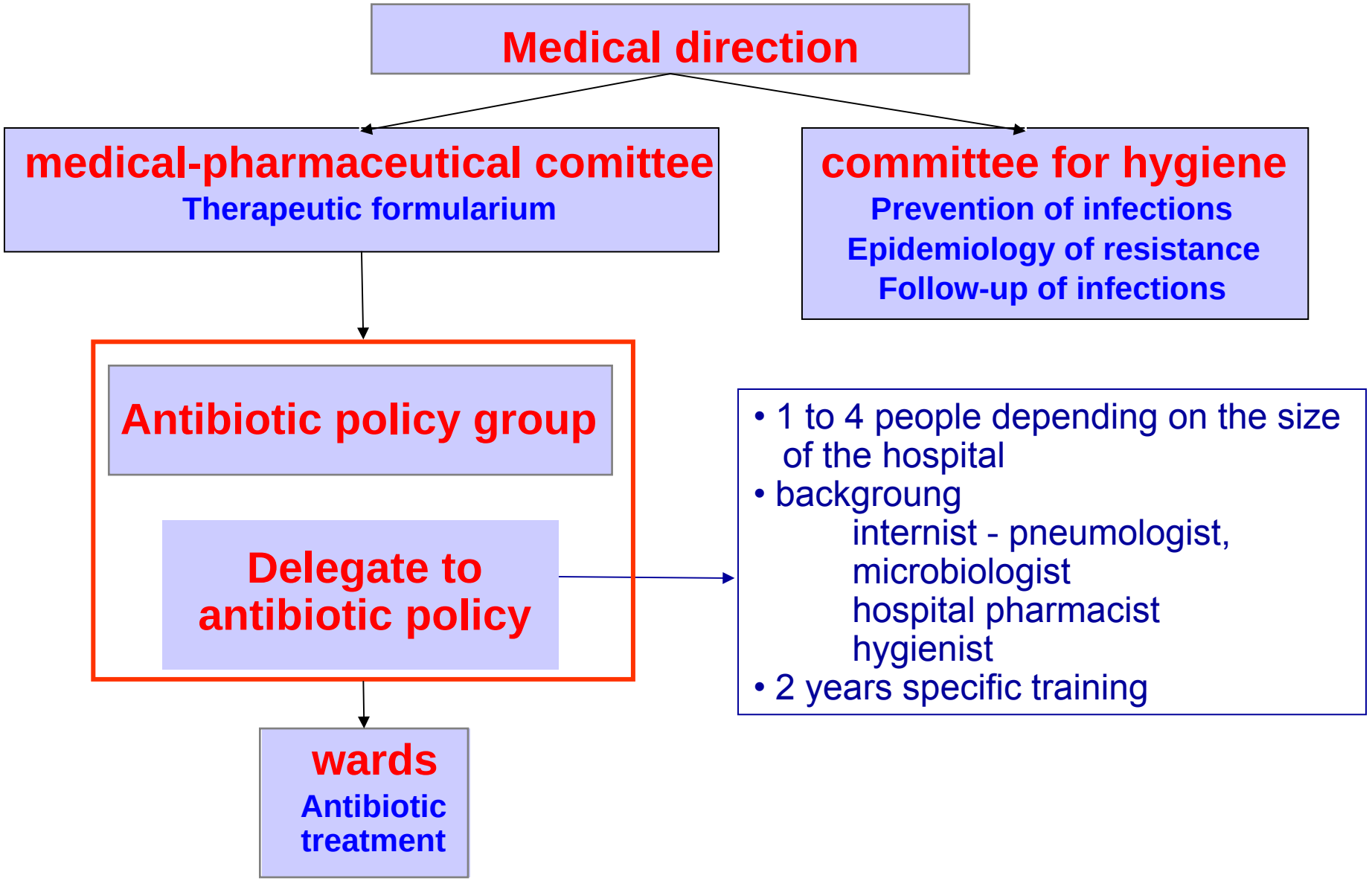
microbiologist

pharmacist

MD from departments using antibiotics

infection control specialist

Position within the hospital organigram



Priority tasks

- **Mandatory interventions**
  - Hospital formularium
- **Required interventions**
  - Guidelines
  - Local epidemiology
- **Priority interventions**
  - Evaluation of consumption
  - Link between consumption and epidemiology
  - Providing advice about antibiotic use
  - Limitation and control of antibiotic usage
  - Staff education
  - Annual report for the commission coordinating antibiotic policy

One example of intervention of the antibiotic policy group in Belgium

St Luc hospital, Université catholique de Louvain

University hospital, ~ 950 beds

22 pharmacists
Among them, 6 full-time in clinical pharmacy

One example of the situation in St-Luc Hospital before implementation of Antibiotic Management

Follow-up of the use of broad spectrum antibiotics

Results	Meropenem	Pip-tazo	Ceftriaxone
Clinically justified Prescriptions	84 %	83%	86%
Bacteriologically justified prescriptions	56 %	28 %	17%
Clin. and bacteriol. justified prescriptions	52 %	26 %	17 %
Treatment duration appropriate	84.5 %	90 %	76%
% correct posologies	86 %	76 %	95 %

Conclusions part #2

- The Belgian experience shows that useful programs can be initiated on a coordinated fashion nationwide;
- This involves the Ministry of Health which acts through specialized national programmes and agencies, universities, hospitals, and general practitioners;
- 4 actions are essential: Antibiotic Management (hospital), Guidelines, Epidemiology, Infection Control
- BAPCOC (Belgian Antibiotic Policy Coordination Committee is the keystone of most of these activities, with epidemiological studies coordinated by the National Institute of Health.

Time for questions and answers

Programme

- Presentation #1:
  Resistance to antibiotics and risks for Vietnam

  Questions and Answers

- Presentation #2:
  Potential solutions...
  The Belgian experience

  Questions and Answers

- Presentation #3:
  Suggestions for Vietnam

  General discussion

1. Epidemiological surveys

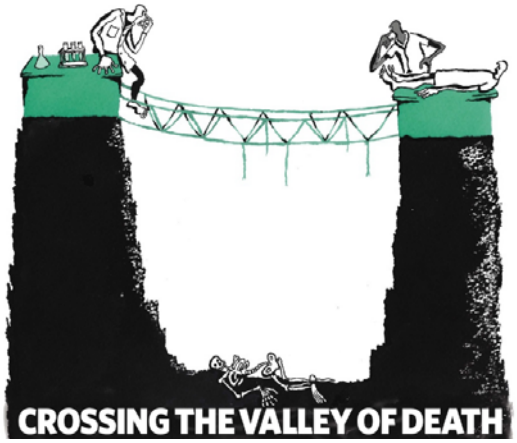
- Collection of representative strains in key centers (sentinels) carefully selected across the country (both community and hospitals):
- Centralized analysis of the data in specific centers (including quality control of the sampling);
- Accurate identification (environment vs. true human pathogens);
- MICs distributions to be preferred to Susceptible/Resistant only;
- Periodic reports including statistical analysis to be communicated to Ministry of Health and to practitioners with recommendations for improvement;
- Data to be used for elaborating or updating therapeutic guidelines, defining essential antibiotics, and rationalizing antibiotic policies.

2. Promoting a better use of antibiotics in the Community

- Training of Pharmacists (both after graduation and during their studies)
- Training of the Assistant Pharmacists
- Promotion of Family Doctors
- Addressing the issues of delivery without prescription
- Increase the awareness of the public about risks of inappropriate use
- Effective control of promotion by Industry Representatives

3. Antibiotic Management groups in hospitals

- Improving co-working between all currently involved healthcare practitioners
- Make the microbiologist more involved in the decision and the follow-up process of infectious diseases management
- Adding and developing clinical pharmacy (both centralized and in the ward)
- Follow-up of local situations in each hospital and rapid reaction in case of infectious problem (Infection Control Team)



Nature (2008) 453:840-842

4. “VAPCOC”

- Promote at the level of the Ministry of Heath a National Coordination Center susceptible to centralize the various activities and programmes already initiated about antibiotic resistance by different stakeholders (Vietnamese Antibiotic Policy Coordination Committee [VAPCOC]);
- Have VAPCOC
  - create new initiatives as fitted to the Vietnamese situation (such as Clinical Pharmacists, Hospital Antibiotic Management Team, ...) and to liaise with the newly formed Vienamese Drug Center;
  - stimulate coordinated epidemiological surveillance systems that meet the requirements of Vietnam (e.g., specific alert systems, quality control, specific infections,...);
  - defining the priorities for action and the proposed strategies.

5. Change of economical model (1)

- In the current economic framework, Pharmaceutical Industry is looking for mass sales as this is how they win money;
- the situation is exacerbated by the emergence of generics where lower prices can only be compensated by larger sales (hospital and community)

This creates a situation intrinsically in contradiction with a prudent use of antibiotics (limited sales for serious indications and restricted use of most potent antibiotics)

5. Change of economical model (2)

- Alternative models can and must be developed

- One potential model is where Government and Industry make an agreement on
  - volume of sales (DDDs, or other)
  - prices

  in a tender system where the winner also takes responsibility for promoting the appropriate use of antibiotics

The goal is to dissociate volume of sales and incomes and to discourage excessive sales

Time for questions and answers