Cooperation

Wallonie-Bruxelles – Hanoi University of Pharmacy

Activities and Visit to Uong Bi Hospital

Antibiotic consumption: why and how ?

Why do you need to know about antibiotic consumption ?

1. Antibiotics are like any drug: you need to know what you do …
2. Antibiotics are expensive, and knowledge of consumption helps to contain costs
3. Antibiotics are perceived as “general drugs” but have actually specific indications
4. Antibiotic consumption leads to resistance … and the loss of antibiotic

But remember that antibiotics save life …
as long as they are active…

How do you measure antibiotic consumption ?

- The simple approach: no. of mg, kg, …
- A more pharmaceutical approach:
  - no. of boxes, vials, …
  - DDDs
- A more close to reality approach
  - DDA
  - no. of prescriptions
  - no. of patients receiving antibiotics (prevalence)
  - route of administration (IV, oral…)
- An incisive approach
  - no. of prescriptions by departments
  - no. of prescriptions by prescriber
- A clinical approach
  - Level of prescription by pathology / indication
- The “Wall street” approach: $, €, VTN …

The simple approach : mg , kg

- Mostly useful
  - For producers
    ➔ as evidence of their capacity of production, of sales …)
  - for Public Health Authorities
    ➔ for comparison between countries and evaluation of general antibiotic pressure between target groups (humans vs. animals, inter-regions comparisons, …)

How much colisitin is used in animals ?

Not truly informative for clinicians beyond what is above …

no. of boxes, vials - DDDs

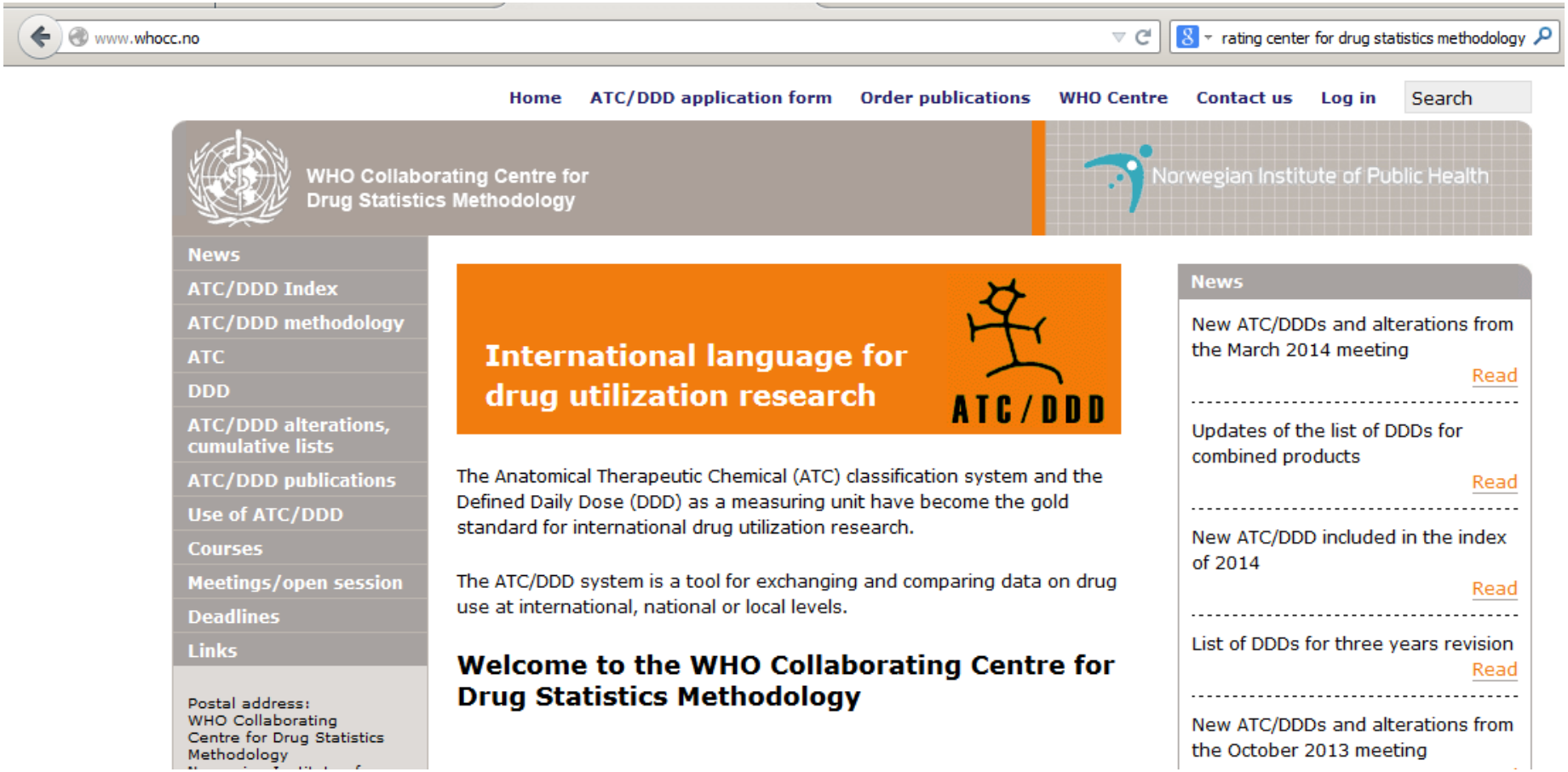
- Boxes, vials
  - ☆ easy and immediate perception…
  - 💣 not really informative in clinical terms (how many pills/box, how many vials/patient ?
  - 💣 Subject to temporal and geographical variations (often marketing-driven)
- DDD = Defined Daily Doses
  - ☆ provides a link to the clinics
  - ☆ allows comparisons between wards, hospitals, countries…
  - ☞ requires some work and may not always correspond to reality

Where do we find the DDDs ?

- ATC/DDD
  - ATC: Anatomical Therapeutic Chemical classification
  - DDD: Defined Daily Dose
- History
  - 1976: The Nordic Council on Medicines (NLN) published the Nordic Statistics on Medicines using the ATC/DDD methodology
  - 1996: WHO recognized the need to develop use of the ATC/DDD system as an international standard for drug utilization studies.
- Aim
  - presentation and comparison of drug consumption statistics at international and other level

Where do we find the DDDs ?

http://www.whocc.no/



Codes ATC

- Drugs are classified in groups at five different levels.
  - 1st level
    - fourteen main groups according to the organ or system on which they act
  - 2nd level
    - pharmacological/therapeutic subgroup
  - 3rd and 4th levels
    - chemical/pharmacological/therapeutic subgroups
  - 5th level
    - chemical substance
- Be aware for change of ATC codes

Codes ATC

Code (level 1)	Description
A	Alimentary tract and metabolism
B	Blood and blood forming organs
C	Cardiovascular system
D	Dermatologicals
G	Genit urinary system and sex hormones
H	Systemic hormonal preparations, excl. sex hormones
J	General antiinfectives for systemic use
L	Antineoplastic and immunomodulating agents
M	Musculo-skeletal system
N	Nervous system
P	Antiparasitic products
R	Respiratory system
S	Sensory organs
V	Various

ATC: code J and subcodes

- J **ANTIINFECTIVES FOR SYSTEMIC USE**
- J01 **ANTIBACTERIALS FOR SYSTEMIC USE**
- J02 **ANTIMYCOTICS FOR SYSTEMIC USE**
- J04 **ANTIMYCOBACTERIALS**
- J05 **ANTIVIRALS FOR SYSTEMIC USE**
- J06 **IMMUNE SERA AND IMMUNOGLOBULINS**
- J07 **VACCINES**

ATC: example of amoxicillin

J	Anti-infectives for systemic use	*1st level, anatomical main group*
J01	Antibiotics for systemic use	*2nd level, therapeutic subgroup*
J01C	Beta-lactam-antibiotics, penicillins	*3rd level, pharmacological subgroup*
J01CA	Broad spectrum penicillins	*4th level, chemical subgroup*
J01CA04	Amoxicilline	*5th level, chemical substance*

DDDs: pros …

- **The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (70 kg)**

- **normally one DDD for each drug, independent of the package**
  - DDD amoxicilline-clavulanic acid IV = 3 G
- **systematic update by experts**
- **provide a fixed unit to assess trends in drug consumption and to perform comparisons between population groups**
- **international unit (publications)**

DDDs: cons …

- no doses for pediatric use
- does not necessarily reflect the recommended or prescribed daily dose
  - DDD piperacillin-tazobactam IV = 14 G (may be true …)
- doses for individual patients and patient groups will often differ from the DDD and will necessarily have to be based on individual characteristics (e.g. age and weight) and pharmacokinetic considerations
- be aware of DDD changes

DDAs: Daily Dose of Administration

- The DDA is the assumed average maintenance dose per day for a drug used for its main indication in adults (70 kg) **specific for a formulation**
  - DDA piperacillin tazobactam IV 2 G = 7000 MG
  - DDA piperacillin tazobactam IV 4 G = 14000 MG 3.5 G
- National unit (can not be used for international comparison) more related to actual practice
- List with DDD (WHO) and DDA (Belgium) be available on line (in French) (http://www.nsih.be/download/GM/2014/Surv_AB_register2014.xls)

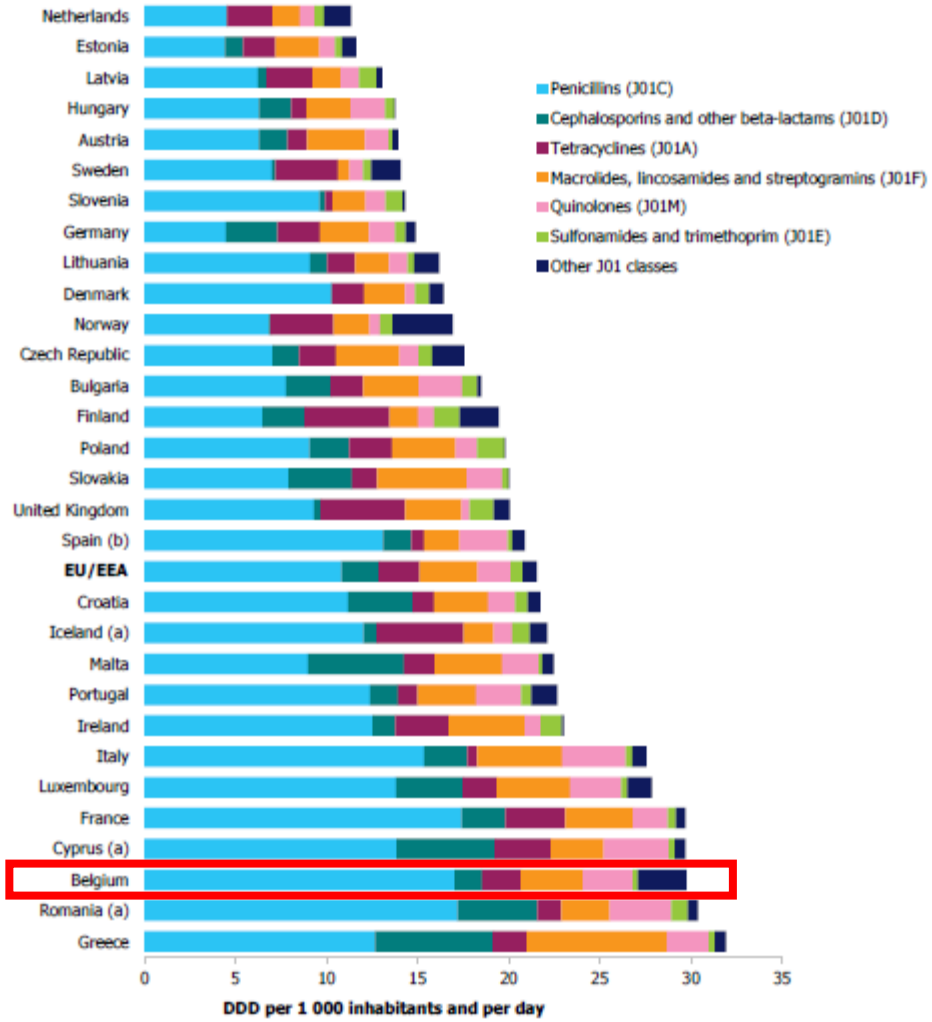
may be useful for creating a Vietnamese equivament…

DDDs and DDAs need a denominator

- **Patient-days (per 100 or 1000 patient-days)**
  - Occupied beds
  - In practice: administrative bed-days
- **Inhabitant days**
  - For antimicrobial consumption in primary health care
  - Should not be used for hospitals
- **Admissions or discharges**
  - For calculating % patients exposed to antibiotics

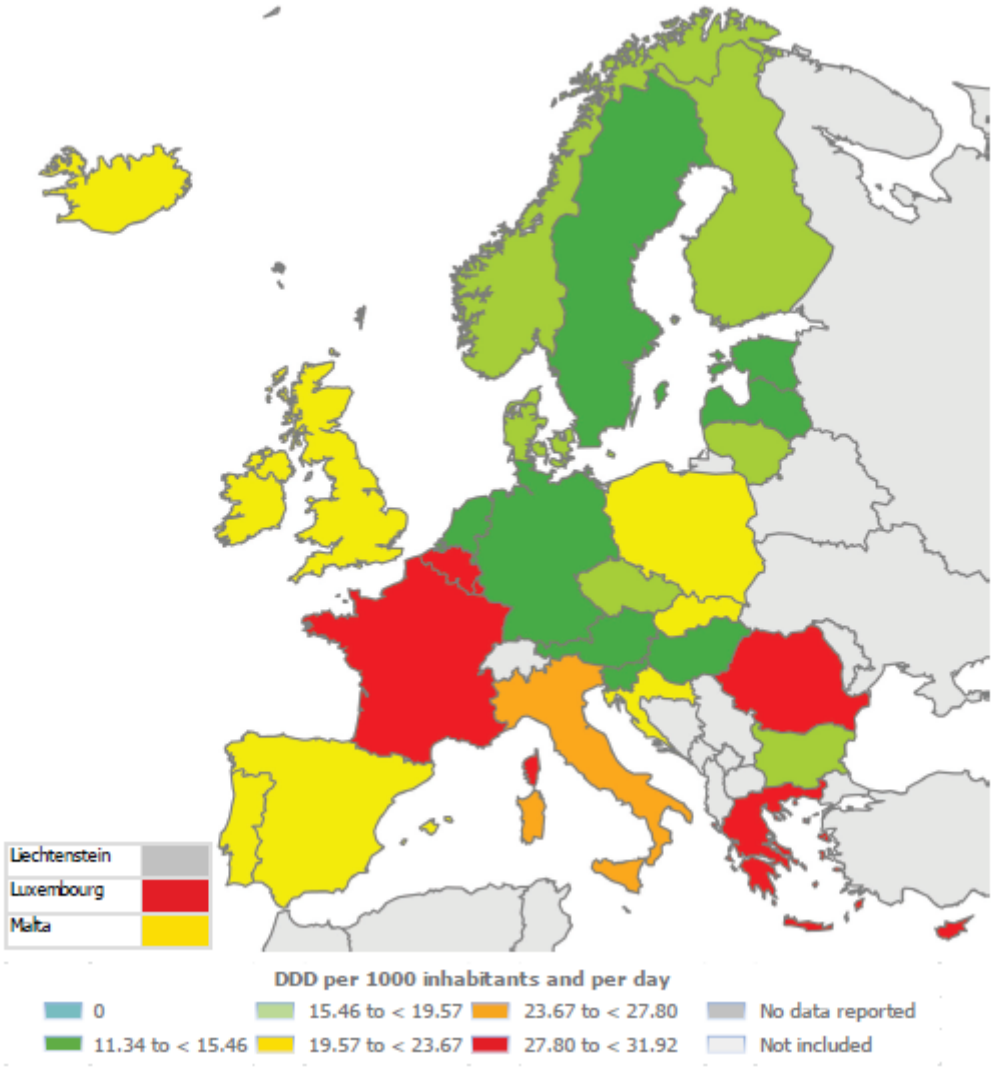
Examples of DDSs with denominator

Figure 3.1. Consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



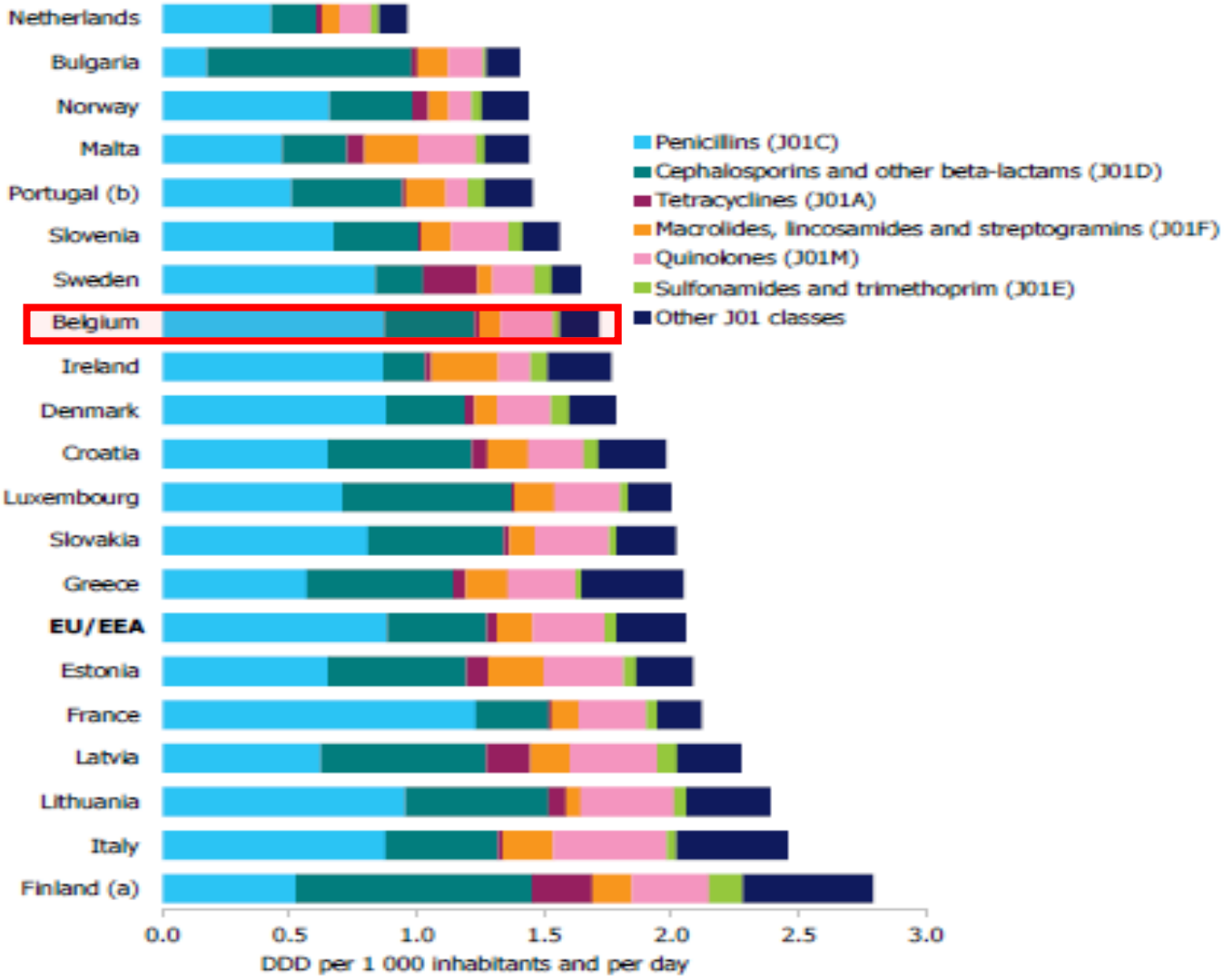
Examples of DDSs with denominator

Figure 3.2. **Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day**



Examples of DDSs with denominator

Figure 4.1. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector in EU/EEA countries, 2012, at group level 3, expressed as DDD per 1 000 inhabitants and per day



No. of prescriptions

- can easily be collected for **hospitalized patients**
- for outpatients: it all depends from the collaboration of the retail pharmacists … and the level of coverage by Social Security (reimbursements)
- allows for a direct assessment of the **medical activities** if taken globally … but individualization is also possible (see more later…)
- comes as very useful complement to DDS…

No of patient receiving an antibiotic

- very useful to assess the **exposure of a given population** to antibiotics
- is amenable to **prevalence studies**
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- is amenable to **prevalence studies**

American Journal of Infection Control 40 (2012) 840-4

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Antibiotic use in Vietnamese hospitals: A multicenter point-prevalence study

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No of patient receiving an antibiotic

- very useful to assess the **exposure of a given population** to antibiotics
- is amenable to **prevalence studies**
- very useful to assess the **exposure of a given population** to antibiotics
- is amenable to **prevalence studies … including out of the hospital**

Nga *et al. BMC Pharmacology and Toxicology* 2014, **15**:6
http://www.biomedcentral.com/2050-6511/15/1/6

BMC Pharmacology & Toxicology

RESEARCH ARTICLE Open Access

Antibiotic sales in rural and urban pharmacies in northern Vietnam: an observational study

Do Thi Thuy Nga[1*], Nguyen Thi Kim Chuc[2], Nguyen Phuong Hoa[2], Nguyen Quynh Hoa[3], Nguyen Thi Thuy Nguyen[2], Hoang Thi Loan[2], Tran Khanh Toan[2], Ho Dang Phuc[4], Peter Horby[1,5], Nguyen Van Yen[6], Nguyen Van Kinh[7] and Heiman FL Wertheim[1,5]

Consumption by route of administration

- mainly used to compare IV and oral for antibioutics with high oral bioavaiability
- allows to foster the switch to oral route whenever possible
  - lesser risk of blood stream infections and catheter-related infections (biofilms…)
  - often associated with a large decrease of price…

Pré. 4 days 8 days

Formation of a biofilm on a catheter

Goto *et al* 1999 IJAA 11:227-232

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Clinicians' Knowledge, Beliefs and Acceptance of Intravenous-to-oral Antibiotic Switching, Hospital Pulau Pinang

S L Lee, MPharm, Sarriff Azmi, BPharm, Pharm D, P S Wong, MBBS, MRCP

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Med J Malaysia Vol 67 No 2 April 2012

No. of prescriptions by department / by physicians

- can be **extremely informative**
- but must be **manipulated with caution**
  (the goal should be to inform, not to penalize)

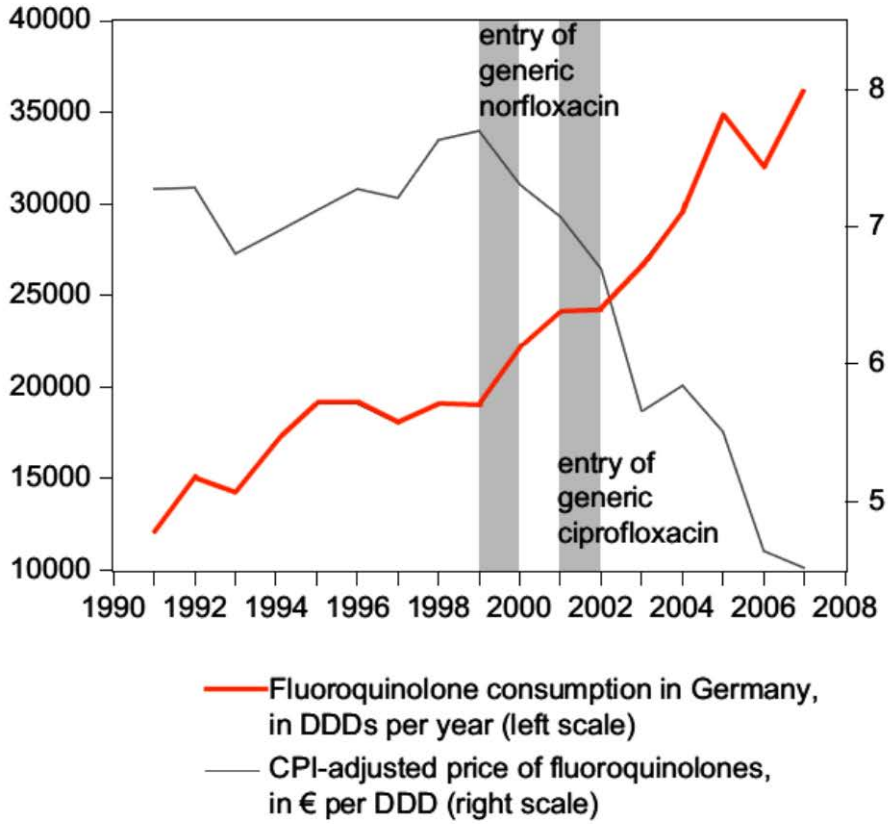
A clinical approach

- consumption by **pathology**
  - allows to identify the true areas of large consumption
  - allows to detect obvious deviations (too long treatments, too long prophylaxis, e.g.)
  - good to compare practices between prescribers around a specific domain
  - must be made by or with support of MDs knowledgeable in the pathologies
- consumption by **indication**
  - requires that the indication is known (including common “off label” indications) and can be well defined
  - can be made by pharmacists (under medical control)
  - good to compare consumption between hospitals for specific applications (e.g., community-acquired pneumonia)

The “Wall street” approach ($, €, VND…)

- Should be part of a comprehensive financial analysis (antibiotics are usually cheap…)
- Is only meaningful locally or in unified markets
- Subject to huge temporal variations (without commensurate change in antibiotic exposure)
- can be totally misleading in terms of antibiotic policy
- but is of interest for Governments … and is of prime interest for Industry…

What if you only consider the “Wall street” results ?



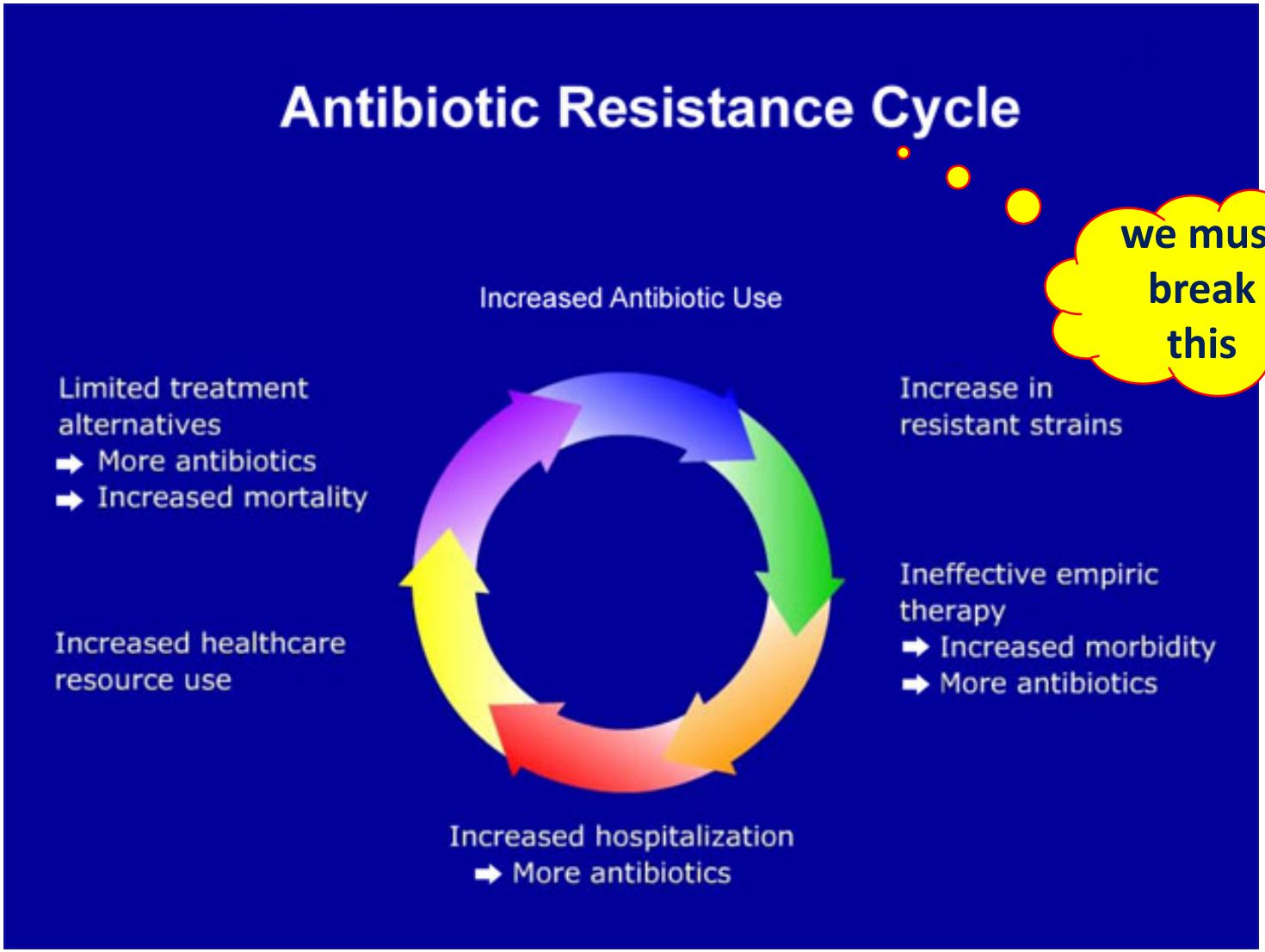
consumption goes up

prices go down

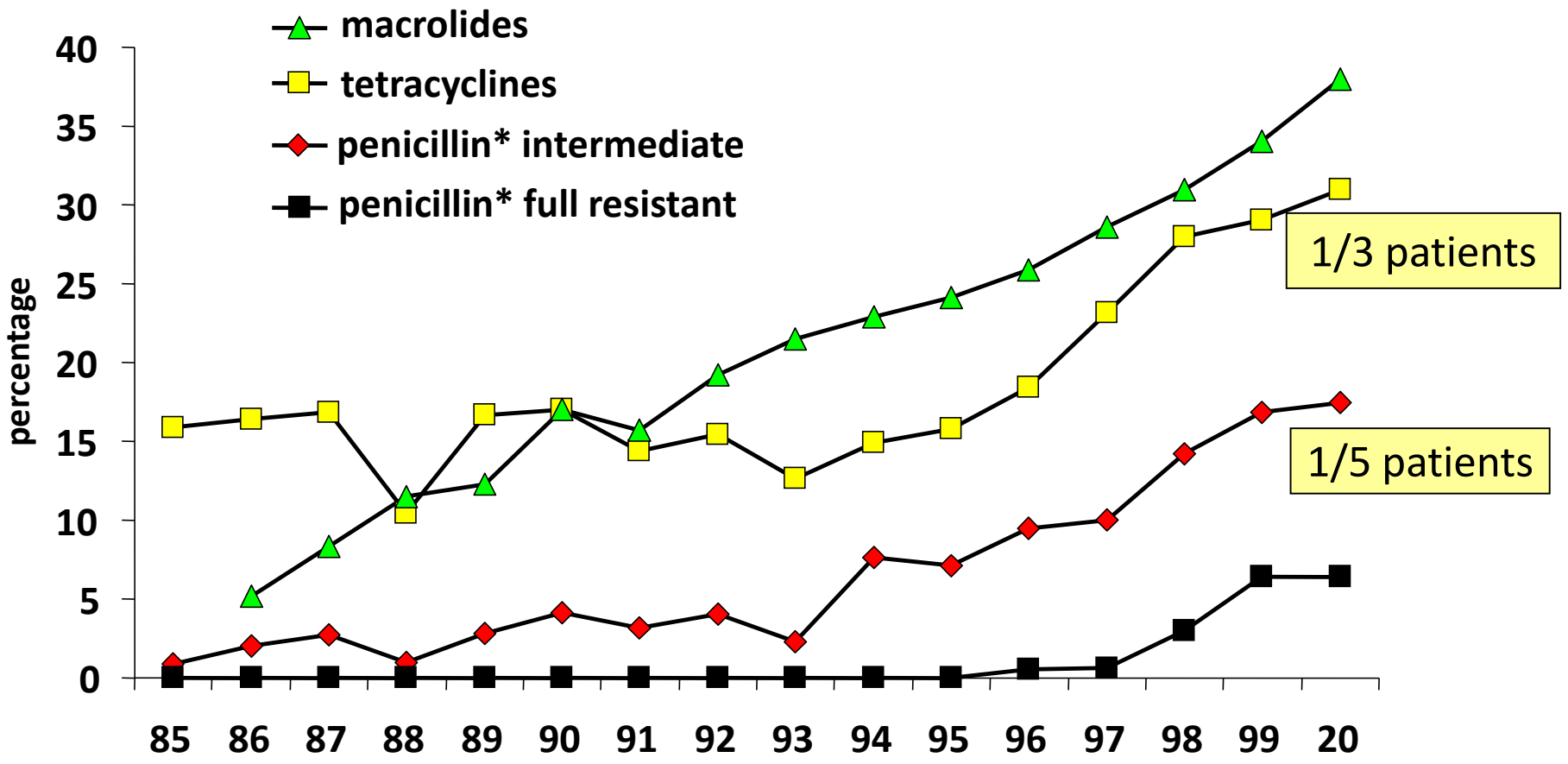
Figure 1. Fluoroquinolone consumption in Germany (SHI-related prescriptions, 1991–2007). SHI = statutory health insurance; DDD = defined daily doses; CPI = consumer price index

Klaus Kaier: The impact of pricing and patent expiration on demand for pharmaceuticals: an examination of the use of broadspectrum antimicrobials
Health Economics, Policy and Law (2013) 8:7-20

But after all, do not forget why we must control the consumption of antibiotics



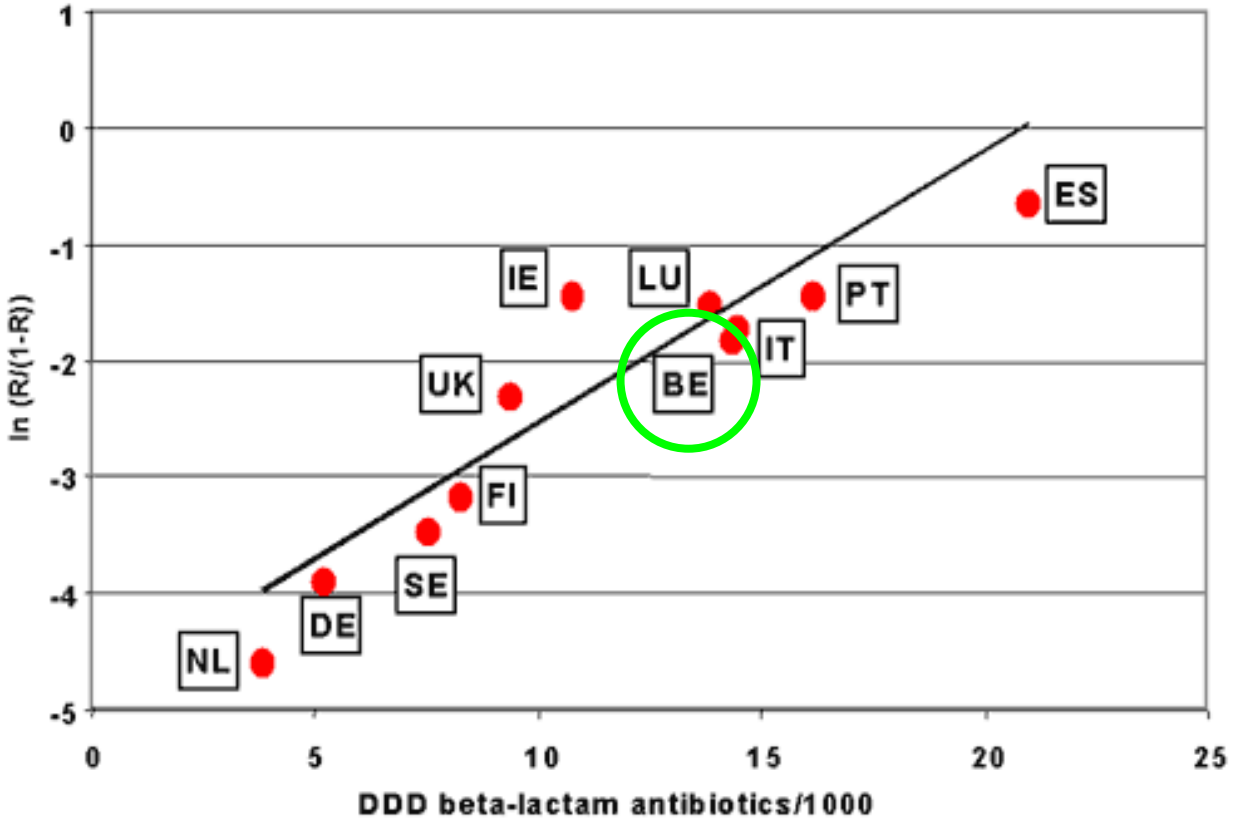
The case of *S. pneumoniae* in Belgium…



* all β-lactams (= penicillins, cephalosporins, …)

Belgian Reference Laboratory for pneumococci, Louvain (*Leuven*), 2000

Relation consumption-resistance



Risk of resistance to β-lactams 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 doses**

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

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

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