Use of antibiotics around the world

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Why to study consumption?

Correlation between antibiotic use and resistance
How to evaluate consumption?

• **DDD**: Defined Daily Dose
  (as per WHO recommendation)

  average maintenance dose per day for a drug used for its main indication in adults.
  The DDD is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose.

  ➔ Packages of different brands with the same active ingredient but with different strength and pack size can be aggregated.

• **DOT**: Days Of Treatment
DDD vs DOT

### DDD vs DOT

<table>
<thead>
<tr>
<th>Measurement method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defined Daily Dose (DDD)</td>
<td>(1) Allows standardized comparisons of aggregate antibiotic use between hospitals in different locations and countries; (2) allows for an estimate of use in countries with limited access to computerized pharmacy data; (3) will change the estimate of drug use if the recommended daily dose is altered and the approved DDD does not change</td>
<td>(1) Will not accurately estimate DOT when the administered daily dose is not equal to the DDD and, therefore, cannot be used to compare relative use between different antibiotic classes; (2) cannot be used in children; (3) will underestimate use for drugs that require reduced dosage when excretory function is impaired, such as with renal impairment; (4) approved DDDs may change as new dosages are approved for existing drugs, which can create confusion when comparing use over time</td>
</tr>
<tr>
<td>Days of Therapy</td>
<td>(1) Can be used to measure antimicrobial use in children; (2) not influenced by changes in the recommended DDD; (3) not influenced by discrepancies between the DDD and the preferred daily dose</td>
<td>(1) Will overestimate use for drugs that are given in multiple doses per day; (2) more difficult to measure without computerized pharmacy records</td>
</tr>
</tbody>
</table>
Antibiotic consumption in the community

Consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the community, EU/EEA countries, 2010, expressed as DDD per 1 000 inhabitants and per day.
Antibiotic consumption in the community

Consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the community, EU/EEA countries, 2010, expressed as DDD per 1,000 inhabitants and per day

This is mainly a question of antibiotic policy …

No difference in climate …

No difference in pathologies …
Does this translate in differences of resistance?

Correlation between antibiotic use and resistance
Antibiotic consumption in the community

1 DDD for 4-1 % of total population each day in the community …
Antibiotic consumption in the hospital

1DD for 0.4-0.1 % of total population each day in the hospital environment …

But this does not give an idea of antibiotic use within the hospital …
Antibiotic consumption in the hospital

Patterns of Antibiotic Use
In European Hospitals

Fiona M. MacKenzie
Aberdeen Royal Infirmary, Scotland
Antibiotic consumption in the hospital

Antibiotic use data: Distribution (n = 140) 2005

- Median = 50 (37,67)
- Minimum = 5
- Maximum = 121

Median total antibiotic use: 2001
By Geographical Region, n = 140

- Central/ East: n=33
- South-East: n=8
- North: n=19
- West: n=52
- South: n=28

p < 0.001
Antibiotic consumption in the hospital

- J01A Tetracyclines
- J01B Amphenicols
- J01C β-lactams, Penicillins
- J01D Other β-lactams
- J01E Sulfonamides & Trimethoprim
- J01F Macrolides, Lincosamides, Streptogramins
- J01G Aminoglycosides
- J01M Quinolones
- J01X Other antibacterials

DDD /100 bed-days, Median values (n = 140)
Distribution of antibiotic use
Antibiotic consumption in the USA
Antibiotic consumption in the community

801 prescriptions/1000 inhabitants/year
Comparison with other countries

Type: Graphic
Publications: Extending the Cure: Policy Responses to the Growing Threat of Antibiotic Resistance

The United States is among the most intensive users of antibiotics in the world

- FRANCE
- GREECE
- ITALY
- BELGIUM
- UNITED STATES
- CANADA
- AUSTRALIA
- SPAIN
- CZECH REPUBLIC
- UNITED KINGDOM
- GERMANY
- NETHERLANDS

DDD per 1,000 inhabitants per day

Sources: United States and Canada (McManus, Hammond et al. 1997), Australia (National Prescribing Service 2005), European countries (Goossens, Ferech et al. 2003).

Note: DDD = defined daily doses, a standardized measure of antibiotic consumption.
Index of resistance in the community

Between 1999 and 2010, the Urinary Tract Infection Drug Resistance Index (UTI-DRI) increased by 35%. Following an initial decline from a baseline of 16.8 in 1999 to 15.1 in 2001, the UTI-DRI increased steadily for eight years, reaching 22.8 in 2010.

In contrast, the Skin and Soft Tissue Infection DRI (SSTI-DRI) increased sharply (~70%) in the beginning of the period, but has been declining since 2005. After 2008-2009, the two indices have been diverging, with SSTI-DRI showing lower values and declining.
Antibiotic consumption in the hospital

An example for selected antibiotics…

Comparison of aggregate drug use by defined daily dose (DDDs) per 1000 patient-days and days of therapy (DOTs) per 1000 patient-days for 10 common antibacterial drugs.

<table>
<thead>
<tr>
<th>Parenteral antibiotic</th>
<th>No. of hospitals</th>
<th>Mean DDDs per 1000 patient-days ± SD</th>
<th>Mean DOTs per 1000 patient-days ± SD</th>
<th>P</th>
<th>Mean difference between DDD and DOT, %</th>
<th>Importance of the mean difference&lt;sup&gt;a&lt;/sup&gt;</th>
<th>DDD, g/day&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Mean administered daily dose, g/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>130</td>
<td>80.3 ± 35.4</td>
<td>94.3 ± 27.7</td>
<td>&lt;.0001</td>
<td>-17.4</td>
<td>Moderate</td>
<td>3</td>
<td>2.46</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>123</td>
<td>75.6 ± 57.5</td>
<td>74.9 ± 55.8</td>
<td>.3</td>
<td>0.7</td>
<td>Minor</td>
<td>0.5</td>
<td>0.51</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>53</td>
<td>56.5 ± 67.9</td>
<td>52.1 ± 48.6</td>
<td>.4</td>
<td>7.9</td>
<td>Moderate</td>
<td>0.4</td>
<td>0.42</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>130</td>
<td>44.9 ± 28.2</td>
<td>62.9 ± 35.9</td>
<td>&lt;.0001</td>
<td>-28.6</td>
<td>Major</td>
<td>2</td>
<td>1.46</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>130</td>
<td>46.1 ± 39.0</td>
<td>52.7 ± 26.6</td>
<td>.013</td>
<td>-6.6</td>
<td>Moderate</td>
<td>2</td>
<td>1.63</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>127</td>
<td>30.3 ± 20.3</td>
<td>42.7 ± 28.5</td>
<td>&lt;.0001</td>
<td>-40.9</td>
<td>Major</td>
<td>14</td>
<td>10.1</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>126</td>
<td>28.1 ± 14.3</td>
<td>32.8 ± 15.4</td>
<td>&lt;.0001</td>
<td>-7.0</td>
<td>Moderate</td>
<td>1.5</td>
<td>1.32</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>130</td>
<td>20.8 ± 17.1</td>
<td>18.0 ± 14.8</td>
<td>&lt;.0001</td>
<td>13.4</td>
<td>Moderate</td>
<td>0.5</td>
<td>0.55</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>123</td>
<td>18.0 ± 22.1</td>
<td>13.5 ± 16.3</td>
<td>&lt;.0001</td>
<td>24.9</td>
<td>Moderate</td>
<td>0.5</td>
<td>0.72</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>129</td>
<td>21.7 ± 12.5</td>
<td>22.3 ± 10.8</td>
<td>.23</td>
<td>-2.8</td>
<td>Minor</td>
<td>1.8</td>
<td>1.79</td>
</tr>
</tbody>
</table>

**NOTE.** The larger the difference between the administered daily dose and the DDD, the larger the difference in the measure of aggregate use by DDDs per 1000 patient-days and DOTs per 1000 patient-days.

<sup>a</sup> Major (>25% difference), moderate (>5% and <25% difference), and minor (<5% difference) importance.

<sup>b</sup> World Health Organization–defined DDD (2005 values [10]).

same order of magnitude as in Europe

Antibiotic consumption in Asia

Population density

Large population → high pressure
Sales increase rapidly ...
What about Vietnam?

SITUATION ANALYSIS
Antibiotic Use and Resistance in Vietnam

The GARP - Vietnam National Working Group
Dr. Nguyễn Văn Kính, Chairman

October 2010
Consumption in the hospital

DDD per 100 bed-days of Antibiotics in 2008-2009

- J01A-Tetracyclines
- J01B-Amphenicols
- J01CA-Penicillins with expanded spectrum
- J01CE-Beta lactam sensitive Penicillins
- J01CF-Beta lactam resistance Penicillins
- J01CG-Sulbactam
- J01CR-Beta-lactam and Inhibitors
- J01DB-First gen. Cephalosporins
- J01DC-Second gen. Cephalosporins
- J01DD-Third gen. Cephalosporins
- J01DE-Forth gen. Cephalosporins
- J01DH-Carbapenem
- J01FA-Macrolides
- J01F-Lincosamides
- J01G-Aminoglycosides
- J01M-Fluoroquinolones
- J01X-Others

2008

2009
Variations among hospitals

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

Reminder: European median: 50 DDD/100 beds

First report on antibiotic use and resistance in Vietnam hospitals

28/10/2013 WBI - cooperation - Uong Bi hospital
Link between consumption and resistance

Resistance to Antibiotics to 4 Common Gram-negative Bacteria

- P. aeruginosa
- Acinetobacter
- Klebsiella
- E. coli

- 4th gen. cephalosporin
- 3rd gen. cephalosporin
- Aminoglycoside
- Fluoroquinolones
- Carbapenem

% Resistance
Hospital vs. community

Sales of antibiotics in Vietnam

Vietnam: 90 Mio inhabitants: 2.8 units/inhab. [commun.]; 0.6 units/inhab [hosp.]
Belgium: 11 Mio inhabitants: 0.03 DDD/inhab [commun.]; 0.003 DDD/inhab [hosp]
Use in children in the community

AB use children during one month

- No Antibiotic Use 38%
- Antibiotic Use 62%
- Cephalosporins 27%
- Ampicillin or Amoxicillin 49%
- Trimetoprin Sulpha 11%
- Macrolides 3%
- Other 3%

Source antibiotics:
- Self treatment 16%
- Drug store 30%
- Private clinic 24%
- Public clinic 31%

Source: QH Nguyen 2010

Too much ....

3.5 days average duration antibiotic course

Too short ....

Number of children

Days of antibiotic use in an antibiotic course
Antibiotics in the community

Pharmacy study

Antibiotic purchase and dispensing behaviour

<table>
<thead>
<tr>
<th>Customer</th>
<th>Urban</th>
<th>Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Buy antibiotic</td>
<td>440</td>
<td>34,0</td>
</tr>
<tr>
<td>With prescription</td>
<td>41</td>
<td>9,3</td>
</tr>
<tr>
<td>- Comply with prescription</td>
<td>33</td>
<td>80,5</td>
</tr>
<tr>
<td>- Dont comply with prescription</td>
<td>8</td>
<td>19,5</td>
</tr>
<tr>
<td>Without prescription</td>
<td>399</td>
<td>90,7</td>
</tr>
<tr>
<td>- Customer demand</td>
<td>175</td>
<td>43,9</td>
</tr>
<tr>
<td>- Drug seller advice</td>
<td>224</td>
<td>56,1</td>
</tr>
</tbody>
</table>

Not allowed in EU or USA
Is patient’s pressure a problem?

A study at the Mexican-American border

<table>
<thead>
<tr>
<th>Total number of products purchased</th>
<th>USA resident (n=109)</th>
<th>Mexican resident (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>157</td>
<td>154</td>
<td></td>
</tr>
<tr>
<td>Average number of medicines purchased per client ± SD</td>
<td>1.4 ± 0.74</td>
<td>1.3 ± 0.55</td>
</tr>
<tr>
<td>% products purchased with prescription</td>
<td>29</td>
<td>58</td>
</tr>
<tr>
<td>% antibiotics purchased with prescription</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>% antibiotics purchased without prescription that were self-prescribed</td>
<td>83</td>
<td>56</td>
</tr>
<tr>
<td>% antibiotics purchased without prescription recommended by professional</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>% antibiotics purchased without prescription recommended by pharmacy clerk</td>
<td>13</td>
<td>44</td>
</tr>
<tr>
<td>Characteristics of the end user of the products purchased</td>
<td>(n=153)</td>
<td>(n=157)</td>
</tr>
</tbody>
</table>

Prescription only

No prescription

Americans are ready to travel to get « free » antibiotics
How to improve the situation: a European view

• **in the community:**
  - antibiotics on prescription only
  - education of pharmacists
  - education of the public on appropriate use

• **at the level of the country:**
  - collect epidemiological data
  - collect consumption data
  - propose treatment guidelines taking into account local epidemiology
How to improve the situation: a European view

• in the community:
  - antibiotics on prescription only
  - education of pharmacists
  - education of the public on appropriate use

• in the hospital:
  - antibiotic/infection control committees in hospitals
    - to develop local guidelines
    - to evaluate consumption
    - to survey resistance
    - to set up preventive measures (hygiene, isolation, prophylaxis)
Need of close collaboration between clinicians and microbiologists

How to improve the situation: a European view

• in the community:
  antibiotics on prescription only
  education of pharmacists
  education of the public on appropriate use

• in the hospital: antibiotic/infection control committees in hospitals
  to develop local guidelines
  to evaluate consumption
  to survey resistance
  to set up preventive measures (hygiene, isolation, prophylaxis)

• at the level of the country:
  collect epidemiological data
  collect consumption data
  propose treatment guidelines taking into account local epidemiology
Recommendations from the GRAP for improving situation in Vietnam

<table>
<thead>
<tr>
<th>Policy option</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics are prescription only drugs.</td>
<td>Develop national action plan for antibiotic resistance.</td>
</tr>
<tr>
<td>Make antibiotics prescription-only</td>
<td>Enforce current law.</td>
</tr>
<tr>
<td>Make hospitals’ drug and therapeutics committee effective</td>
<td>Enforce requirement for committees, define their functions and standards, and develop audit mechanisms. Give committees tools and guidance on antibiotic stewardship. Provide up-to-date, accurate resistance data.</td>
</tr>
<tr>
<td>Establish infection-control committees in hospitals</td>
<td>Give committees sufficient resources to carry out their activities and improve infrastructure. Establish standardized indicators to monitor progress, such as hospital-acquired infection rates by department and hand-washing compliance.</td>
</tr>
<tr>
<td>Track patterns in antibiotic resistance</td>
<td>Develop national testing and quality control guidelines. Fund resistance testing, quality control, training, and reporting. Issue annual national report on both antibiotic use and resistance.</td>
</tr>
<tr>
<td>Monitor antibiotic use in hospitals</td>
<td>Standardize antibiotic usage indicators to international units (e.g., defined daily dosage per 100 bed-days). Issue annual national report on both antibiotic use and resistance.</td>
</tr>
<tr>
<td>Develop curriculum for medical and pharmacy schools</td>
<td>Teach and train professionals on antibiotic resistance and appropriate antibiotic use.</td>
</tr>
<tr>
<td>Develop treatment guidelines</td>
<td>Ensure timely and evidence-based updates of treatment guidelines for infectious diseases.</td>
</tr>
<tr>
<td>Establish pharmacovigilance center</td>
<td>Engage pharmacovigilance center in curbing inappropriate antibiotic prescribing.</td>
</tr>
<tr>
<td>Conduct public education campaign</td>
<td>Create awareness and educate Vietnamese public about appropriate and inappropriate antibiotic use.</td>
</tr>
</tbody>
</table>