# Are public campaigns effective to reduce antibiotic overconsumption? Did we fail to provide what is needed by the general practitioner?



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Based on work performed with in collaboration with Jean-Marc Feron, Michel Boutsen, and Gilles Moreau<sup>3</sup>

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## 3<sup>rd</sup> Global Microbiologists Annual Meeting

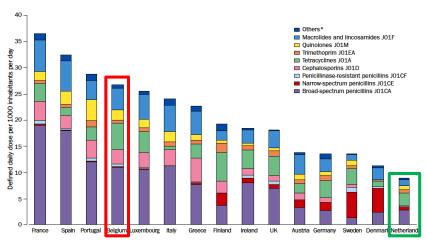
August 15-17, 2016 Portland, Oregon, USA

#### Where has this material been published and/or presented?

- Slides 3 through 16 (antibiotic consumption data 2000-2016): presented at
  - ASM Microbe 2016 (American Society for Microbiology), Boston, Mass., 16-20 June 2016, as an oral presentation (Session Title: Antimicrobial Stewardship I June 17, 2016)
     <a href="http://www.facm.ucl.ac.be/posters/2016/ASM-Microbe-2016/Tulkens-antibiotic-consumption-and-public-campaigns-ASM-microbe-2016.pdf">http://www.facm.ucl.ac.be/posters/2016/ASM-Microbe-2016/Tulkens-antibiotic-consumption-and-public-campaigns-ASM-microbe-2016.pdf</a>
- Slides 17 through 34 (qualitative research): partly presented at the
  - 27ème Réunion Interdisciplinaire de Chimiothérapie Anti-Infectieuse (RICAI),
     Paris, France, 6-7 décembre 2007 (focus group studies), as an oral presentation (no. 235)
    - http://www.facm.ucl.ac.be/posters/2007/RICAI/Feron-et-al-RICAI-2007-oral-235.pdf
  - 18th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) Barcelona, Spain, 19-22 April 2008 (Lot Quality Assurance Group study) as an oral presentation (O249) http://www.facm.ucl.ac.be/posters/2008/ECCMID/Feron-et-al-ECCMID-2008-O-249.pdf
  - 26th International Conference on Chemotherapy, Toronto, Ont., 18-21 June 2009 (large survey), as a poster (P313)
     <a href="http://www.facm.ucl.ac.be/posters/2009/ICC-2009/P-313-Feron-Motivations-ICC-2009.pdf">http://www.facm.ucl.ac.be/posters/2009/ICC-2009/P-313-Feron-Motivations-ICC-2009.pdf</a>

### Why public campaigns for less use of antibiotics in the community in Belgium?

#### 1997



Outpatient antibiotic sales in 1997 in the European Union

\*Includes sulphonamides, penicillinase-resistant penicillins, amphenicols, aminoglycosides, and glycopeptides.

Cars et al. Lancet. 2001;357:1851-3 - PMID: 11410197



#### The message was clear and understood:

- Belgium consumes too much antibiotics in the community, which creates resistance...
- If you reduce antibiotic pressure (DDDs) in the community, you will reduce resistance!

#### 1997 - 1999

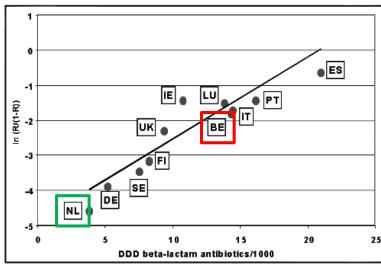


Figure 2. The logodds of resistance to penicillin among invasive isolates of *Streptoccus pneumoniae* (PNSP; In(R/[1-R])) is regressed against outpatient sales of beta-lactam antibiotics in 11 European countries; antimicrobial resistance data are from 1998 to 1999 and antibiotic sales data are from 1997. DDD = defined daily dose; BE = Belgium; DE = Germany; FI = Finland; IE = Ireland; IT = Italy; LU = Luxembourg; NL = the Netherlands; PT = Portugal; ES = Spain; Se = Sweden; UK = United Kingdom.

Bronzwaer et al. Emerg Infect Dis. 2002;8:278-82. PubMed PMID: 11927025

#### So, we started public campaigns targeted to the community...

2000-2003



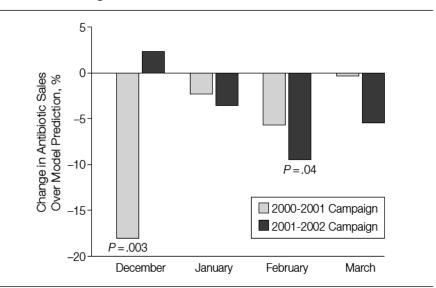
http://www.red-antibiotica.org/ (Dutch) http://www.antibiotiques.org/ (French)

And these first campaigns were modestly but significantly successful in reducing the number of DDD's per month in the winter periods of 2000-2001 and 2001-2002



use less often and better

**Figure 2.** Monthly Change in Antibiotic Sales Controlled for Influenza-like Illnesses During Each Campaign (December-February) and the Following Month (March)



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.

Bauraind et al. JAMA. 2004;292:2468-70 - PMID: <u>15562124</u>

## So, public campaigns targeted to the community were repeated <u>each year</u> with various themes...



http://www.belgium.be/fr/actualites/2013/news\_campagne\_antibiotiques\_2013



http://www.gebruikantibioticacorrect.be/nl/lees-tante-biotica-online

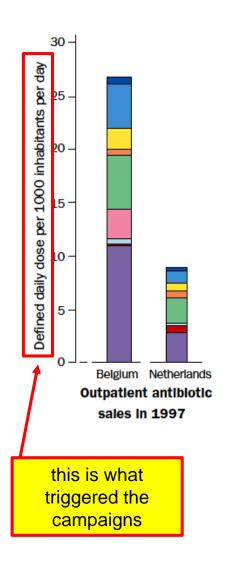


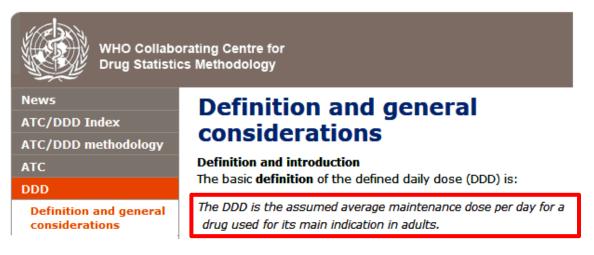


but what are the results?

## What and how did we analyze the antibiotic pressure in the community?

#### What is a Defined Daily Dose and why did we use it?





http://www.whocc.no/ddd/definition\_and\_general\_considera/

"Introduction to Drug Utilization Research"

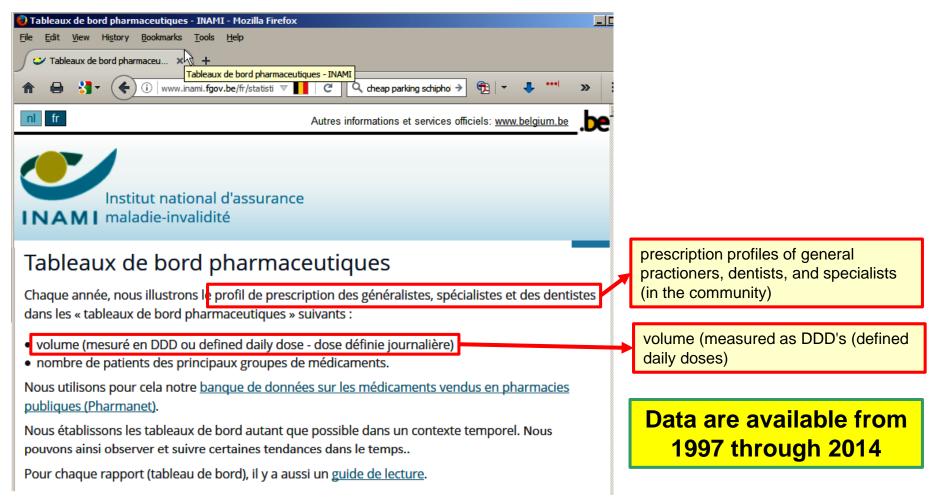


The use of DDD / 1,000 inhabitants / day allows for direct comparisons between countries, regions and health facilities without confounding factors such as

- differences in size of packages (prescription drugs are mostly sold as packages, NOT as units in Europe)
- differences in prices (markedly influenced by the introduction of generics, taking place to an increased extent since 2005 in Europe)

http://www.whocc.no/filearchive/publications/drug\_utilization\_research.pdf

### Public data from the National Institute for Health and Disability Insurance (NIHDI [INAMI / RIZIV]\*)



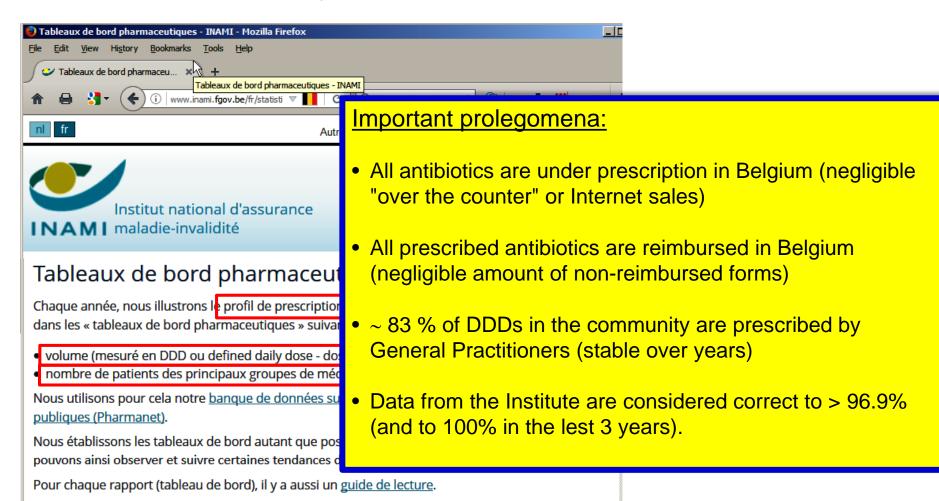
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Full URL: <a href="http://www.inami.fgov.be/fr/statistiques/medicament/Pages/statistiques-medicaments-pharmanet-01.aspx#.V1wBn6JYyE0">http://www.inami.fgov.be/fr/statistiques/medicament/Pages/statistiques-medicaments-pharmanet-01.aspx#.V1wBn6JYyE0</a> (French)

Full URL: <a href="http://www.inami.fgov.be/nl/statistieken/geneesmiddel/Paginas/statistieken-geneesmiddelen-farmanet-01.aspx#.V1wDHKJYyE0">http://www.inami.fgov.be/nl/statistieken/geneesmiddel/Paginas/statistieken-geneesmiddelen-farmanet-01.aspx#.V1wDHKJYyE0</a> (Dutch)

<sup>\*</sup> Institut national d'assurance maladie-invalidité / Rijksinstituut voor ziekte- en invaliditeit verzekering

### Public data from the National Institute for Sickness and Invalidity Insurance (INAMI / RIZIV\*)



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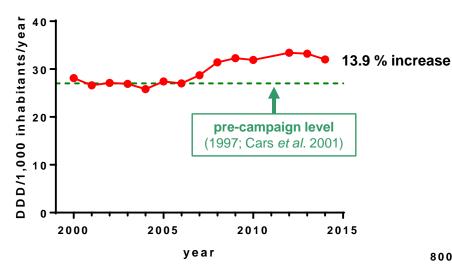
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#### What did we find?

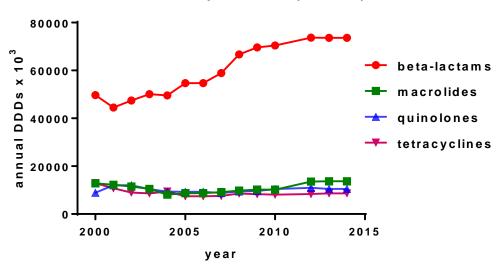




\* defined as DDD's of ATC class J drugs (anti-infectives for systemic use) reimbursed in the community (~ 85% antibiotics)

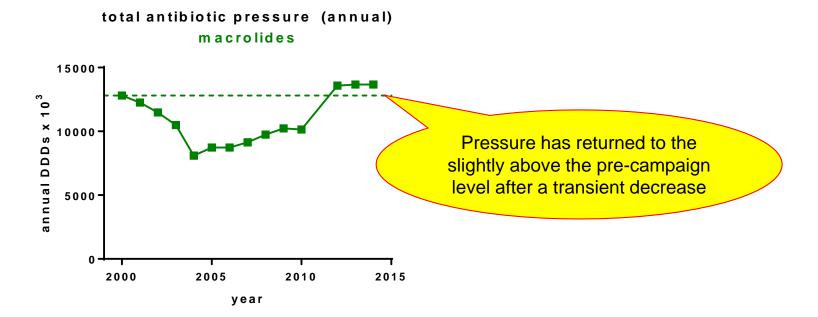
#### But which antibiotics?





#### Were targeted efforts rewarded?

1. S. pneumoniae full resistance to macrolides in clinically confirmed CAP and clinically-confirmed confirmed COPD is ~ 25 % in Belgium \* and is, therefore, no longer recommended as first line ...

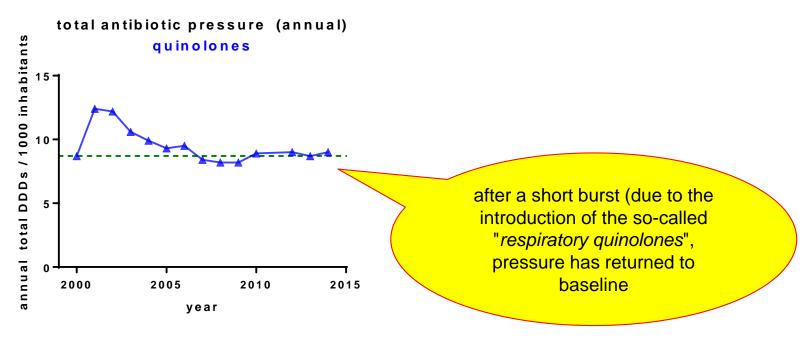


<sup>\*</sup> Lismond *et al.* Intern J Antimicrob Agents (2012) 39:208–216 - PMID: <u>22245497</u>

Vandevelde *et al.* Intern J Antimicrob Agents (2014) 44:209–217 - PMID: <u>25123808</u>

#### Were targeted efforts rewarded?

2. Many actions were taken to reduce what was considered as an exaggerated prescription of quinolones in Belgium \* (31% of total DDDs in 2000)

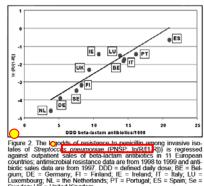


- \* see, for example,
- the limited recommendations of fluoroquinolones in the antibiotic guidelines for GPs (available at <a href="http://www.health.belgium.be/fr/antibiotiques-guide-belge-des-traitements-anti-infectieux-en-pratique-ambulatoire">http://www.health.belgium.be/fr/antibioticabelgische-gids-voor-anti-infectieux-en-pratique-ambulatoire</a> <a href="http://www.health.belgium.be/nl/antibioticabelgische-gids-voor-anti-infectieuze-behandeling">http://www.health.belgium.be/nl/antibioticabelgische-gids-voor-anti-infectieuze-behandeling</a>)
- information letters and GP's profiling made by the National Institute for Health and Disability Insurance (NIHDI [INAMI / RIZIV]) available at <a href="http://www.inami.fgov.be/fr/recherche/pages/default.aspx?k=antibiotiques#.V10T4KJYyE1">http://www.inami.fgov.be/fr/recherche/pages/default.aspx?k=antibiotiques#.V10T4KJYyE1</a>
   http://www.inami.fgov.be/nl/zoeken/paginas/default.aspx?k=antibiotica#.V10Ux6JYyE0

#### A problem of metrics?

DDDs are not perfect and may not represent actual prescribed doses ...
 → but they are the metric used to trigger actions about resistance...





#### Other metrics are available... but may have other problems

- packages (in Europe): assumed to better represent prescriptions ... and showing a decrease of 17% between 2002 and 2009 vs. an increase in DDDs of 12 % (see Coenen et al. J Antimicrob Chemother. 2014;69:529-34 PMID: 24084641)
  - but package sizes change over time ... <u>as mainly decided by Industry</u> ... (e.g., major changes for amoxicillin and amoxi-clav in Belgium, largely but not only for commercial positioning...) and may not express the overall antibiotic pressure and <u>risk of resistance</u>... ... and a recent analysis of data for French-speaking Belgum indicates that the no. of prescription has slightly increased between 2004 and 2013 (unpublished data)
- **prices**: useful for business and some politicians ... but highly variable between countries ... and markedly influenced by the introduction of generics... (e.g., the price of levofloxacin was halved (incl. for the original) upon introduction of generics in Belgium)

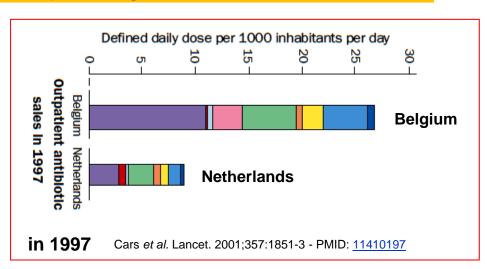
#### At the end, the real questions...

Why do we do public campaigns?

#### → To reduce unnecessary usage of antibiotics?

If such, would a decreased number of packages explain the large differences in DDDs between Belgium and the Netherlands?

Or, is the antibiotic pressure really different?



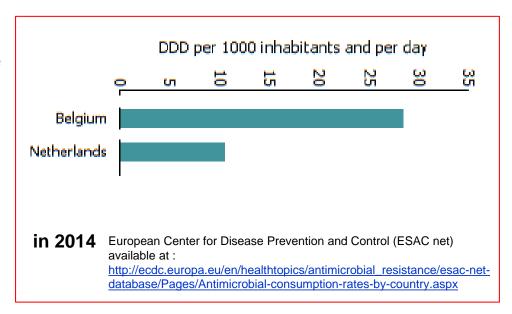
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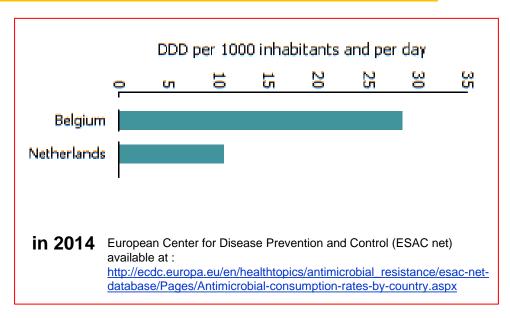
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Or, is the antibiotic pressure really different?



- → To reduce the rate of emergence of resistance?
- → To save money ?

#### And why could campaigns be ineffective? \*

- Did we address the REAL questions for the doctor?
- and for the patient...

The next series of slides will present a summary of studies undertaken between 2006 and 2010, i.e. in the middle of the period examined for antibiotic consumption and when the campaigns were in full swing....

#### Three studies with General Practitioners

- Qualitative research: Focus groups with active general practitioners (4 groups of 10 practitioners)
- Qualitative research: Lot Quality Assurance Group: in depth analysis of the actual act of antibiotic prescription with 30 General Practitioners
- Large scale survey with 400 practitioners

#### Qualitative research

- Qualitative research approach aims at discovering and assessing motives (not facts)
- It allows building an in-depth understanding of human behavior and of its underlying motives
- It is hypothesis-generating.

I would study not what you (or me) presented here but why you (I) did it ...

#### Qualitative studies and focus groups

- Qualitative research methods research has been well defined and applied in a in health care number of situations <sup>1</sup>
- It often uses the method of the semi-structured interviews with groups (focus groups <sup>2</sup>) analyzed using the grounded theory approach.
  - > several stakeholders are asked about their attitude towards a service, a concept, or other point of common interest, with emphasis on participants' interactions.
  - ➤ The grounded theory is a research method in which categories of concepts are formed from an objective analysis of the data and used as the basis for the creation of a theory.<sup>3,4</sup>

<sup>1.</sup> Pope & Mays: BMJ 1995; 311, 42-5; Huston & Rowan: Can Fam Physician 1998; 44, 2453-8; Malterud: Lancet 2001; 358, 397-400; Malterud: Lancet 2001; 358, 483-8; Giacomini & Cook: JAMA 2000; 284, 357-62.

<sup>2..</sup>Kitzinger: BMJ 1995; 311, 299-302.

<sup>3 .</sup>Glaser & Strauss A. (1967): *The discovery of grounded theory: strategies for qualitative research*, Aldine, New York; Glaser (1978): *Advances in the methodology of grounded theory: theoretical sensitivity*, Sociology Press, Mill Valley.

<sup>4.</sup> Spinewine et al. BMJ 2005; 331, 935.

#### Focus groups interview guide

- 1. You are consulted by an adult patient who is complaining about symptoms of common cold (cough, tiredness, recently occurred). What comes to your mind? What is your approach?
- 2. Which clinical clues do you seek in your diagnosis approach?
- 3. Once you have made a good probability diagnosis, in which case do you decide to prescribe an antibiotic? In which case do you always/never prescribe an antibiotic?
- 4. What does the patient seek when consulting you for an acute respiratory tract infection? If she/he has a special demand, how do you manage it?
- 5. What are your information sources regarding antibiotic use in respiratory tract infection? What do you think about them? Can you give some examples?
- 6. Are there some structural aspects in our health care system that may influence you in your decision to prescribe? Why?
- 7. Do you want to add anything?

Conceptual group	Emergent theme	
Clinical approach	- perceived severity of the disease	
	- fragility of the patient	
	- uncertainty of the etiological diagnosis	
Socio-cultural and structural elements	- patient's demand	
	- provider-client relationship	
	- reimbursement scheme	
Training and information	- guidelines	
	- experts' opinion and guidance	

Conceptual group	Emergent theme				
Clinical approach	- perceived severity of the	e disease	Му ра	atients are reall	y sick
	- fragility of the patient	This is a	child,	and elderly	
	- uncertainty of the etiolo	ogical diag	nosis <mark>I</mark>	How do I know	it is v
Socio-cultural and structural elements	<ul><li>patient's demand</li><li>provider-client relations</li><li>reimbursement scheme</li></ul>	-			
Training and information	<ul><li>guidelines</li><li>experts' opinion and gu</li></ul>	ıidance			

Conceptual group	Emergent theme		
Clinical	- perceived severity of the disease		
approach	- fragility of the patient		
	- uncertainty of the etiological diagnosis		
Socio-cultural and structural elements	<ul> <li>patient's demand My patients ask for!</li> <li>provider-client relations I must "deliver" something</li> <li>reimbursement scheme It is so cheap (for the patient)</li> </ul>		
Training and information	- guidelines - experts' opinion and guidance		

Conceptual group	Emergent theme		
Clinical	- perceived severity of the disease		
approach	- fragility of the patient		
	- uncertainty of the etiological diagnosis		
Socio-cultural	- patient's demand		
and structural elements	- provider-client relationship		
	- reimbursement scheme		
Training and information	- guidelines Most guidelines are anapplicable!		
	- experts' opinion and guidance guidance is for money only!		

#### Qualitative research: Lot Quality Assurance Group

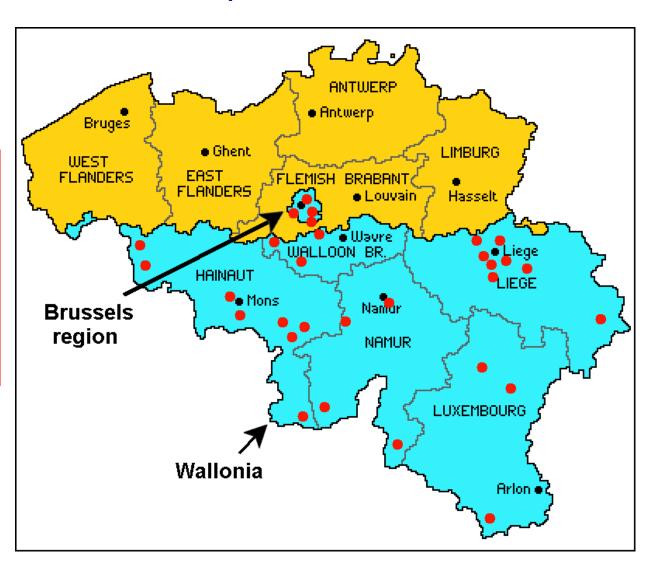
- In-depth analysis of a process performed by a limited number of individuals but for which the extent of knowledge gained by examining all critical aspects of the process compensates for the small number of cases examined.
- Originally developed in the manufacturing sector to control the quality of finished products (to reduce the actual number of pieces examined: better examine in details a few than superficially many)
- Introduced in medicine to assess health care services, health behaviors, and disease burden against pre-defined standards.<sup>1</sup>

<sup>1.</sup> Lanata et al. *Lancet* 1988; **1**, 122-3; Lanata et al. *Int J Epidemiol* 1990; **19**, 1086-90; Monte et al. *Am J Manag Care* 2008; **14**, 190-6.

#### Qualitative research:

#### Lot Quality Assurance Group: who did we examine?

30 general practitioners spread over the French-speaking part of Belgium as a function of the population density



#### Qualitative research: Lot Quality Assurance Group: what did we examine?

Туре	Actual data collected
Medical notes	<ul><li>hand-written / computer-based</li><li>other (including none)</li></ul>
Reasons for encounter	- global picture of the consultation.
Characteristics of the patient	<ul> <li>patient already seen (yes/no)</li> <li>sex, age</li> <li>medical history (known pathologies)</li> <li>smoking (yes/no)</li> <li>professionally active (yes/no)</li> </ul>
General clinical status of the patient	- non-severe / severe / alarming
Anamnesis	<ul> <li>cough (dry / productive), wheezing, dyspnoea</li> <li>sore throat, headache, muscular pain, thoracic pain</li> <li>coloured sputum, rhinorhea, otorhea</li> <li>necessity of work or school leave</li> <li>other</li> </ul>

#### Qualitative research: Lot Quality Assurance Group: what did we examine?

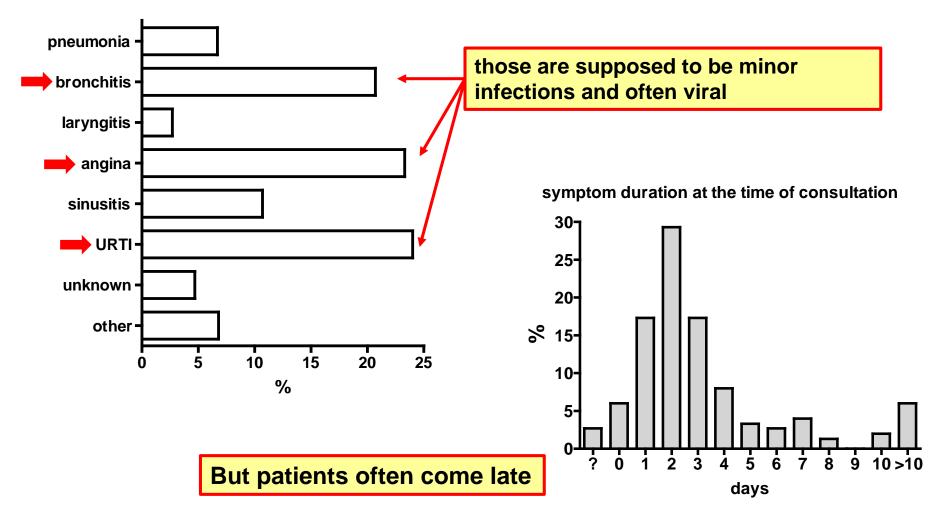
Alteration of the general status	-	fever
	-	fatigue
	-	loss of appetite
	-	inability to perform normal work
	-	patient feeling ill
	-	other
Clinical examination	-	pathological throat or amygdale
	-	nasal congestion
	-	abnormal tympanum
	-	abnormal auscultation
	-	adenopathies
	-	sinus tenderness
	_	other
Patient's demand	_	important - moderate - not important
Falletii 5 Ueilialiu	-	important - moderate - not important

#### Qualitative research: Lot Quality Assurance Group: what did we examine?

complentary examinations	<ul><li>biological investigations</li><li>RX</li><li>other</li></ul>
certainty of the clinical diagnostic	- ranked from 1 (doubtful) to 5 (certain)
antibiotic(s) prescribed	<ul><li>trade name, dosage, schedule</li><li>additional non-antibiotic treatments (yes/no)</li></ul>
decisive criteria for antibiotic prescribing	- entry left free for expression by GP
compliance with official guidelines (according to the prescriber)	<ul><li>yes / no / not known</li><li>if no or not know, why ?</li></ul>

#### Qualitative research: Lot Quality Assurance Group: main findings

Main diagnostics (ICPC-2 classification)



#### Qualitative research: Lot Quality Assurance Group: main findings

Main reasons for prescribing an antibiotic against the guidelines and the messages of the public campaigns

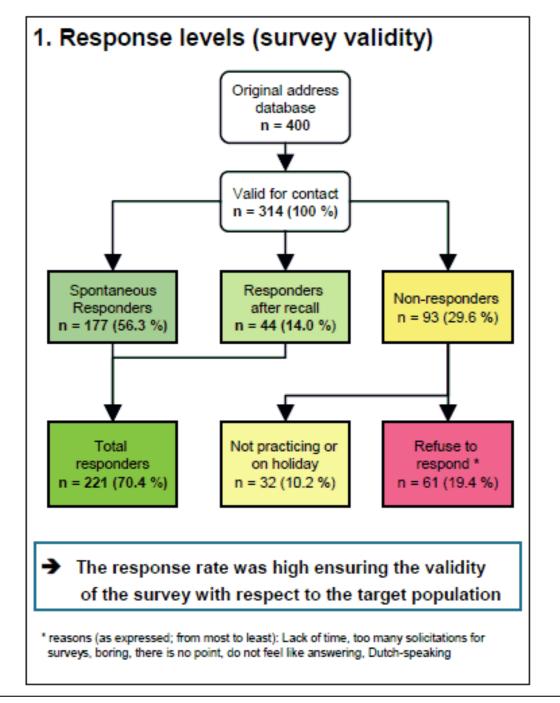
Category	Subcategory
Medical	<ul> <li>perceived severity of the disease or disease considered as requiring antibiotic treatment</li> </ul>
	- fragility of the patient or whit risk
	- uncertainty of the etiological diagnostic
	- insufficient time to spend with the patient
Socio-cultural	- patient's demand to which it is difficult to resist
	- provider-client relationship favouring the "delivery of a prescription"
Training and information	- guidelines considered as inappropriate or inapplicable

### Not a real surprise...

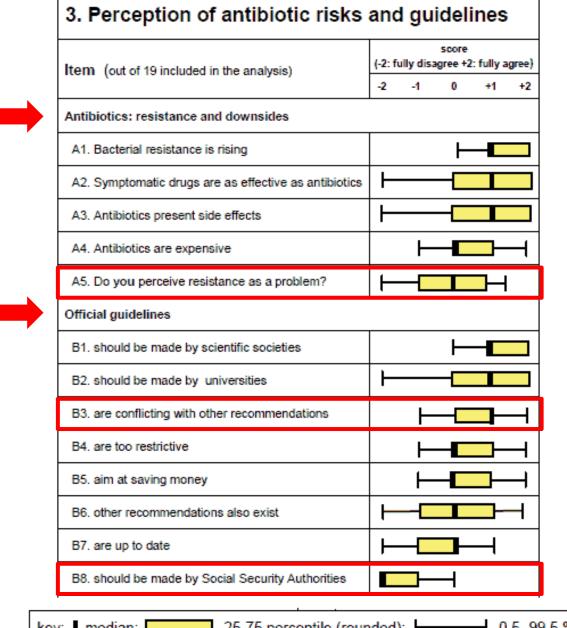
## Large scale survey

Self-administered questionnaire sent to practicing GPs (selected at random in French-speaking Belgium [Brussels/Wallonia addressing

- (i) actual practice data;
- (ii) (ii) how the GPs assessed bacterial resistance, official guidelines, public campaigns, feed-back campaigns;
- (iii) questions related to two frequent situations (clinical vignettes: acute sore throat; acute cough) in which antibiotics should normally not be prescribed.

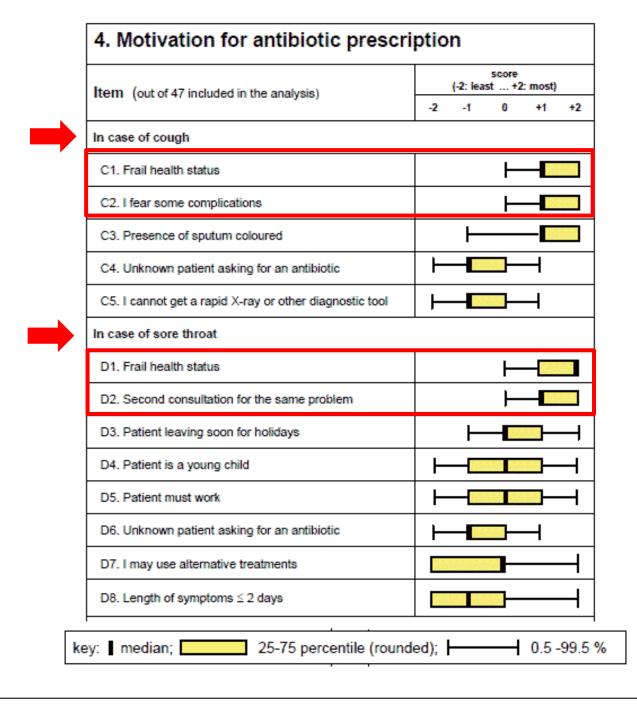


# Large scale survey: Results



key: ■ median; \_\_\_\_\_\_ 25-75 percentile (rounded); \_\_\_\_\_\_ 0.5 -99.5 %

# Large scale survey: Results



#### So, why could campaigns be ineffective?

- Did we address the REAL questions for the doctor?
  - → What is the diagnostic?
  - → What are the risks of not giving an antibiotic?
  - → Will the patient go and see another doctor?
- and for the patient...
  - → am I going to take a risk for my-self?
  - → what for my child, my elder parent, ...?

#### To sum up...

- Public campaigns targeting the public are potentially interesting actions for trying to curb exaggerate use of antibiotics and, thereby, for reducing antibiotic resistance in the community...
- However, there is so far little demonstration of real, important, and long-lasting effects of public antibiotic campaigns on actual antibiotic pressure, and, more critically, on resistance levels...
- The main reasons for failure may be that public campaigns
  - (i) miss the real targets, i.e. the <u>sick patient</u> and the <u>attending</u> <u>physician</u>...
  - (ii) do not address the real questions of importance for these two key actors, such as <u>uncertainty of diagnostic</u> and <u>risk</u> of missing what could be <u>a real threat</u>...