MD. MS. Giorgio Zanetti
Service of Infectious Diseases
and Division of Hospital
Preventive Medicine
University Hospital
46, Bugnon Street
1011 Lausanne
giorgio.zanetti@chuv.ch

4049-112739
01.10.2005-30.09.2006

Prof. Dr. Kathrin Mühlemann
Institut für
Infektionskrankheiten,
Universität Bern
kathrin.muehlemann@imm.
unibe.ch

Prof. Dr. Christian Ruef
Klinik für
Infektionskrankheiten
und Spitalhygiene,
Universitätsspital Zürich
christian.ruef@dim.usz.ch

Dr. OlivierBugnon
Laboratoire de Pharmacie,
Policlinique Médicale
Universitaire, Lausanne
olivier.bugnon@hospvd.ch

Prof. Dr. André Pannatier
Service de Pharmacie, CHUV,
Lausanne
andre.pannatier@chuv.ch

PD Dr. Georges Zelger
Pharmacie des Hôpitaux du
Nord Vaudois et de la Broye,
Yverdon-les-Bains
georges.zelger@phnvb.ch

Use of antibiotics in Switzerland: Investigation of a monitoring system

Objectives To date, continuous monitoring of bacterial resistance is being implemented in Switzerland within the project "Sentinel Surveillance of Antibiotic Resistance in Switzerland" (SEARCH). In contrast, there is no monitoring of antibiotic consumption, and information on consumption can only be purchased from a private provider of health market data. The present project proposes to explore the performance of sentinel surveillance based on an alternative source of data, i.e. hospital and community pharmacists. This alternative source appears reliable and less expensive than commercially available data. It also provides some additional information. It would allow the setting up of continuous monitoring. In addition to being a useful complement to SEARCH, it would be a useful tool for future research and intervention.

Conclusions Antibiotic use data from a **sentinel hospital network** ensured high quality information and flexibility. Although hospital representativeness remains to be improved, the study results confirmed that the development of a network for continuous monitoring of antibiotic use seems to be an achievable objective for the future. A major added value of the sentinel hospitals network, as compared to health market data based on manufacturers' sales, is the ability to analyse the density of antibiotic use. Moreover, the sentinel network is closer to actual clinical use. For instance, it allows analysis of antibiotic use separately by hospital size or hospital wards. Wards of special interest – such as intensive care units – can be analysed in detail, while others can be excluded (e.g. paediatric wards for which the DDD (Defined Daily Doses) methodology is not appropriate). Focused research projects can also be considered, such as correlation of antibiotic use with markers of case-mix or activity. Finally, the sentinel network allows benchmarking, and therefore offers interesting feedback to participating hospitals.

In **the community**, the data gathered by the Swiss Association of Pharmacists on prescription of antibiotics by sentinel groups of primary care physicians (physicians-pharmacists quality circles and control group) appear interesting in several respects. The data are close to actual consumption in the ambulatory setting, and the validation by health insurances increases their reliability. Quality circles offer an access to the prescription profile of individual practitioners, which makes it possible to assess in detail the impact of interventions, incentives or political decisions. At the present time, access to the data is limited to some groups of primary care physicians in the French-speaking part of Switzerland. However, these physicians are important players in the field of antibiotic policies. Moreover, it would be technically possible to extend the analysis to the whole country and to all categories of physicians, provided confidentiality rules are applied.

To conclude, the sentinel networks based on delivery data from either hospital or community pharmacies accurately reflect antibiotic use and allow in-depth analyses and comparisons of the prescription patterns. Furthermore, the collected data can be analysed with the SEARCH system. These pilot projects can be extended to represent a larger proportion of hospitals and practitioners, thus gaining in accuracy. Monitoring of antibiotic use is a necessary basis to investigate interventions on quality of antibiotic use. Sentinel networks are a possible option to set up continuous monitoring of antibiotic consumption, which is a necessary complement to the monitoring of antibiotic resistance (SEARCH).

Main results and findings

ANTIBIOTIC USE IN PUBLIC ACUTE CARE HOSPITALS

Sources of data Two sources of data on 2004-2005 antibiotic consumption in hospitals were compared:
- a private provider of health market data based on manufacturer's sales to all Swiss hospitals (IMS Health GmbH, Hergiswil);
- a sentinel network of pharmacists in public acute care hospitals. This network was set up in the context of the present project.

Antibiotic consumption data were converted into defined daily doses (DDD).

Setup of the sentinel network of hospital pharmacists Participants were recruited among members of the Swiss Society of Public Health Administration and Hospital Pharmacists (GSASA). GSASA members were invited to join the sentinel network if they were chief pharmacists in an acute care hospital or hospital group. Purely paediatric or psychiatric hospitals were excluded. Thirty-three of the 37 chief pharmacists (89%) responded. Twenty-eight (76%) volunteered to provide delivery data, which accounted for 48 and 50 hospitals for the years 2004 and 2005, respectively.

One additional hospital could join the network, because its 2004 antibiotic consumption report, published for another purpose, was available to the present project. Therefore, the sentinel network included 50 (49 for 2004 data) of the 158 Swiss public acute care hospitals indexed by Hplus, the association of Swiss hospitals. This represented 49% of all beds in this category of hospitals in Switzerland.

Comparison between the sentinel network and the private survey of the Swiss market
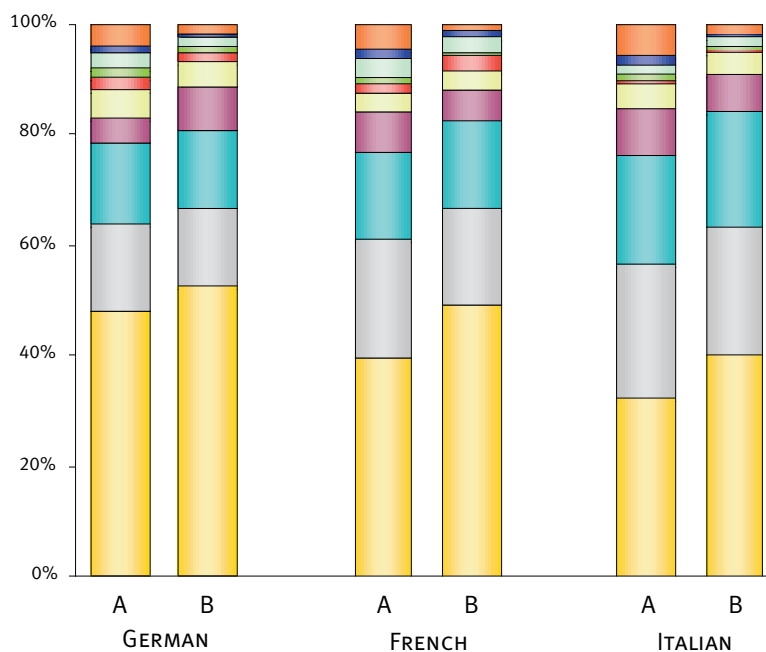
a) Total antibiotic use

Total antibiotic use was stable over the 2 study years. The sentinel network captured 36% of the total use in Switzerland in 2004 and 33% in 2005. The proportion of the Swiss hospital market covered by the sentinel network varied across language regions. This variation correlated for a large part with the proportion of acute hospital beds represented in the sentinel network for each region. Indeed, sentinel hospitals in the German-speaking region (37% of all public beds) accounted for 26% and 22% of antibiotic consumption in 2004 and 2005, respectively. In the French-speaking region, sentinel hospitals represented 81% of public beds and 61% of antibiotic use. With 54% of the public beds, sentinel hospitals in the Italian-speaking region represented 62% and 59% of the total antibiotic use.

b) Distribution of antibiotic families

Antibiotics were grouped in accordance with the Anatomic Therapeutic Chemical (ATC) classification. The proportions of penicillins and cephalosporins use differed slightly between data from sentinel hospitals and market survey. The 2 sources of data provided very close results regarding the proportions of other antibiotic families. In 2004, the use of penicillins, cephalosporins and quinolones represented 77.7% of the total in the sentinel hospitals and 82.5% in the hospital market survey. Comparable proportions were found in 2005 (77.6% and 81.3% in the sentinel network and the private survey of the hospital market, respectively) (Figure 1). The penicillin family ranked first for consumption in the three language regions. Its importance was highest in hospitals of the German-speaking region. The use of cephalosporins and quinolones was higher in Italian-speaking hospitals than in the other language regions.

Figure 1

Use of antibiotic families by language region in 2004, expressed as proportion of total use. A: data from the sentinel hospital network; B: data from the private survey of the hospital market. The family named "Others" grouped together the ATC codes: J01X (without J01XA Glycopeptides), J01DF (monobactams), J01EA (trimethoprim and derivates), J01FF (lincosamides), J01FG (streptogramins).

At this point, we conclude that the implementation of a sentinel network made up of a limited sample of hospitals is feasible. Findings from the sentinel data showed characteristics and trends similar to of the data from the private surveyor of manufacturers' sales. The hospitals' participation through pharmacists could be improved to be more representative in the future, especially in the German-speaking region.

Examples of further analyses made possible by the sentinel hospital network The hospital pharmacists can provide interesting details that are not available from a market survey based on manufacturers' sales. Examples include data to adjust antibiotic consumption to hospital activity (density of use, see below), or ward-specific consumption data.

a) Density of total antibiotic use in the language regions

For the whole sentinel network, the density of total antibiotic use expressed in DDD per 100 patient days ranged from 21.0 to 97.5 (median = 50.9, IQR = 19.0) in 2004 and from 21.0 to 101.0 (median = 50.7, IQR = 18.1) in 2005. It remained stable over the study years in every language region (Figure 2). However, it was significantly different across the regions ($p < 0.001$, test for homogeneity of incidence rates). The Swiss Italian hospitals in the sentinel network showed the highest antibiotic use, with a median of 60.8 DDD per 100 patient days in 2004, and 60.1 in 2005. The lowest antibiotic use was found in the German-speaking region (medians 43.1 in 2004 and 45.0 in 2005); it was slightly higher in the French-speaking region (47.8 and 53.9). Of note, two pharmacists provided agglomerated data for several hospitals. These hospitals' groupings were excluded for calculating medians, percentiles, minimum and maximum values.

Figure 2

Box plot of total density of antibiotic use expressed as DDD per 100 patient days in each language region. The red line in the box indicates the median value of the data set. The upper and the lower edges of the box represent the 75th and the 25th percentiles of the data set. The minimum and maximum data values are shown as capped bars. The number of participating hospitals (N, %) is shown by language region and year.
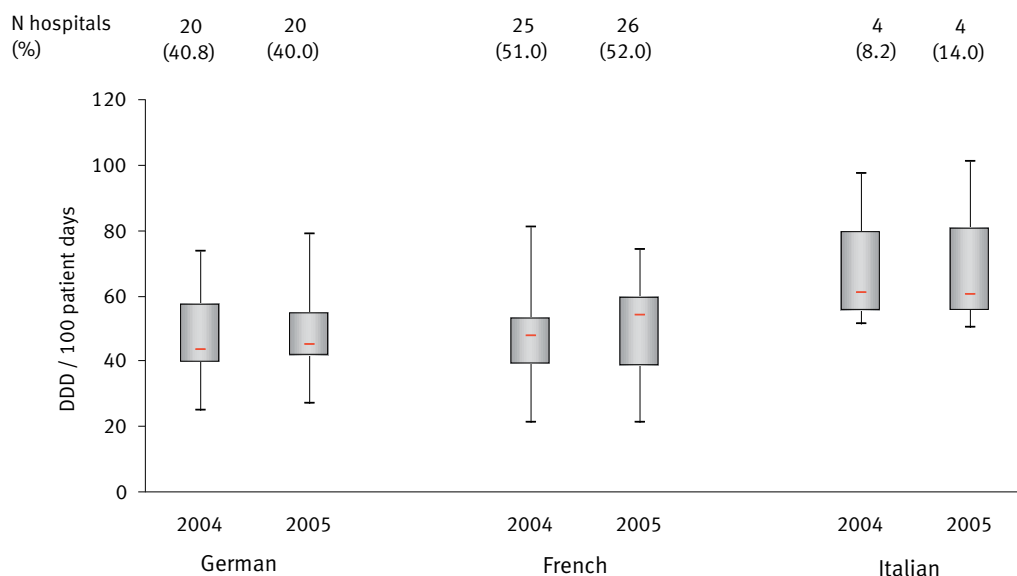
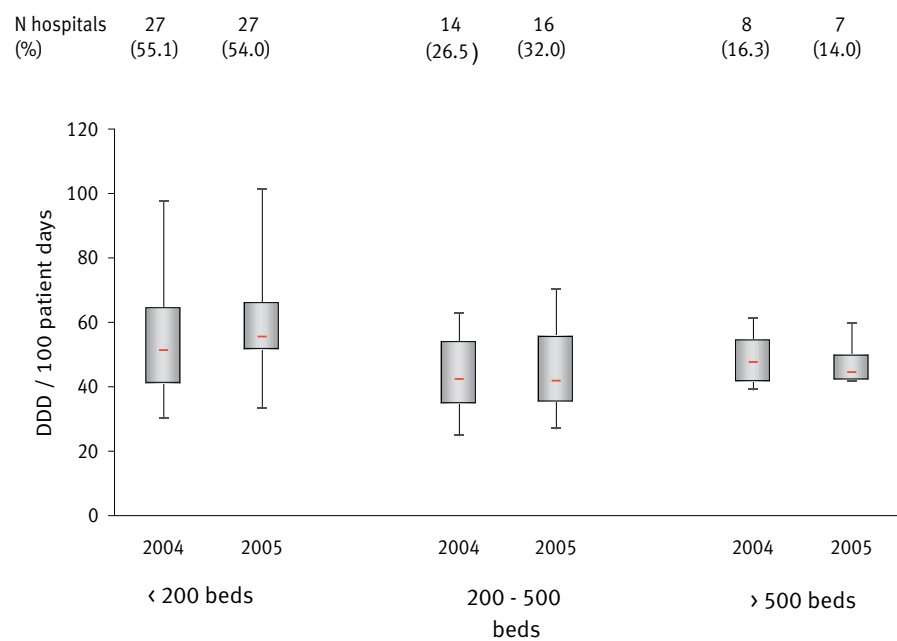b) Density of use of antibiotic families in the language regions

A weighted mean was calculated for each year by aggregating data on antibiotic use and patient days from all hospitals. The distribution of antibiotic families remained stable over 2004 and 2005 in every language region. Most of the difference between the Italian region and the others was explained by the use of cephalosporins, quinolones and macrolides, which was about twice higher in this region. In contrast, the use of penicillins was quite similar in the three language regions. Combinations of penicillins and betalactamase inhibitors (ATC code J01CR) were the most frequently prescribed antibiotics in the three regions. They represented 75.8% ± 1.4 of the density of use for penicillins in 2004 and 75.7% ± 2.8 in 2005. Regarding cephalosporins, the density of third and fourth-generation use was higher in Swiss Italian hospitals (4.4 and 7.5 DDD per 100 patient days, respectively) than in Swiss German (1.8 and 2.0) and Swiss French hospitals (3.2 and 2.0) in 2004. The density of use ranged from 6.2 (Swiss German hospitals) to 12.5 DDD per 100 patient days (Swiss Italian hospitals) for quinolones and from 2.0 (Swiss German hospitals) to 5.0 DDD per 100 patient days (Swiss Italian hospitals) for macrolides in 2004.

c) Density of total antibiotic use per hospital size

Sentinel hospitals were stratified in three categories of size: fewer than 200 beds (small), 200 to 500 beds (medium), more than 500 beds (large). The density of antibiotic use remained stable over 2004 and 2005 in each category of hospitals (Figure 3). It was significantly higher in smaller hospitals (p<0.001, test for homogeneity of incidence rates). A large variation in antibiotic use was found among participating hospitals, especially among small-size hospitals.

Figure 3

Density of total antibiotic use by hospital size in 2004 and 2005. The red line in the box indicates the median value of the data set. The upper and the lower edge of the box represent the 75th and the 25th percentiles. The minimum and maximum values are shown as capped bars. The number of participating hospitals (N, %) is shown by hospital size and year.

| N hospitals (%)	27 (55.1)	27 (54.0)	14 (26.5)	16 (32.0)	8 (16.3)	7 (14.0)

d) Density of use of antibiotic families per hospital size

The distribution of antibiotic families varied less than the total consumption across hospital sizes (Figure 4). Penicillins were the most frequently prescribed antibiotic family in 2004 and 2005. In 2004 for instance, they made up 40.1% (small-size hospitals), 46.8% (medium) and 43.7% (large) of all antibiotic use. The use of cephalosporins represented 22.7% in small, 17.7% in medium and 18.0 % in large hospitals. The percentages of penicillins and cephalosporins were similar in 2005. A majority of penicillins were given in combination with betalactamase inhibitors in the three size categories. In 2004, for instance, these combinations represented 77.4% ± 5.4 of penicillin use. Quinolones accounted for 14.0% (large hospitals) to 17.1% (small) of the total antibiotic use in 2004, while the proportions for macrolides ranged from 5.0% (large hospitals) to 7.7% (small).

Figure 4

Density off antibiotic families expressed in DDD per 100 patient days in the sentinel network per hospital size in 2004 and 2005. The family named "Others" grouped together the ATC codes: J01X (without J01XA Glycopeptides), J01DF (monobactams), J01EA (trimethoprim and derivates), J01FF (lincosamides), J01FG (streptogramins).
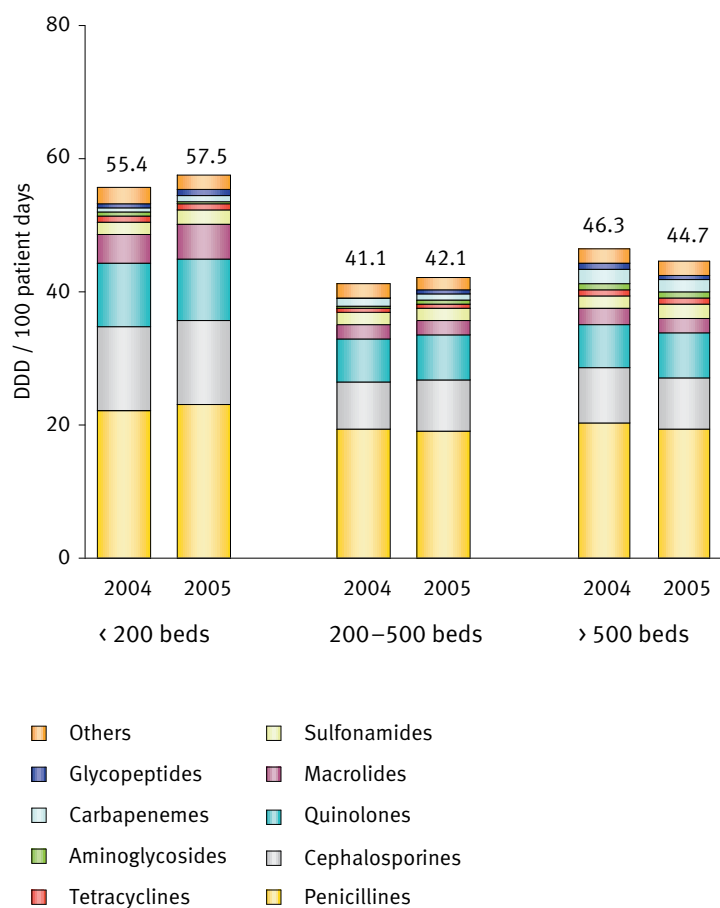
ANTIBIOTIC USE IN THE COMMUNITY

Sources of data Two sources of data on 2002-2004 antibiotic consumption in the outpatient setting were compared:
– a private provider of health market data based on manufacturers' sales to all Swiss pharmacies and dispensing doctors (IMS Health GmbH, Hergiswil);
– sentinel groups of primary care physicians (physicians-pharmacists quality circles and control group): the details of their prescriptions paid by health insurances were available through the billing data of the Swiss Association of Pharmacists (SAPh) elaborated by the Office de Facturation (OFAC, Geneva) and delivered by 80% of the Swiss pharmacies.

Antibiotic consumption data were aggregated as numbers of packages, and converted into DDD either globally or according to the ATC classification. Results were then expressed as DDD per 1000 inhabitants per day (DID). Population statistics were provided by IMS Health GmbH for the market survey. For the sentinel groups, census data were used from the Swiss Federal Statistical Office for the regions of interest; the data was extrapolated using the proportion of inhabitants by primary care physician in these regions.

Focus of the comparison Because the availability of SAPh data is restricted by confidentiality rules, data for sentinel groups were limited both geographically and regarding the profile of the physicians who prescribed the billed drugs. Data were collected for:
- a group of 160 primary care physicians (PCP) who participate in physicians-pharmacists quality circles in the Cantons of Fribourg, Valais and Neuchâtel. Physicians in this group gave informed consent for the analysis of their individual prescription data;
- a subgroup of the above, made up of 26 PCP who have participated in quality circles in the Canton of Fribourg since 1998. This subgroup of pioneers was of interest for some of the analyses, because it had been exposed to continuous interventions on cost (e.g. promotion of generics) and prudent use of antibiotics (e.g. restrictive use of newer compounds, promotion of guidelines on respiratory tract infections, uncomplicated urinary tract infections);
- a control group of 320 anonymous PCP from the Cantons of Fribourg, Valais, Neuchâtel, Geneva, Jura and Vaud.

Data from the health market survey could be split in 200 regions, which enabled precise matching of the regions covered by the sentinel groups of PCP for the purpose of comparison.

Representativity of the sentinel groups Antibiotic use in the sentinel groups accounted for 46 to 64% of the DID reported by the market survey in the corresponding regions (Figure 5). Because DID were very close in the 2 sentinel groups (quality circles and control), we assumed that they were representative of the prescriptions by PCP. Therefore, the difference between sentinel groups and the market survey presumably reflects antibiotics prescribed by physicians other than PCP. The distribution of the various antibiotic families in the sentinel groups was close to that in the market survey (Table 1). The slight differences suggested that PCP prescribed fewer penicillins than other physicians but more cephalosporins. This observation was reproducible over the 3 study years.

Figure 5
Density of antibiotic in one sentinel group of primary care physicians from Fribourg, Neuchâtel and Valais involved in physicians-pharmacists quality circles (PCP quality circles), in one random sample of primary care physicians from the French-speaking cantons (PCP – control) and in a market survey of Fribourg, Neuchâtel and Valais.
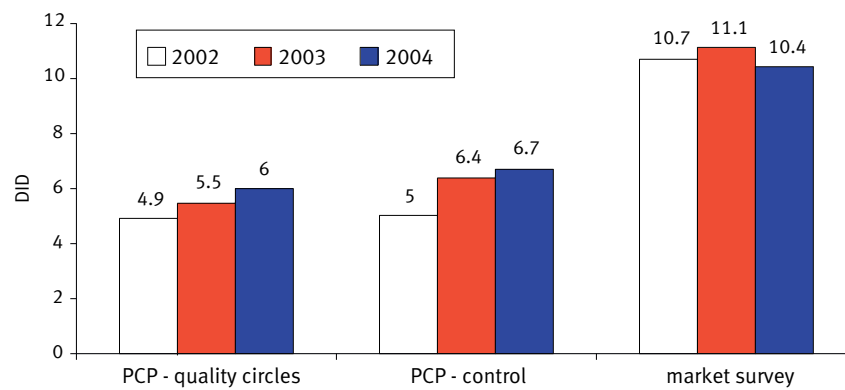
DID : Defined daily doses per 1,000 inhabitants per day
PCP : primary care physicians

Table 1
Use of antibiotic families, as percent proportions of total use, in 2 sentinel groups of primary care physicians in the Cantons of Valais, Neuchâtel and Fribourg (physicians involved in physicians-pharmacists quality circles and physicians in a control group) and in a market survey of the same cantons.

Antibiotic families	PCP[1] – quality circles			PCP[1] – control			Health market survey		
	2002	2003	2004	2002	2003	2004	2002	2003	2004
Tetracyclines	5[2]	5	6	6	7	8	7	6	7
Penicillins	35	38	36	35	37	38	40	42	44
Cephalosporins	14	15	13	16	15	13	11	11	10
Sulfonamides and trimethoprim	3	3	3	4	4	4	5	5	4
Macrolides	21	21	19	18	17	17	17	17	16
Quinolones	20	19	23	22	20	20	21	19	20

[1] : primary care physicians
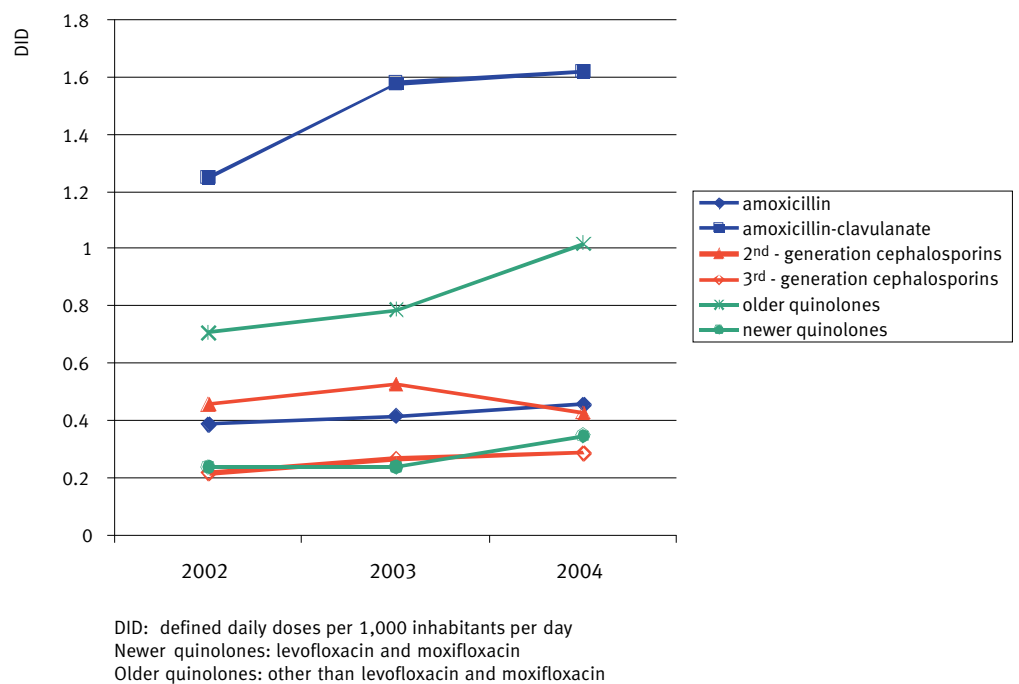[2] : all data in percents of total antibiotic use

Knowledge of prescription practice by PCP is interesting at least in two respects. First, PCP represent a substantial amount of the total use of antibiotics in the community. Second, PCP have to deal more often than others with grey zones of antibiotic therapy, such as upper and lower respiratory tract infections. These are domains where it is the most difficult to put the principles of prudent antibiotic use into practice and are therefore domains with room for improvement. In this respect, the quality circles are of great interest for sentinel monitoring, as they gather physicians and pharmacists who volunteer for interventions, the impact of which could then be assessed.

Profile of antibiotic prescription by primary care physicians in the sentinel groups: the example of year 2004 PCP in the control group were compared to the pioneers of the quality circles from Fribourg. Amoxicillin and the association of amoxicillin plus clavulanic acid represented more than 90% of the prescribed penicillins. The observed data demonstrate some effects of the collaborative local approach promoted in the physicians-pharmacists quality circles. The pioneers of quality circles used amoxicillin more often than PCP in the control group. A similar difference was observed with cephalosporins and with quinolones.

Trends in antibiotic prescription by PCP A global increase in the drugs prescribed by PCP in the quality circles (+ 34%) and in the control group (+ 22%) was observed over the 3 study years. This was true for most of the antibiotic families (Figure 6).

Figure 6

Trends in density of antibiotic use in one random sample of primary care physicians in the French-speaking cantons (control group of the physicians-pharmacists quality circles programme) over the 3 study years.

DID: defined daily doses per 1,000 inhabitants per day
Newer quinolones: levofloxacin and moxifloxacin
Older quinolones: other than levofloxacin and moxifloxacin

Publications of the NRP 49 project

In preparation.