



## Hospital antibiotic consumption in Switzerland: comparison of a multicultural country with Europe

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### SUMMARY

The consumption of antibiotics in the inpatient setting of Switzerland was assessed to determine possible differences between linguistic regions, and to compare these results with European results. Data on antibiotic consumption were obtained from a sentinel network representing 54% of the national acute care hospitals, and from a private drug market monitoring company. Aggregated data were converted into defined daily doses (DDD). The total consumption density in Switzerland was close to the median consumption reported in European surveys. Between 2004 and 2008, the total consumption of systemic antibiotics rose from 46.1 to 54.0 DDD per 100 occupied bed-days in the entire hospitals, and from 101.6 to 114.3 DDD per 100 occupied bed-days in the intensive care units. Regional differences were observed for total consumption and among antibiotic classes. Hospitals in the Italian-speaking region showed a significantly higher consumption density, followed by the French- and German-speaking regions. Hospitals in the Italian-speaking region also had a higher consumption of fluoroquinolones, in line with the reported differences between Italy, Germany and France. Antibiotic consumption in acute care hospitals in Switzerland is close to the European median with a relatively low consumption in intensive care units. Some of the patterns of variation in consumption levels noticed among European countries are also observed among the cultural regions of Switzerland.

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### Introduction

Epidemiological studies and mathematical models support a close correlation between the variation in antibiotic consumption and bacterial resistance.<sup>1</sup> Since there may be a time-lag between the consumption of antibiotics and the variation in resistance, continuous monitoring of consumption might be as important as the monitoring of resistance and can be helpful for several reasons: (i) to understand the main determinants of bacterial resistance; (ii) to predict the evolution of this resistance; (iii) to plan interventions

fostering appropriate consumption; and (iv) to assess the impact of such interventions.<sup>2</sup> In this context, hospitals represent 'hot spots' for selective pressure on micro-organisms, especially in intensive care units (ICUs).<sup>3</sup> Therefore surveillance programmes have been developed at regional, national or international levels to monitor patterns of antibiotic consumption in hospitals.<sup>4</sup>

The first goal of our study was to describe the antibiotic consumption in the Swiss sentinel network. The second goal was to assess possible differences in hospital antibiotic consumption between the three major linguistic regions of Switzerland (German-, French- and Italian-speaking). In particular, we aimed at revealing whether the regional differences described in the ambulatory care setting were also observed in the hospital setting.<sup>5,6</sup> Finally, our third goal was to compare the consumption of antibiotics in Swiss hospitals with those reported in European surveys.

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## Methods

### Design and sources of data on antibiotic consumption in Switzerland

This observational, multicentre study was based on two sources of data for the 2004–2008 antibiotic consumption in hospitals. (i) Data provided by a private drug market investigation company (IMS Health GmbH, Hergiswil, Switzerland) were purchased for 2004 and 2005. This exhaustive data set included the antibiotic quantities sold to all institutions with acute, intermediate and long term care. (ii) A sentinel network of acute care hospitals was set up in 2004. This network allows detailed analyses that would not be possible with the market data, e.g. adjustment to hospital activity with measurement of antibiotic consumption by linguistic region. We collected antibiotic consumption data from 42 acute care hospitals in 2004 and 57 in 2008, of which 37 were small size hospitals (<200 beds), 14 medium size (200–500 beds), and six large size (>500 beds, which includes the five Swiss university hospitals). Thirty-one were located in the German-, 22 in the French- and four in the Italian-speaking regions of Switzerland. The network represented 54% of the total number of acute somatic care hospitals (excluding psychiatric and rehabilitation centres) and 47% of all beds in this category in Switzerland (33% of all beds) and 49%, 73% and 100% in the German-, French- and Italian-speaking regions, respectively. Of the 42 hospitals that participated in the sentinel network in 2004, 39 (93%) provided data in 2008. Twenty-five hospitals (13 small, eight medium, and four large size) also provided data on adult ICUs. Their number increased to 37 (19, 14, and four, respectively) in 2008, representing 51% of the hospitals equipped with ICU beds in Switzerland.

### Sources of data on antibiotic consumption in Europe

From the literature 15 studies or reports were selected from European countries assessing the consumption of antibiotics;

results were compared with the Swiss data for all hospitals and their ICUs.<sup>7–16</sup>

### Data collection

Data were collected on antibiotic agents for systemic consumption group J01 of the Anatomical Therapeutic Chemical (ATC) classification.<sup>17</sup> Antibiotic consumption (in grams or millions of International Units) was converted into defined daily doses (DDD) using the 2009 release of the DDD by the World Health Organization Collaborative Centre for Drug Statistics Methodology.<sup>17</sup>

For the sentinel network, data were collected from the entire hospitals, and separately from the adult ICUs when possible. Regarding drug market data, IMS Health GmbH used the classification of the European Pharmaceutical Marketing Research Association (EphMRA). By contrast with the ATC classification, EphMRA does not include metronidazole, sulfadiazine, and fosfomycin in its definition of the J01 group.

Data on hospital occupied bed-days and admissions within the sentinel network were collected, enabling expression of the consumption density as DDD per 100 occupied bed-days (DDD per 100 BD) and as DDD per 100 admissions (DDD per 100 A). To compare the Swiss consumption with the studies using the DDD per 1000 inhabitants per day, we used IMS data and demographic features of the Swiss population.

### Data analysis

A one-level mixed model for repeated measurements was used to compare antibiotic consumption across linguistic regions over the years. In the model, the independent variables 'time' and 'linguistic region' were treated as fixed repeated-measures factors, and hospital was treated as a random effect. Two dummy variables were created for the categorical variable 'linguistic region' and were compared to the reference, which corresponded to the German-speaking area in our case. Two-sided  $P < 0.05$  was considered statistically significant.

**Table 1**

Use of systemic antibiotics (ATC J01 code, expressed in defined daily doses per 100 bed-days) in 2004 and 2008 in all Swiss sentinel hospitals, and by linguistic region (German-, French- and Italian-speaking)

	All participating hospitals				German-speaking hospitals		French-speaking hospitals				Italian-speaking hospitals			
	2004	2008	Trend 2004–2008		2004	2008	2004	2008	Comparison with German-speaking hospitals		2004	2008	Comparison with German-speaking hospitals	
			Coef. <sup>a</sup>	P-value					Coef. <sup>a</sup>	P-value			Coef. <sup>a</sup>	P-value
Total antibiotic use	46.2	53.4	0.4	0.208	46.7	52.9	41.6	54.3	1.3	0.659	68.5	63.9	13.2	0.023
Penicillins (J01C)	19.0	23.7	0.2	0.323	22.1	26.7	18.4	24.9	–2.9	0.070	21.5	23.7	–2.6	0.397
Combinations of penicillins and β-lactamase inhibitors (J01CR)	16.1	19.8	0.0	0.824	16.9	21.2	14.6	17.8	–3.2	0.047	16.2	16.8	–4.2	0.193
Cephalosporins (3rd and 4th generation <sup>b</sup> )	5.2	5.6	–0.2	0.011	4.3	4.7	5.3	6.8	2.3	<0.001	13.3	8.2	5.6	<0.001
Carbapenems <sup>c</sup>	1.6	2.8	0.2	<0.001	1.3	1.5	1.9	3.2	0.6	0.066	1.5	3.1	1.0	0.156
Fluoroquinolones (J01MA)	6.3	8.2	0.0	0.666	6.0	8.0	5.6	8.2	0.3	0.685	12.6	10.5	4.3	0.002
Macrolides (J01FA)	2.6	3.3	–0.1	0.296	2.1	2.8	3.1	4.1	0.9	0.086	5.0	4.2	1.8	0.089
Vancomycin (J01XA01)	0.4	0.8	0.0	<0.001	0.4	0.6	0.6	1.1	0.3	0.003	0.7	1.2	0.5	0.003

<sup>a</sup> A one-level mixed model for repeated measurements used 'time' and 'linguistic region' as fixed effect and 'the hospitals' as random effect. The German-speaking area was used as the reference. The coefficients correspond to the effect of time or linguistic region on the antibiotic use.  $P < 0.05$  was considered statistically significant.

<sup>b</sup> Fourth generation cephalosporins were only represented by cefepime in Switzerland.

<sup>c</sup> Only meropenem and imipenem were used in Switzerland.

**Table II**  
Comparison of antibiotic use density in defined daily doses per 100 bed-days in ICUs between Switzerland and various countries

Country	Study name	Ref.	Period of data collection	Hospital type	ICUs (type and number)	Total antibiotic use <sup>a</sup>	Penicillins	Combinations of penicillins	3rd generation cephalosporins	Carbapenems	Macrolides	Fluoroquinolones	Glycopeptides	
Switzerland	Present study		2008	<200 beds	19	114.3 (57.7–159.8)	33.3	22.3	8.3	10.1	9.4	6.3	2.0	
					200–500		14	35.9	25.9	8.1	13.3	10.7	6.8	3.5
					University hospitals		4	33.8	23.3	6.0	15.3	8.2	8.6	6.9
Europe	Care-ICU	<sup>7</sup>	2005	University, general hospitals (8 countries)	35	125.4 (34.8–499.2)	NA	NA	NA	NA	NA	NA	NA	
Germany	MABUSE-INTER-REGIO II	<sup>8</sup>	2002	NA	Inter-ICU (25)	104 <sup>b</sup> (14.4–182.9)	74.1	NA	NA	NA	7.7	12.7	0.8	
					MICU (15)		70	NA	NA	7.5	10.9	1.0		
					SICU (13)		75.7	NA	NA	3.2	12.2	1.8		
	MABUSE-INTER-UNI-II	<sup>9</sup>	1998–1999–2000	University hospitals	MICU (8)	187 <sup>c</sup>	22.2	NA	NA	NA	31.4	NA	9.8	
					SICU (8)		146	16.5	NA	NA	7.9	NA	5.1	
SARI	<sup>10</sup>	Feb 2000–Jun 2002	NA	Inter-ICU (14)	125.2	NA	NA	15.1	4.2	NA	9.1	2.2		
				MICU (10)		148.3	NA	NA	19.4	6.1	8.7	NA		
				SICU (11)		138.6	NA	NA	17.5	11.3	8.2	3.6		
France	INTER-CCLIN	<sup>11</sup>	2007	NA	86	146.6 <sup>d</sup>	NA	NA	NA	3.7	3.8	19.2	5.2	
Sweden	ICU-STRAMA	<sup>12</sup>	1999	Tertiary care	9	154.1	NA	NA	NA	14.3	NA	NA	NA	
				County hospitals	17	117.0	NA	NA	NA	11.0	NA	NA	NA	
				Local hospitals	4	107.2	NA	NA	NA	5.8	NA	NA	NA	
		<sup>13</sup>	2003	Academic and non-academic hospitals	14	151.0	NA	NA	NA	NA	NA	NA	NA	

NA, not available; Inter-ICU, interdisciplinary intensive care unit; MICU, medical ICU; SICU, surgical ICU.

<sup>a</sup> Total antibiotic use (code ATC J01, antibiotics for systemic use), median (range) except if specified otherwise.

<sup>b</sup> Weighted mean.

<sup>c</sup> Three-year mean.

<sup>d</sup> Overall antibiotic use includes ATC codes J01, oral imidazole derivatives P01AB, rifampicin J04AB2.

Statistical analyses were conducted using the Stata™ software 10.0 (Statacorp., Lakeway, TX, USA).

## Results

### Total antibiotic consumption in the sentinel network of Swiss hospitals

The total consumption of systemic antibiotics in the sentinel hospitals rose from 46.2 DDD per 100 BD (weighted mean, range: 21.0–97.4) in 2004 to 53.4 DDD per 100 BD (range: 16.6–78.7) in 2008, a mean annual increase of 4% (Table I). Measuring antibiotic consumption in DDD per 100 admissions showed a comparable 5% annual increase, from 387.2 in 2004 to 407.0 in 2008. The upward trend was observed in 70% of the hospitals within the network. The density of penicillin consumption ranked first over the five years and ranged from 19.0 to 23.7 DDD per 100 BD. The various combinations of a penicillin and a  $\beta$ -lactamase inhibitor were the most frequently prescribed antibiotics (range: 16.1–19.8 DDD per 100 BD). We observed an increased consumption for most antibiotic families, except for tetracyclines and aminoglycosides.

In the 14 ICUs who submitted data between 2004 and 2008, the total consumption of systemic antibiotics rose from 99.9 DDD per 100 BD (weighted mean, range: 42.1–161.9) in 2004 to 111.2 DDD per 100 BD (range: 57.7–159.8) in 2008, a mean annual increase of 2%. Thirty-seven ICUs participated in 2008, and their total consumption of systemic antibiotics was 114.3 DDD per 100 BD (range: 57.7–159.8) (Table II). The consumption of each antibiotic family in the ICUs increased over the five years, except for cephalosporins.

### Differences in antibiotic consumption between linguistic regions

The density of antibiotic consumption was higher in the Italian-speaking sentinel hospitals (weighted mean: 68.5 and 63.9 DDD per 100 BD in 2004 and 2008, respectively) than in the German-speaking (46.7 and 52.9) and French-speaking (41.6 and 54.3) hospitals (Table I). The difference between Italian- and German-speaking hospitals was statistically significant for total antibiotic consumption for the third and fourth generation

cephalosporins as well as for fluoroquinolones and vancomycin. Consumption in French-speaking hospitals was significantly higher than in German-speaking hospitals for third and fourth generation cephalosporins and vancomycin, and significantly lower for combinations of penicillins and  $\beta$ -lactamase inhibitors.

According to the mixed model, consumption in ICUs in Italian-speaking hospitals was significantly higher than in ICUs of German-speaking hospitals for third and fourth generation cephalosporins (+9.3 DDD per 100 BD,  $P < 0.01$ ) and vancomycin (+2.8 DDD per 100 BD,  $P < 0.01$ ). The difference between the ICUs in the French- and German-speaking hospitals was statistically significant for macrolides (+5.2 DDD per 100 BD,  $P < 0.001$ ), as well as for vancomycin (+1.2 DDD per 100 BD,  $P < 0.05$ ).

### Comparison with Europe

IMS data showed a consumption density of 2.1 DDD per 1000 inhabitants per day in 2005. Swiss hospitals lie slightly higher than the European median reported by the ESAC hospital subproject for 2005 (1.7; range: 0.8–3.4). The total consumption in the Swiss sentinel hospitals (53.4 DDD per 100 BD) was close to the median values of the ARPAC hospitals from Western (53.6) and Northern (48.3) countries, where there was less dispersion of the data.<sup>14</sup> Studies conducted in neighbouring countries showed a higher total antibiotic consumption in Italian hospitals (76.8 DDD per 100 BD) compared with German and French hospitals, similar to the regional differences in Switzerland (Table III).<sup>11,15,16</sup> Regional differences were also observed among antibiotic families. More fluoroquinolones were used in the Italian-speaking area of Switzerland (12.5 and 10.0 DDD per 100 BD in 2004 and 2008, respectively) than in German- (6.0 and 7.1) and French- (5.4 and 7.1) speaking areas. Similarly, Italian hospitals showed a higher consumption of fluoroquinolones (14.6) than German- (6.0–8.0) and French- (5.2) speaking hospitals.<sup>11,15,16</sup> Compared to the data from the European Survey of Antimicrobial Consumption (ESAC), Swiss sentinel hospitals showed a proportion of penicillins in association with  $\beta$ -lactamase inhibitors (74%) and cefepime (18%) among the highest in Europe (range: 1–87% and 0–15%, respectively). Quinolone consumption was also relatively high in Swiss hospitals (15% in 2005), whereas the range varied in Europe

**Table III**

Use of systemic antibiotics (ATC code J01) in hospitals: comparison between Switzerland and various countries

Country	Study name	Ref.	Year of data collection	Hospitals	Total antibiotic use <sup>a</sup>
Switzerland	Present study		2008	31 German-speaking	51.2
				23 French-speaking	54.2
Europe	ESAC	b	2005	4 Italian-speaking	63.9
				All Swiss hospitals	2.1
				13 countries	1.7
Germany	GERMAP	c	2001	139 (30 countries)	49.6
			2004	1800	50
			2002	40	49
Italy	NA	15	2003	145	49.6
			2004	5	76.8
France	INTER-CCLIN	11	2007	530	35.9 <sup>g</sup>
Netherlands	NETHMAP	d	2008	53	58.1
Denmark	DANMAP	e	2008	18	74.9
Sweden	SWEDRES	f	2008	All Swedish hospitals	53.6

NA, not available.

<sup>a</sup> Data are median values expressed in defined daily doses (DDD) per 100 occupied bed-days, except for Switzerland-2005 and Europe-ESAC-2005 (weighted mean expressed in DDD per 1000 inhabitants per day).

<sup>b</sup> <http://www.esac.ua.ac.be> (accessed 1 March 2011).

<sup>c</sup> <http://www.bvl.bund.de> (accessed 1 March 2011).

<sup>d</sup> <http://www.swab.nl> (accessed 1 March 2011).

<sup>e</sup> <http://www.danmap.org> (accessed 1 March 2011).

<sup>f</sup> <http://en.strama.se> (accessed 1 March 2011).

<sup>g</sup> Overall antibiotic use includes ATC codes J01, oral imidazole derivatives P01AB, rifampicin J04AB.

between 4% in Norway to 17% in Finland.<sup>18</sup> ICUs in the Swiss sentinel network showed the lowest total antibiotic consumption compared with ICUs that participated in European studies (Table II). At the antibiotic families level, this lower consumption was observed for penicillins and third generation cephalosporins.

## Discussion

Surveillance of antibiotic consumption in Switzerland offers a unique opportunity to study three well-defined cultural regions. Our findings revealed that, although the regulation of antibiotic delivery is similar in the three linguistic regions, we found a higher antibiotic consumption in the hospitals of the Italian-speaking area, followed by those in the French- and German-speaking areas. The difference was statistically significant, a finding consistent with other studies. Higher antibiotic consumption in the Italian- and French-speaking part of the country was also observed in outpatient settings.<sup>5</sup> Also, the two Europe-wide surveys (ESAC and ARPAC) that measured the features of antibiotic consumption in hospitals showed a higher consumption in Southern countries (e.g. Italy).<sup>14,18</sup>

Sociocultural factors are well-known determinants of prescribing habits.<sup>19,20</sup> Switzerland lies at the intersection of three cultural influences (German, French and Italian) and thus reproduces variations observed at the European level. Total antibiotic consumption increased in Switzerland between 2004 and 2008 whereas it decreased in some other European countries (e.g. France, Malta). Hypothetically, the relatively low rate of antibiotic resistance in Switzerland may contribute to a lower awareness of prudent use in Swiss prescribers compared with other countries. Moreover, the study by Filippini *et al.* in the outpatient setting showing that Switzerland had the lowest antibiotic consumption in Europe may have wrongly reassured prescribers in hospitals.<sup>5</sup> Differences in use in the ICUs have also been observed across linguistic regions, especially with respect to vancomycin, the consumption of which was higher in the French- and Italian-speaking ICUs than in the German-speaking ones. In the current study there was also an upward trend in consumption of vancomycin, although resistance to meticillin remained stable over the study period among staphylococci.

We do not think that our findings were driven by existing guidelines or stewardship programmes at the regional and/or the national level, as such interventions on antibiotic use policies in hospitals have still to be developed in Switzerland. A review by Huttner *et al.* showed that public campaigns have to take into account the heterogeneity of culture.<sup>21</sup> Our results should encourage Swiss stakeholders to follow this recommendation in future initiatives such as guidelines, or campaigns targeting the general population or healthcare professionals.

The rate of antibiotic resistance is relatively low in Switzerland, but differences in resistance levels have also been observed between geographical regions. For example, French-speaking hospitals have reported higher carbapenem resistance rates among *Enterobacter* spp. compared with other regions, which correlates with the consumption of carbapenems in this region. Only a prolonged longitudinal monitoring of antibiotic consumption and resistance would allow better deciphering of this mutual relationship.

Vander Stichele *et al.* highlighted a correlation of total antibiotic consumption between out- and inpatient settings within the countries participating in the ESAC study.<sup>18</sup> The correlation between in- and outpatients was not observed in our country. For example, Switzerland exhibited the lowest outpatient antibiotic consumption among 26 European countries but was close to the European average regarding acute care hospitals.<sup>5</sup> By contrast, quinolone consumption was also relatively high in the Swiss hospitals, similar

to what was observed for ambulatory care [i.e. 20% in Switzerland vs 7% (mean) in other European countries]. This is a matter of concern since quinolones represent one of the antibiotic families whose high consumption is most often associated with development of resistance, including cross-resistance to other antibiotics.

Our study has several limitations. First, a sentinel network is a surveillance system comprising a non-exhaustive group of hospitals. Nevertheless, the high proportion of all Swiss acute care hospitals included in our study (54%, i.e. 47% of total beds) suggests that the data are representative. Second, the DDD methodology allows comparisons between hospitals, but it may inaccurately reflect the dosages chosen in some of them, thus limiting the qualitative appraisal of different prescribers' profiles.<sup>22</sup> Third, adjustment to case-mix would be an improvement, as the population of patients can differ in similar-sized hospitals.<sup>23</sup> Fourth, comparing antibiotic consumption between countries can be biased by differences in methodology, differences in antibiotics involved, the inclusion or not of wards where antibiotic consumption is presumably low (e.g. psychiatric wards) or with long lengths of stay (e.g. rehabilitation wards).<sup>24</sup>

In conclusion, Swiss acute care hospitals showed an antibiotic consumption density close to the European median. Differences between linguistic regions mimic the differences observed between European countries.

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## Conflict of interest statement

None declared.

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