Antibiotic use in adult outpatients in Switzerland in relation to regions, seasonality and point of care tests

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Abstract

The use of antibiotics is highest in primary care and directly associated with antibiotic resistance in the community. We assessed regional variations in antibiotic use in primary care in Switzerland and explored prescription patterns in relation to the use of point of care tests. Defined daily doses of antibiotics per 1000 inhabitants (DDD_{1000pd}) were calculated for the year 2007 from reimbursement data of the largest Swiss health insurer, based on the anatomic therapeutic chemical classification and the DDD methodology recommended by WHO. We present ecological associations by use of descriptive and regression analysis. We analysed data from 1 067 934 adults, representing 17.1% of the Swiss population. The rate of outpatient antibiotic prescriptions in the entire population was 8.5 DDD_{1000pd}, and varied between 7.28 and 11.33 DDD_{1000pd} for northwest Switzerland and the Lake Geneva region. DDD_{1000pd} for the three most prescribed antibiotics were 2.90 for amoxicillin and amoxicillin-clavulanate, 1.77 for fluoroquinolones, and 1.34 for macrolides. Regions with higher DDD_{1000pd} showed higher seasonal variability in antibiotic use and lower use of all point of care tests. In regression analysis for each class of antibiotics, the use of any point of care test was consistently associated with fewer antibiotic prescriptions. Prescription rates of primary care physicians showed variations between Swiss regions and were lower in northwest Switzerland and in physicians using point of care tests. Ecological studies are prone to bias and whether point of care tests reduce antibiotic use has to be investigated in pragmatic primary care trials.

Keywords: Antibiotics, epidemiology, point of care tests, primary care, Switzerland

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Background

There is growing evidence from observational studies that antibiotic overuse is an important risk factor for the emergence of antibiotic resistance [1,2]. In primary care, most antibiotics are prescribed for upper and lower respiratory tract and urinary tract infections. Antibiotic resistance has been recognized as an increasing public health problem. Therefore the European Surveillance of Antimicrobial Consumption project was established to collect data on outpatient antibiotic use in a uniform format [3]. Highly variable rates of antibiotic prescriptions were found, with higher rates of defined daily doses (DDD) in the Mediterranean countries, compared with those in the northern European countries. Striking seasonal fluctuations and higher rates of antibiotic resistance were observed in particular in high-prescribing countries [3]. Switzerland has one of the lowest rates of antibiotic consumption in Europe [4]. Contrary to many European countries, point of care tests are widely used by primary care providers in Switzerland [5]. First intervention trials indicate that point of care tests may contribute to a more diligent use of antibiotics in primary care [6,7]. However, there is conflicting evidence from epidemiological data of outpatient antibiotic use in relation to the use of such tests. Based on prescription records of the largest social health insurer, we investigated differences in outpatient antibiotic use in Switzerland in relation to regions, seasons and use of point of care tests.

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Methods

We analysed reimbursement data of systemic antibiotic use in ambulatory care from 2007 of the Helsana Group, the largest social health insurer in Switzerland. This insurer covers, according to regions, between 11.5% and 22.8% of the Swiss population.

Information on drug prescriptions was received from invoices. Antibiotics were identified by the pharma code, an index for the identification of the drug, application form, doses and package size used in Switzerland and provided by e-mediat AG, Bern, Switzerland [8]. According to regions, between 95.8% and 97.9% of invoices are sent or processed electronically and centrally stored by the health insurer, guaranteeing high completeness of data for the particular calendar year. All antibiotics analysed have to be covered by the social health insurance, although individuals with high deductibles may not send their bills to the health insurer.

We considered only outpatient antibiotic use provided by self-dispensing physicians or pharmacies. We classified each antibiotic with the anatomic therapeutic chemical (ATC) classification codes [9]. We included only antibiotics with systemic and oral administration and excluded all antifungals, antimycobacterial drugs, and all topical antibiotics. For each ATC code and drug, we calculated defined daily doses (DDD) based on the World Health Organisation (WHO) definitions [9]. For the calculation of $DDD_{1000\ per\ day\ (pd)}$, the study population was standardized by age and gender. The reference was the Swiss population of 2007 [10]. The number of Swiss residents being insured with the Helsana Group for the year 2007 and the total person days involved was calculated for each region. This allowed us the calculation of the DDD per 1000 persons per day (DDD_{1000pd}) by summing up the DDD either per month or by year and dividing it by the number of insured individuals for the respective unit of time. We explored regional differences in antibiotic use based on the seven major regions as defined by the Swiss Federal Statistical Office (for a map see reference [11]).

We further analysed for each antibiotic prescription whether the reimbursement claims included compensations for office-based point of care tests, a laboratory test or radiographs ordered within 7 days prior to or 2 days following the procedure date. Point of care tests included urine analysis for leucocyte counts and urine culture, white blood cell count, C-reactive protein (CRP), pharyngeal-smear for antigen testing or culture of group A *Streptococcus*. Primary care physicians in Switzerland may run their own radiology facilities for conventional radiographs, or refer their patients to radiology centres.

In Switzerland deductibles are mandatory for all patients and according to individual budget and insurance package may range between Swiss Francs 300–2500 per year. Patients whose invoices are below the limit of the deductible sometimes do not send their bills to the insurance company but pay them directly. This results in incomplete information regarding their actual health care utilization. Therefore, we included for this part of the analysis only patients with data on point of care tests where the expenses exceeded the deductible. This restriction ensures that only individuals with complete information on antibiotic prescriptions and point of care tests were considered for the analysis, which reduced our number of prescriptions by 12.7%. We further restricted our analysis of point of care tests to primary care physicians and general internists (by excluding all specialists) and to physicians with at least four prescriptions per antibiotic group in order to avoid coefficients with zero values. This additional restriction reduced our initial number of prescriptions for the analysis of point of care tests by another 54.1% and resulted in a final total of 126 048 (40.0% of all prescriptions).

We used linear regression analysis to calculate the ratio between the number of prescriptions per patient group and the percentage of point of care tests for these prescriptions. All patients of one physician were divided into four patient groups according to gender and age (18–64 and >65 years). For each antibiotic group, the outcome variable (e.g. the number of prescriptions) divided by the number of patients per patient group and physician was calculated. Because our outcome variable was skewed to the left we used a log-transformation and obtained normally distributed dependent variables and residuals. In addition, the percentage of point of care tests per antibiotic prescription and region was calculated for all patients with costs in excess of the deductible. All statistical analyses were carried out with the open software R version 2.7.

Results

This analysis is based on data from 1 067 934 Swiss residents aged 18 or older that had mandatory health insurance with the Helsana Group, representing 17.1% of the Swiss population. In 2007, the mean age of this served population was 1.6 years above the national average age of 41.1 years, and compensation costs for this population were 7.6% above the national average [10,12]. Overall, 52.5% of the population were female and 26% were aged over 65 years. General

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practitioners comprised 41.5%, general internists 17.3% and specialists 41.2% of 11 208 antibiotic prescribing physicians, with a total of 314 915 prescriptions.

The rate of outpatient antibiotic prescriptions in the entire population was 8.5 DDD_{1000pd} and varied by a factor of 1.5, with the highest rate in the region of Lake Geneva (11.33 DDD_{1000pd}) and the lowest prescription rate in northwest Switzerland (7.28 DDD_{1000pd}) (Fig. 1). In general, regions with higher overall prescription rates had also higher prescriptions per antibiotic group, with the exception of central Switzerland where consumption of amoxicillin and amoxicillin-calvulanate was lower (Fig. 1). In all regions, fluoroquinolones were the second most prescribed antibiotics, with DDD_{1000pd} ranging between 1.45 and 2.28. Macrolides were the third most prescribed antibiotics, with DDD_{1000pd} between 1.13 (east Switzerland) and 1.94 (Lake Geneva). Espace Midland, Lake Geneva and Ticino had a higher prescription rate for other betalactams (all betalactams excluding amoxicillin and amoxicillin/clavulanate), with DDD_{1000pd} ranging between 0.69 and 1.29 when compared with ranges of prescription rates of 0.34 and 0.48 DDD_{1000pd} in the remaining regions.

In order to explore seasonal variation we calculated mean DDD_{1000pd} per month according to regions and antibiotic groups (Fig. 2). There was a high variation between summer and winter months for amoxicillin and amoxicillin-clavulanate for the two regions Lake Geneva and Ticino, with the highest prescription rates and less seasonal variation in the remaining regions with lower overall prescriptions for amoxicillin and amoxicillin-clavulanate. We found a very similar pattern for macrolides and other betalactam antibiotics, although the absolute difference in seasonal prescription variation was lower for theses groups of antibiotics.

Table 1 shows the use of point of care tests according to regions. We found a consistent pattern for each antibiotic, with a higher use of point of care tests in regions with lower antibiotic use. The use of all point of care tests was highest in the northwest, northeast and the Zurich regions and lowest in the Ticino and Lake Geneva regions. In a further analysis, we modelled the ratio of the number of prescriptions divided by the number of patients per physician and groups of antibiotics in relation to the use of point of care tests. The use of a point of care test was for all antibiotics consistently associated with fewer antibiotic prescriptions (Table 2). For example, if physicians conducted any point of care test the number of antibiotic prescriptions for amoxicillin and amoxicillin-clavulanate and fluoroquinolones was reduced by a factor of 0.79 (95% CI, 0.74–0.84) and 0.68

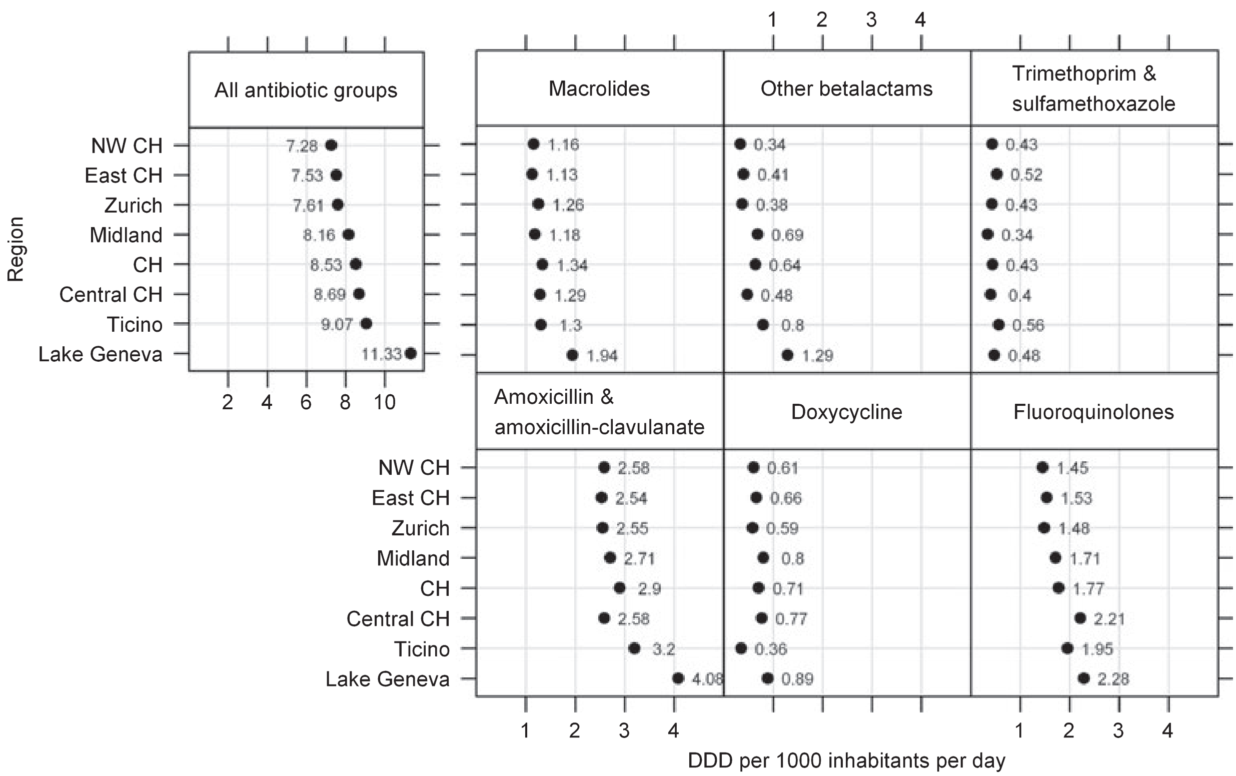

FIG. 1. Standardized DDD per 1000 inhabitants per day, for outpatient prescriptions in 2007 for all antibiotics and selected antibiotics for seven Swiss regions and Switzerland. Measures are standardized for age and sex to the Swiss population. NW, northwest; CH, Switzerland.

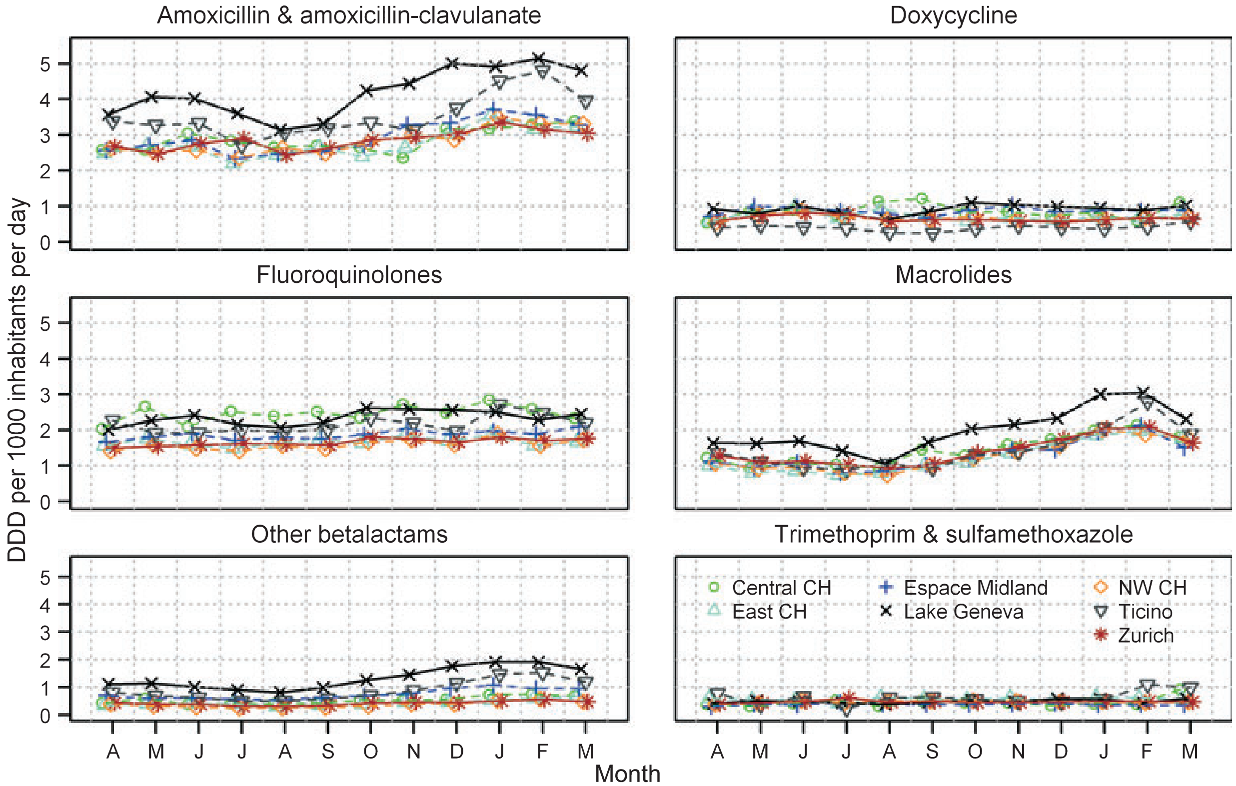

FIG. 2. Monthly average DDD per 1000 inhabitants per day, for outpatient prescriptions in 2007 for seven regions in Switzerland. For better visibility of seasonal fluctuations the first month shown is April 2007 (A) and the last month shown is March 2007 (M). Measures are standardized for gender and age to the Swiss standard population. NW, northwest; CH, Switzerland.

(95% CI, 0.65–0.72%), respectively. Thus, the use of point of care tests was associated with a 21% (95% CI, 16–26%) and 32% (95% CI, 28–45%) reduction in prescriptions of these antibiotics. With the exception of fluoroquinolones, female patients were less likely to receive an antibiotic prescription for each antibiotic class. Age was consistently associated with a higher use of antibiotics for each antibiotic class. The variance of antibiotic prescriptions and drug class explained by our model, however, was modest (adjusted R^2).

Discussion

In this study, data from roughly one-fifth of the adult Swiss population are represented. We confirm a very low rate of outpatient antibiotic prescriptions with important variation between regions within Switzerland. Overall DDD_{1000pd} were highest for the French and Italian speaking parts (Lake Geneva and Ticino) of Switzerland. However, rates in these regions were still in the range of low prescribing European countries such as the Netherlands [3]. Similar to the pattern in other European countries, we found a higher seasonal variation of antibiotic prescriptions in high prescribing regions. Amoxicillin and amoxicillin-clavulanate continue to be the most used antibiotics for outpatients in Switzerland [4]. Use of macrolids and fluoroquinolones, however, is relatively high in Switzerland and constitutes a known risk factor for antibiotic resistance, in particular for *S. pneumoniae* [13–15]. Increased use of amoxicillin-clavulanate and fluoroquinolones has also been noted in other European countries [16]. We found a consistent inverse relation between use of any point of care test and antibiotic prescriptions for all classes of antibiotics that are mostly used in upper and lower respiratory tract and urinary tract infections.

This study has several strengths. Contrary to other studies, we used a single and rather comprehensive data source for antibiotic use from the reimbursement system of the largest Swiss social health insurer. This source guarantees a uniform data collection system that is based on information on drug use for antibiotics that were actually delivered to patients. Thus, our analysis is not based on data of drug sales as used in previous studies [3,4], which may introduce bias in ecological analyses [3,17]. In addition, our database allowed us to identify the prescription behaviour at the individual physician level. We used the ATC classification system and report DDD measurement units in standardized formats

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TABLE 1. Percentage of antibiotic prescriptions with point of care per region in patients with health consumptions above the deductible

Antibiotic group (number of prescriptions/number of physicians)	Region	Percentage of tests: CRP	Leucocyte counts	Pharyngeal swab[a]	Urine[b]	Radiograph[c]	Any[e]
Amoxicillin and amoxicillin-clavulanate (58 550/5274)	CH total[d]	26	25	4	8	08	34
	NW CH	31	29	3	8	9	38
	East CH	33	31	3	9	10	42
	Zurich	33	31	4	10	8	41
	Midland	25	23	4	7	8	33
	Central CH	36	34	4	10	10	44
	Ticino	15	14	3	5	7	23
	Lake Geneva	7	08	3	5	5	14
Other betalactams (15 100/2972)	CH total[d]	24	23	5	7	9	34
	NW CH	32	29	6	6	10	40
	East CH	32	31	7	11	7	45
	Zurich	42	38	6	9	10	50
	Midland	23	21	5	7	10	33
	Central CH	41	41	6	11	12	54
	Ticino	20	19	5	6	8	29
	Lake Geneva	06	7	5	5	6	16
Doxycycline (8041/2347)	CH total[d]	21	22	01	11	6	31
	NW CH	23	24	2	7	7	30
	East CH	23	23	1	12	7	34
	Zurich	32	32	1	14	6	42
	Midland	17	17	1	12	6	28
	Central CH	22	23	1	12	6	32
	Ticino	12	12	0	7	6	18
	Lake Geneva	6	8	1	6	9	14
Fluoroquinolones (76 423/5363)	CH total[d]	24	24	1	41	5	57
	NW CH	26	26	1	41	6	58
	East CH	27	29	0	46	5	64
	Zurich	30	29	01	45	6	63
	Midland	23	22	0	43	4	57
	Central CH	31	31	1	40	7	61
	Ticino	18	18	0	32	6	45
	Lake Geneva	9	12	0	33	4	40
Macrolides (40 230/4802)	CH total[d]	34	31	4	4	13	40
	NW CH	41	37	5	4	14	46
	East CH	41	38	4	4	13	47
	Zurich	48	43	5	5	15	52
	Midland	30	26	4	3	12	36
	Central CH	47	42	5	5	15	53
	Ticino	20	15	3	2	08	25
	Lake Geneva	7	8	3	2	09	14
Trimethoprim-sulfamethoxazole (12 295/3187)	CH total[d]	15	17	1	43	3	52
	NW CH	12	15	1	43	3	50
	East CH	16	19	0	45	3	56
	Zurich	20	22	1	43	4	56
	Midland	12	16	1	49	2	56
	Central CH	21	23	0	45	4	60
	Ticino	9	15	0	36	2	44
	Lake Geneva	5	7	1	28	3	32

NW, northwest; CH, Switzerland.
[a]Tested for *Streptococci* group A either by antigen test or by culture.
[b]Urine analysis and culture.
[c]Any type of radiograph.
[d]Not standardized for age and gender.
[e]Performed in a time window of 7 days prior to 2 days following an issued prescription.

that allow for comparison of our data with other countries [9]. We restricted our analysis to adults in order to avoid bias, because DDDs do not take into account different doses for children.

We could show an important and statistically significant reduction in the range of 21% to 37% for prescriptions of the five most frequently used classes of antibiotics with the use of any point of care test. Although these findings are important and interesting from the public health perspective, they have to be interpreted with caution. No causal association can be drawn from our ecological study. Our findings could be confounded by other factors related to physicians or patients we were unable to measure. Physicians who use more tests may reassure patients and themselves that antibiotics are not needed. In a primary care study on patients' expectations for antibiotics in respiratory tract infections, reassurance was more strongly related to patient satisfaction than actually receiving an antibiotic prescription [18]. Thus, the association of lower antibiotic prescription rates with the use of point of care tests could simply reflect testing patients with low probability of bacterial infection. As we lack data on the type and the severity of infections, we

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TABLE 2. Ratio of the number of antibiotic prescriptions and number of patients of primary care physicians for antibiotic compounds according to point of care tests and patient characteristics

	Amoxicillin and amoxicillin-clavulanate	Fluoroquinolones	Macrolides	Other betalactams	Trimethoprim-sulfamethoxazole	Doxycycline
	Coefficients (95% CI)[a] [*P*-value]					
Any radiograph[b]	1.03 (0.91, 1.18) [0.604]	1.01 (0.90, 1.12) [0.926]	0.91 (0.81, 1.01) [0.087]	0.81 (0.65, 1) [0.046]	0.71 (0.45, 1.12) [0.142]	0.95 (0.63, 1.45) [0.822]
Any POCT[c]	0.79 (0.74, 0.84) [<0.001]	0.68 (0.65, 0.72) [<0.001]	0.76 (0.72, 0.81) [<0.001]	0.63 (0.56, 0.71) [<0.001]	0.68 (0.6, 0.77) [<0.001]	0.91 (0.73, 1.13) [0.387]
Female patients	0.77 (0.74, 0.79) [<0.001]	1.02 (1.00, 1.05) [0.105]	0.85 (0.82, 0.89) [<0.001]	0.79 (0.73, 0.85) [<0.001]	0.76 (0.68, 0.84) [<0.001]	0.77 (0.68, 0.87) [<0.001]
Age group[d]	1.30 (1.26, 1.35) [<0.001]	1.60 (1.56, 1.64) [<0.001]	1.11 (1.06, 1.16) [<0.001]	1.26 (1.17, 1.36) [<0.001]	1.47 (1.35, 1.60) [<0.001]	1.18 (1.03, 1.34) [0.014]
Adjusted R^2	0.110	0.188	0.046	0.113	0.159	0.039

[a]Back-transformed coefficients with confidence intervals (CI) for antibiotic prescriptions: coefficients >1 indicate more and coefficients <1 less prescriptions.
Regression model: $\log(Y_i) \sim \beta_0 + \beta_1 \times \text{AnyXRay}_i + \beta_2 \times \text{AnyPoct}_i + \beta_3 \times \text{gender}_i + \beta_4 \times \text{age}_i + \epsilon_i$, where: Y_i, number of prescriptions/number of patients; i, antibiotic group, physician and patient group; AnyPoct_i, number POCT_i/number of antibiotic prescriptions_i $0 \le \text{Any POCT} \le 1$; gender_i, [male, female].
[b]Any radiograph_i, number of radiographs (including all $\text{radiographs})_i$/number of antibiotic prescriptions_i, $0 \le \text{Any radiograph} \le 1$.
[c]POCT, point of care test.
[d]Age_i [18–64, 65+].

cannot rule out such bias. Because health insurers in Switzerland reimburse physicians for office-based laboratory tests, there exists an economic incentive to use such tests. Issues of liability due to complications may be another reason for laboratory testing or patients may request testing to exclude a serious infection. Patient pressure has been reported as an important factor in patient referral and additional clinical investigations, even when general practitioners judge the need for such activities as not high [19].

Previous observational studies from Scandinavia have shown a reduction in antibiotic prescriptions with the use of CRP in primary care [20,21]. Whether a diagnostic test leads to fewer antibiotic prescriptions without compromising patient outcome is ideally best addressed in a clinical trial evaluating two or more diagnostic strategies and their clinical consequences for patient-relevant outcomes [22]. Trials conducted in primary care and in emergency departments found no reduction of antibiotic prescriptions for respiratory tract infections with CRP testing [23–25], whereas one trial using a more complex intervention with general practitioner training and use of CRP tests did show a reduction of antibiotic prescription in patients with acute bronchitis [7].

Our study has several limitations. The population served by the Helsana Group was slightly older and generated higher costs than the average Swiss population. Therefore, antibiotic consumption eventually may be higher in this population than in the remaining Swiss population. In some areas with self-dispensing physicians, patients with high deductibles may not send the invoice to the health insurer but rather pay them directly. From previous unpublished studies, we estimate that 2–3% of all invoices are directly paid and not reimbursed by the Helsana Group [26]. Social health insurers do not get full and accurate information regarding the exact diagnosis from the physician-patient encounter. Therefore, we were unable to link antibiotic prescriptions and the use of point of care tests to a particular diagnosis. Data from a Swedish surveillance study indicate that CRP in primary care is overwhelmingly used in respiratory tract infections [27]. In addition, our study lacks detail regarding important characteristics of the study population that goes beyond crude estimates of age and gender distributions.

In conclusion, this study shows that the regions of the northwest and east of Switzerland have one of the lowest antibiotic prescription rates in ambulatory care in Europe. Swiss regions with higher prescription rates show higher seasonal variability in antibiotic use. The use of any point of care test was associated with an important reduction in the prescription of the most frequently used antibiotics. Our findings need confirmation from other countries and indicate that more research for new point of care tests and better integration of already existing point of care tests into primary care may be a promising strategy to reduce antibiotic consumption and thereby the emergence of antibiotic resistance in the community.

Transparency Declaration

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author had full access to all data in the study and had the final responsibility for the decision to submit the manuscript.

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