

Appropriateness of antimicrobial prescribing in a Swiss tertiary care hospital: a repeated point prevalence survey

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Summary

AIMS OF THE STUDY: Inappropriate use of antimicrobials is associated with the emergence of antimicrobial resistance and adverse events. Antimicrobial stewardship programmes may both optimise treatment of infections and reduce antimicrobial resistance but are implemented in only a minority of Swiss hospitals. In addition, data on prescribing patterns and quality are scarce. We conducted a repeated point prevalence survey to evaluate the quality of antimicrobial prescribing in a single tertiary care centre.

METHODS: Antimicrobial use was audited twice (summer 2017 and winter 2018) among all patients admitted to the University Hospital Basel, Switzerland. Data were collected from the electronic health record. Appropriateness of antimicrobial use was evaluated according to previously published rules and local national guidelines.

RESULTS: We evaluated 1112 patients of whom 378 (34%) received 548 prescriptions in total (30% for prophylaxis). Penicillins with β -lactamase inhibitors were most commonly used (30%), followed by cotrimoxazole (12%) and ceftriaxone (7%). Intravenous administration was chosen in 56% of patients. Prior to antimicrobial therapy, blood cultures were collected in 69% of patients. Overall, 182 (33%) prescriptions were not appropriate; reasons included lack of indication (11%), incorrect dosing (7%), delay in intravenous to oral switch (9%) or non-adherence to local guidelines (15%). A minority of patients received antimicrobials despite documented allergies (2%). Almost 38% of empirical prescriptions were inappropriate, compared with only 19% of prophylactic and 20% of targeted prescriptions. Penicillins with β -lactamase inhibitors and cephalosporins were most commonly involved in inappropriate prescribing (>50%) followed by carbapenems (30%), narrow-spectrum penicillins (17%) and cotrimoxazole (6%), with oral administration being involved less frequently than intravenous administration (15 vs 37%). Infectious diseases consultation and presence of immunosuppression were associated with reduced odds (odds ratio

[OR] 0.38, 95% confidence interval [CI] 0.21–0.70 and OR 0.31, 95% CI 0.17–0.54, respectively) of inappropriate prescription in the per-patient multivariable analysis, whereas being admitted to a surgical or intensive care unit was associated with increased odds (OR 1.83 and 5.67) compared with a medical unit.

CONCLUSION: Almost one third of prescriptions were inappropriate in our tertiary care centre despite local guidelines and an on-demand infectious diseases consultation service. Our results underscore the need for expanding current antimicrobial stewardship efforts, including national initiatives such as stewardship and prescribing guidelines, repeated surveys and identification of areas for improvement including timely intravenous to oral switches in order to reduce the consequences of inappropriate prescribing and of multidrug resistant organisms.

Keywords: antimicrobial stewardship, point prevalence survey, Switzerland, antimicrobial agents, appropriateness of antimicrobial therapy

Background

Antimicrobial resistance (AMR) of microorganisms, in particular of gram-negative bacteria, is a growing global concern. It is associated with prolonged in-hospital stays, higher treatment costs, and increased morbidity and mortality [1–3]. The four key drivers of increasing resistance, persistence and spread of resistant microorganisms are: (i) the development of adaptive resistance mechanisms owing to the high selection pressure due to the indiscriminate use of antimicrobial agents; (ii) insufficient stewardship of broad-spectrum agents, propagating the cycle of increasing resistance; (iii) a lack of professional hospital infection control services; and (iv) increasing numbers of patients with severe immunosuppression related to chemo- or immunotherapies, who require frequent and prolonged antibiotic treatments [4]. Misuse and overuse of antibiotics have been recognised as major challenge to overcome [4]. As a result of the shortfall of new effective antimicrobials in development and the clinical challenges of AMR, it is

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Author contributions
MO designed the study. CG and AE collected all data. CG, AE and NG performed the statistical analysis. CG, AE, SB and MO assessed the appropriateness. CG and MO drafted the manuscript, which was further edited by NG, SB, ST, AE and MO. All authors were involved in the interpretation of data, critical revision of the manuscript for important intellectual content, and read and approved the final manuscript.

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necessary to curb inappropriate antibiotic use. Therefore, the World Health Organization (WHO) has called for coordinated action including antimicrobial stewardship programmes (ASPs) [5]. In Switzerland, a comprehensive antimicrobial resistance strategy (StAR) was launched in 2016; this defines the appropriate use of antibiotics as one of eight strategic objectives toward achieving the long-term efficacy of antibiotics [6].

Data collected by the Swiss Centre for Antibiotic Resistance (Anresis) since 2014 suggest low rates of AMR in Switzerland compared with many other European nations [7]. Nevertheless, a continuous trend towards increased resistance rates of commonly used antimicrobials can also be observed in Switzerland. For example, resistance rates of *Escherichia coli* to fluoroquinolones and 3rd/4th generation cephalosporins have more than doubled since 2004 [8]. This increase may be at least partly related to antimicrobial overtreatment and inappropriate prescribing in Swiss hospitals and in the outpatient setting [9].

Previous assessments of the quality of antimicrobial prescribing in Switzerland, performed more than a decade ago, suggest that at least one third of empirical/targeted and one eighth of prophylactic prescriptions were not appropriate [10–12]. Despite such shortcomings and the numerous proven advantages of ASPs, the majority of Swiss hospitals lack a formal ASP, and a national ASP guideline or surveillance programme assessing the quality of antimicrobial prescribing has not been introduced so far [11, 13].

The aim of this study was to provide current estimates of antimicrobial prescribing appropriateness by evaluating the overall quality of antimicrobial prescriptions at a Swiss tertiary care hospital. Furthermore, we sought to identify risk factors associated with inappropriate prescribing to inform future ASP interventions.

Methods

We conducted a repeated point prevalence survey at the University Hospital Basel, an adult tertiary care hospital in Switzerland with approximately 750 beds, three intensive care units and bone-marrow and renal transplantation units. The proportion of antimicrobial-resistant bacteria is low: for example, 2.7% of *Staphylococcus aureus* isolates are methicillin-resistant [14]. However, the proportion of extended-spectrum β -lactamase producing gram-negative bacteria is increasing (10.5% of *E. coli* in 2017). The prescription of antimicrobials is not under any restriction, except for rarely used drugs, such as colistin, ticoplanin, tigecycline, ceftaroline, ceftazidime-avibactam, ceftolozane-tazobactam, linezolid and amphotericin B, which are available only upon request from the hospital pharmacy and after consultation with the infectious diseases service. There is a well-established infectious diseases service, which may be accessed 7 days a week and provides consultations on request. In addition, all positive blood cultures are evaluated daily by the infectious diseases team. Comprehensive institutional infectious diseases guidelines have been developed by the infectious diseases department in collaboration with microbiologists and other specialists and are accessible online for all hospital staff. The contents of these institutional guidelines have been integrated into the Sanford Guide and thus access to this international resource is also provided at our institu-

tion [15]. These guidelines are updated at least annually and include recommendations regarding the diagnosis and treatment of various infections, empirical, prophylactic or targeted treatment, dose and dose adjustments, a validated checklist of criteria for switching antibiotic treatment from intravenous to oral and counselling in the case of allergies against antimicrobials [16]. Updated local resistance data are published annually by the microbiology laboratory and also integrated into the institutional guidelines.

This study was approved by the Ethics Committee of Northwest and Central Switzerland (EKNZ Req-2017-00236) with a waiver of informed consent.

This point prevalence study was performed at two time-points, in July 2017 and January 2018 and included all inpatients who were hospitalised on a given ward at 9:00 a.m. on the day of the survey. In a first step, all patients admitted to the ward at 9:00 a.m. were audited for receipt of at least one antimicrobial agent (antibiotic, antifungal or antiviral) on the day of the evaluation. We excluded all outpatients, patients in the emergency department and all patients receiving preoperative surgical antimicrobial prophylaxis only, whereas patients receiving postoperative surgical prophylaxis or antibiotic prophylaxis because of prolonged neutropenia or corticosteroid therapy were included. In addition, erythromycin treatment was not counted as an antimicrobial treatment, as it is exclusively used as a prokinetic agent in our facility [17]. All data were collected from the hospital's electronic health record.

The appropriateness of every prescription was assessed separately by an infectious diseases physician and an internal medicine fellow with the support of a medical student. Discrepant judgements were resolved by involving a second infectious diseases physician (40 cases, 10.6%). Their assessment was based upon the local epidemiology, presence of comorbidities, allergies, microbiological results and the local guidelines, and if local guidelines were lacking, upon national and international guidelines [15, 18].

Appropriateness was judged according to the following rules and according to previous publications (examples can be found in supplementary table S1 in appendix 1) [10, 11, 16, 19, 20].

The agent was indicated if there were recorded signs of infection or a serious risk of infection related to, e.g. immunosuppression or indicated for the prophylaxis of an infection. Suspected indications had to be clearly documented.

The spectrum of the used agent covered at least 90% of the most likely pathogens, on consideration of local resistance rate and travel history (empirical prescription) or the cultured pathogen (targeted therapy).

The recommended dose, frequency and duration were listed in the local or national guidelines, and were adapted to the patient's kidney function or weight, if applicable.

Allergy mismatch was not present if the patient did not receive an antimicrobial agent that was associated either with a previous allergic reaction and not simply an intolerance or with a relevant risk of cross-reactivity following a documented type 1 hypersensitivity reaction.

Previously in-house validated criteria for intravenous to oral switch were used, including: receipt of intravenous

treatment for more than 24 hours; core (tympanic) temperature below 38°C; signs of clinical improvement; the absence of an undrained abscess, endocarditis or an intravascular/bone/joint infection; a neutrophil count of more than 500 per microlitre; a continuous and uncompromised oral route; and an available oral formulation of the antimicrobial agent [21].

The treatment was according to the local guidelines if there were guidelines available for the specific situation and if the dose, frequency and duration of the antimicrobial agent were as listed in those guidelines (taking into account the renal function of the patient).

The requirement for adaptation of antimicrobial treatment was judged within 48 hours after a relevant positive microbiological test result was available.

Routine therapeutic drug monitoring was advised for the following drugs: voriconazole, posaconazole, gentamicin and amikacin (if used for more than 3 days), tobramycin and vancomycin.

The treatment was judged as appropriate if it fulfilled all the above requirements, and otherwise as inappropriate or indeterminate if data were missing or insufficient to judge the appropriateness.

Immunosuppression was defined as a daily dose of more than 5 mg prednisone or equivalent, treatment with classical immunosuppressive drugs or monoclonal antibodies, a neutrophil count less than 500 per microlitre, human immunodeficiency virus infection CDC category C, and liver cirrhosis. The Charlson Comorbidity Index was used to estimate comorbidities at the time of the survey [22].

All continuous variables were compared using the Mann-Whitney-U test, with median and interquartile ranges (IQR), or the Student's t-test, with mean and standard deviation (SD), where appropriate. We used the chi-square and Fisher's exact tests for comparisons of categorical variables where appropriate. Multivariable logistic regression models including potentially confounding variables were performed to analyse associations between patient variables with the appropriateness of antimicrobial prescribing. Variable selection was based on biological plausibility and/or demonstrated associations from the literature, such as infectious diseases consultation [23]. The results were considered statistically significant if the two-sided p-value was less than 0.05. SPSS 22 software (SPSS; IBM; Chicago, IL) was used for all analyses.

Results

Patient characteristics

Overall, 1112 patients on 28 wards were hospitalised during the two survey periods, and 378 (34%) patients re-

ceived 548 antimicrobial prescriptions. Baseline characteristics are presented in table 1.

In a group excluding patients receiving only prophylactic treatment, blood cultures were collected in 214 patients (68.6%) before antimicrobial treatment was initiated. Other microbiological samples including urine, stool and sputum cultures were collected in 271 of these patients (86.9%) prior to treatment. In 51.9% of patients, a bacterial pathogen was isolated, including species potentially associated with contamination. An infectious diseases consultation had been requested in 113 patients (36.2%) within the previous 4 weeks.

Among the 548 prescriptions, the most commonly used antimicrobial agents were amoxicillin/clavulanic acid (17.9%) followed by piperacillin/tazobactam (12%), cotrimoxazole (11.5%) and ceftriaxone (7%) (table 2).

Parenteral administration was chosen for 307 patients (56%). The purpose of antimicrobial administration was almost equally distributed between empirical (206 prescriptions, 37.8%), targeted (169 prescriptions, 30.8%) and prophylactic treatments (166 prescriptions, 30.3%).

The most common indication for treatment was antimicrobial prophylaxis (166 prescriptions, 30.3%) followed by respiratory tract infection (104 prescriptions, 19%), genitourinary tract infection (46 prescriptions, 8.4%) and bone and joint infection (45 prescriptions, 8.2%).

Appropriateness of antimicrobial prescribing

One hundred and eighty-two (33.2%) prescriptions were judged to be not appropriate, with the remaining prescriptions judged to be appropriate (66.7%) or indeterminate

Table 1: Patient characteristics (n = 378).

Characteristic	Value	
Male, n (%)	207 (54.8)	
Age in years, mean (SD)	70.0 (17.6)	
Weight in kg, mean (SD)*	72.2 (18.4)	
Immunosuppression, n (%)*	111 (29.4)	
Charlson Score, median (IQR)	2 (1–4)	
eGFR in ml/min/1.73m ² , median (IQR) ^{†‡}	81.0 (57–101)	
Treating unit	Medicine, n (%)	170 (45.0)
	Surgery, n (%)	140 (37.0)
	Intensive care, n (%) [§]	37 (9.8)
	Other, n (%)	31 (8.2)
Allergy	Antibiotic allergy, n (%) ^{¶‡}	56 (14.8)
	Antibiotic intolerance, n (%)	3 (0.8)
	Penicillin allergy, n (%)	39 (10.3)

eGFR = estimated glomerular filtration rate; IQR = interquartile range; SD = standard deviation * See methods section for definition; † according to CKD-EPI; ‡ missing data: weight (n = 70), eGFR (n = 4), allergy (not documented in n = 21); § surgical and medical; ¶ allergic reaction type 1 and 4; || other reactions

Table 2: Distribution of the 10 most frequently used antimicrobial prescriptions (n = 411 out of 548) according to the ward.

Ward n (%) [*]	Co-Am	Pip-Taz	Ceftx	Carb	TMP-SMX	Clin	Van	Quin	Val	Flu
Medicine	24 (7.8)	33 (10.8)	16 (5.2)	9 (3.0)	59 (19.3)	1 (0.3)	5 (1.6)	22 (7.3)	40 (13.1)	24 (7.8)
Surgery	58 (36.5)	20 (12.6)	12 (7.5)	8 (5.1)	2 (1.3)	9 (5.7)	6 (3.8)	7 (4.4)	0	0
ICU	7 (14.3)	8 (16.3)	3 (6.1)	5 (10.2)	0	1 (2.0)	0	1 (2.0)	0	2 (4.1)

Co-Am = amoxicillin/clavulanic acid; Pip-Taz = piperacillin/tazobactam; Ceftx = ceftriaxone; Carb = carbapenems; TMP-SMX = trimethoprim/sulfamethoxazole; Clin = clindamycin; Van = vancomycin; Quin = fluoroquinolones; Val = valaciclovir; Flu = fluconazole; ICU = intensive care-unit * Number of prescriptions and percentage (in relation to all antimicrobial prescriptions used in patients of these wards)

(0.7%) (table 3). Of note, an opportunity to optimise the prescription was found in more than one domain in the majority of inappropriate prescriptions (106 [19.3%] compared with 76 [13.9%] prescriptions judged as inappropriate in only one domain). This equals 36.8% of patients receiving at least one inappropriate prescription. The most common reasons for an inappropriate prescription were a lack of indication (10.8%), intravenous administration despite fulfilling the requirements for a switch to oral antibiotics (9.3%) and non-adherence to guidelines (15.1%), with similar percentages in the per patient analysis (table 3). Eight patients (2.1%) received an antimicrobial agent despite a documented allergy. The indication for antimicrobial treatment was not documented in the patients' notes for 26 prescriptions (4.7% of all prescriptions).

In univariable (per patient) analyses, the following factors were associated with receiving an inappropriate prescription: female gender (odds ratio [OR] 1.59, 95% confidence interval [CI] 1.05–2.43; $p = 0.03$), advanced age (OR per year increase 1.02, 95% CI 1.00–1.03; $p = 0.008$) and being admitted to a surgical rather than a medical unit (OR 2.08, 95% CI 1.32–3.30; $p = 0.002$). Conversely, the odds of receiving an inappropriate prescription were lower when blood cultures had been collected prior to therapy (OR 0.59, 95% CI 0.38–0.91; $p = 0.02$), in patients on immunosuppressive therapy (OR 0.3, 95% CI 0.18–0.50; $p < 0.0001$) and after infectious diseases consultation (OR 0.31, 95% CI 0.10–0.51; $p < 0.0001$). Figure 1 displays the percentages of inappropriate prescriptions according to the above-mentioned factors.

In a multivariable (per patient) analysis, the presence of immunosuppression and an infectious diseases consultation remained independently associated with a reduced odds ratio for receiving an inappropriate prescription (OR 0.38, 95% CI 0.21–0.70; $p = 0.002$ and OR 0.31, 95% CI 0.17–0.54; $p < 0.001$, respectively). Being admitted to either a surgical ward (OR 1.83, 95% CI 1.08–3.12; $p = 0.01$) or an intensive care unit (OR 5.67, 95% CI 1.71–18.81; $p = 0.01$) was associated with an increased odds ratio for inappropriate prescription when compared with a medical ward (table S2 in appendix 1).

Inappropriate prescribing was more commonly detected in parenteral (compared with oral, 36.9 vs 14.6%, $p < 0.0001$) and empirical (compared with targeted or prophylactic, 37.6 vs 20.1 vs 18.7%, $p < 0.0001$) treatment (per prescription analysis). Inappropriateness according to the reason for prescription ranged from 19.9% for prophylaxis to

31.1% for bone and joint infection, and from 41.3% for respiratory infection to 50.0% for genitourinary tract infections (table S3)

In total, 33 (19.9%) of all prophylactic prescriptions violated one or more appropriateness criteria, of which 40% concerned extended postoperative surgical prophylaxis (14/33 inappropriate prescriptions). Indeed, the vast majority of prescriptions for surgical prophylaxis was deemed as an inappropriate continuation of perioperative prophylaxis (73.7% of all postoperative/postinterventional surgical prophylaxis prescriptions).

Of the 148 prophylactic prescriptions other than for prevention of surgical site infections, the following reasons for inappropriateness were determined: 8 (5.4%) non-adherence to guidelines, 7 (4.7%) lacking indication and 5 (3.4%) inappropriate duration.

The appropriateness of antimicrobial treatment varied between the different agents from as high as 93.7% for cotrimoxazole, which is mainly used for targeted or prophylactic therapy, to as low as 48% for amoxicillin/clavulanic acid. (table 4) For the latter, inappropriateness was distributed across several quality indicators such as a lack of an evidence-based indication ($n = 28$, 28.6%), an inappropri-

Figure 1: Inappropriateness of antimicrobial prescriptions according to the presence or absence of patient characteristics ($n = 378$; female vs male sex; immunosuppression) and prescribing characteristics ($n = 548$; parenteral vs oral and empirical vs targeted/prophylactic treatment; prophylaxis vs other indications for antimicrobials) or procedures ($n = 378$; infectious diseases (ID) consultation or blood culture sampling prior to antimicrobial treatment).

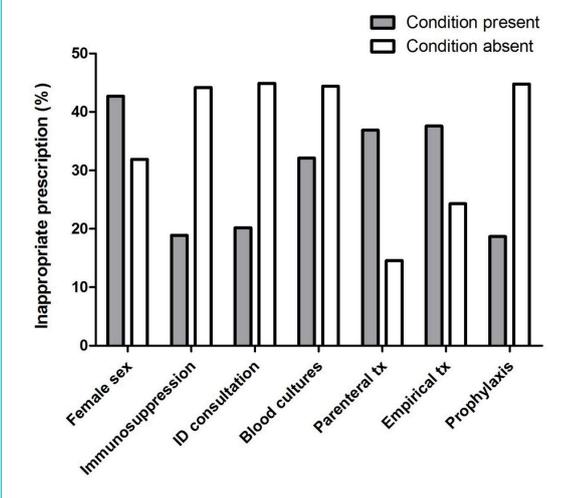


Table 3: Assessment of inappropriateness per prescription and per patient.

Variable (n, %)	Per prescription*	Per patient†
At least one assessment not appropriate	182 (33.1)	139 (36.8)
Inappropriate indication	59 (10.8)	58 (15.3)
Inappropriate spectrum‡	38 (6.9)	35 (9.3)
Inappropriate dose	36 (6.6)	36 (9.5)
Inappropriate frequency of administration	17 (3.1)	17 (4.5)
Inappropriate duration	30 (5.5)	30 (7.9)
Allergy mismatch§	11 (2.0)	8 (2.1)
Not according to guidelines	83 (15.1)	79 (20.9)
Intravenous to oral switch possible¶	51 (9.3)	47 (12.4)
Switch to targeted therapy possible¶	38 (6.9)	23 (6.1)

* For a total of 548 prescriptions; † for a total of 378 patients; ‡ spectrum was assessed as too broad in the majority (82%); § 11 antimicrobials in 8 patients were prescribed although a relevant allergic reaction to this antimicrobial was documented in the notes; ¶ possible, but not yet performed at the time of the survey

ate dose and duration of treatment (21.4 and 18.4%, respectively), noncompliance with the local guidelines and a delayed intravenous to oral switch (29.6 and 18.4%, respectively).

Similar reasons for inappropriateness were identified for ceftriaxone, whereas treatment with piperacillin/tazobactam was mainly judged as inappropriate because a narrow-spectrum alternative would have been sufficient in several instances (n = 17, 26.2%).

Discussion

In this point prevalence study performed at two different time-points in a tertiary care hospital without a formal ASP, we evaluated 1112 patients of whom 378 received at least one antimicrobial agent. A significant number of patients received inappropriate antimicrobial treatments (36.8%), mainly due to non-adherence to guidelines (20.9%), lack of requirement for antimicrobial therapy (15.3%) and a missed opportunity or a delay in the switch from intravenous to oral administration (12.4%). This is in line with previous surveys from the same and other Swiss university hospitals and is of concern as it implies that no progress has been made in Switzerland during the last decade in an area regarded as crucial in the fight against AMR [10, 11].

The fact that antimicrobials were prescribed without indication in a similar fashion is concerning (17.5% in Cuisini et al. and 10.8% in the present survey) [10]. With respect to noncompliance with guidelines, our findings reveal an even higher proportion (15.1%) compared with Cuisini et al. (8%), which may be related to the more detailed guidelines in our institution [10].

Additional areas of concern identified in the present study include the high rate of inappropriately extended postoperative surgical prophylaxis (accounting for 42% of inappropriate prophylactic prescriptions) and a lack of or delay in switching from intravenous to oral administration (9.3% of all prescriptions). Continuation of prophylactic antibiotic treatment postoperatively on surgical wards is of major concern, as no benefit has been demonstrated in previous studies [24–28]. The recommendation to avoid such therapies has been incorporated in the choosing wisely list of the Society for Healthcare Epidemiology of America [29]. In total, 19.9% of prophylactic prescriptions were judged as inappropriate, which is in line with previous observations from Swiss hospitals [13–15].

An early switch from intravenous to oral administration has been advocated for a long time and decision support tools are effective in shortening intravenous therapies without a negative impact on morbidity or mortality [21, 30]. In our institution, a simple algorithm led to a 19% reduction in the number of days on intravenous antibiotics with no increase in the number of complications [21]. Such algorithms need to be reinforced. The introduction of electronic decision support systems in electronic health records might facilitate compliance with these algorithms.

Interestingly, appropriateness rates were among the highest on wards caring primarily for immunosuppressed patients. This may be explained by the fact that these patients often receive prophylactic treatment, which is clearly defined in the guidelines. Furthermore, prescribing physicians are probably more experienced in managing infectious complications and therefore in the appropriate use of antimicrobial treatments, and infectious diseases physicians are often involved in these patients.

The international literature reports a wide range of appropriateness of antimicrobial therapies (41–91%) [31–34]. Inappropriateness of antimicrobial treatment poses a risk for the perpetuation of AMR and based on the threat of AMR, our study adds to the growing body of evidence underscoring the need to implement national point prevalence surveys and ASPs [35]. In Switzerland, the use of antimicrobial agents is assessed only by measuring quantitative pharmacy data on a ward, hospital or national level, i.e. defined daily doses (DDDs) [7]. However, there are many drawbacks when relying on DDDs to judge the use of antimicrobial agents. In particular, assessment of DDDs only informs about the quantity of antimicrobial used, and does not indicate if the treatment was appropriate. Ideally, quantitative data should be supplemented with comprehensive qualitative data from regular point prevalence surveys. This is already standard-of-care in several countries [16, 34, 36]. Our data call for future audits, which should be performed regularly throughout the country in a standardised fashion.

The introduction of ASPs has been associated with a significant reduction in inappropriate antimicrobial prescriptions, a reduction in treatment failures and complications arising from antibiotic therapy, and a decrease in overall antibiotics use and healthcare costs [37, 38]. These programmes include actions such as a requirement for pre-authorisation for certain antimicrobial agents, and/or regular

Table 4: Assessment of appropriateness according to the prescribed antimicrobial treatment (n = 548). Data are shown in detail only for the most frequently used agents.

Assessment n (%)	Co-Am	Pip-Taz	Ceftx	Carb	Nar	TMP-SMX	Quin	Other
Inappropriate indication	28 (28.6)	5 (7.6)	6 (15.0)	0	0	0	4 (12.9)	16 (7.7)
Inappropriate spectrum*	7 (7.2)	17 (26.2)	5 (12.5)	1 (4.3)	0	0	5 (16.1)	3 (1.5)
Inappropriate dose†	21 (21.4)	0	1 (2.5)	3 (13.0)	1 (5.6)	0	1 (3.2)	9 (4.3)
Inappropriate frequency of administration	2 (2.0)	2 (3.1)	0	1 (4.3)	0	1 (1.6)	0	11 (5.3)
Inappropriate duration	18 (18.4)	0	1 (2.5)	1 (4.3)	0	0	0	10 (4.8)
Allergy mismatch	3 (3.1)	2 (3.1)	2 (5.0)	0	1 (5.6)	2 (3.2)	0	1 (0.5)
Not according to guidelines	29 (29.6)	18 (27.7)	5 (12.5)	2 (8.7)	0	0	7 (22.6)	22 (10.5)
Intravenous to oral switch possible	18 (18.4)	12 (18.5)	8 (20.0)	3 (13.0)	0	1 (1.6)	1 (3.2)	8 (3.8)
Switch to targeted therapy possible	6 (6.1)	9 (13.8)	6 (15.0)	3 (13.0)	1 (5.6)	0	4 (12.9)	8 (3.8)
At least one assessment not appropriate	55 (56.1)	31 (47)	19 (47.5)	7 (30.4)	3 (16.8)	4 (6.4)	13 (41.9)	49 (23.4)

Co-Am = amoxicillin/clavulanic acid; Pip-Taz = piperacillin/tazobactam; Ceftx = ceftriaxone; Carb = carbapenems; Nar = narrow-spectrum β -lactams; TMP-SMX = trimethoprim/sulfamethoxazole; Quin = fluoroquinolones; * Spectrum mostly too broad; † dose mostly too low

review of prescriptions and immediate feedback to prescribing physicians.

Despite Switzerland being in favour of a national ASP strategy, comprehensive ASPs are present in only a minority of Swiss hospitals [13]. Although ASPs require a significant investment they may become cost-effective by reducing the financial burden caused by the treatment of multidrug resistant infections and their poor outcomes [39].

Furthermore, reducing inappropriate prescribing may reduce the incidence of *Clostridioides difficile* infections [40]. The risk of *C. difficile* infection is increased not only by unnecessary antimicrobial treatment, but also by the unnecessary use of broad-spectrum antibiotics, which have a greater risk of subsequent *C. difficile* infection, when instead an antimicrobial with a better risk profile could have been used [41, 42].

Our data suggest that direct feedback from trained infectious diseases physicians may optimise appropriateness of therapies. In the present work, consultation with an infectious diseases physician during the previous 4 weeks was associated with an increased proportion of appropriate therapies: 79.8% compared with 55.1% in patients without a consultation. Recent data support our findings: infectious diseases consultation was associated with an increase in the quality of antimicrobial prescription; their impact, however, depends on the level of expertise and experience [23]. On the other hand, infectious diseases consultation is only possible in a minority of patients receiving antimicrobial treatment, and hence additional measures are required including the establishment of antimicrobial stewardship teams. Last but not least, a key aspect of improving antimicrobial prescribing is to empower and assist prescribers to optimise antimicrobial treatment by continuous education and, even more importantly, by using decision support tools such as widely available, clear and easy-to-use-guidelines [36, 43, 44]. In contrast to a comprehensive ASP, this may be a potentially low-cost but very effective stewardship intervention.

Limitations of the present study include the reliance on chart review instead of clinical examination and/or consultation with the treating team. However, chart review is usually sufficient for the assessment of many aspects of the appropriateness of antimicrobial prescriptions. We tried to minimise this bias by also evaluating the written notes of nurses and doctors on the day of evaluation, but it was not feasible to contact prescribers during this study. Still, over- and underestimation of appropriateness may have been possible; for example, the incidence of allergy mismatch may have been overestimated, as the true nature of the allergic reaction was often not documented in the notes, and as a true penicillin allergy can be confirmed in only 20% of those reporting a penicillin allergy [45]. The duration of prescription was assessed only on the day of evaluation, which means that treatments that were stopped too early or treatments that were continued for too long after our assessment could not be evaluated for the present analysis. Further, assessment of appropriateness was conducted by internal medicine and infectious diseases physicians according to their expert opinion, without the use of any standardised assessment tool or algorithm. Importantly, there is no consensus on how to evaluate appro-

priateness of antimicrobial therapy and many methods are currently used, most of which rely on expert opinions as in the present study. Spivak et al. analysed multiple approaches and concluded that there is a lack of a standardised approach to the evaluation of appropriate therapy [19]. Sikkens et al. highlighted the shortcomings of relying only on expert opinions, as in their study agreement was reached in only 80% of cases when appropriateness of antimicrobial treatment was evaluated by a large group of experts (infectious diseases physicians, microbiologists, resident physicians) [46]. Ideally, a nationally standardised survey form should be developed for future point prevalence surveys assessing appropriateness of antimicrobial prescribing in Swiss hospitals.

Conclusion

In conclusion, the proportion of inappropriate antimicrobial prescriptions was significant at a Swiss tertiary care centre, which may contribute to or at least perpetuate increasing AMR. Our results underscore the need for expanding current antimicrobial stewardship efforts, including the empowerment of frontline physicians and identification of areas for improvement including timely intravenous to oral switches. National initiatives including widely available and easy-to-use antimicrobial stewardship guidelines or national prescribing surveys could impact on those rates, as well as on the costs for the treatment of adverse effects as a consequence of inappropriate prescription and of multidrug resistant organisms.

The results of this work have been displayed in part as a poster at the Joint annually meeting 2018 of the Swiss Society for Infectious Diseases, 13–14 September in Interlaken (P86).

Access to data

The data used and analysed in this work are available from the corresponding author on reasonable request.

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Potential competing interests

The authors declare that they have no competing interests.

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Appendix 1

Supplementary tables

Table S1: Examples of assessment of the appropriateness of antimicrobial treatment.

Table S2: Univariate and multivariate variables analysed per patient (n = 378).

Table S3: Assessment of appropriateness per prescription (n = 548) according to the indication/infection.

The appendix is available as a separate file for downloading at <https://smw.ch/en/article/doi/smw.2019.20135/>