Active surveillance of antibiotic resistance prevalence in urinary tract and skin infections in the outpatient setting

A. Kronenberg, S. Koenig, S. Droz and K. Mühlemann

Institute for Infectious Diseases, University of Bern, Bern, Switzerland

Abstract

The aim of the study was to evaluate the need for active surveillance of antibiotic resistance in ambulatory infections. We measured the prevalence of antibiotic resistance in urinary tract infections (UTIs) (n = 1018) and skin infections (n = 213) diagnosed in outpatients between September 2008 and February 2009 in the Canton of Bern, Switzerland. Samples were stratified into 'solicited' (diagnostic work-up for study purpose only) and 'routine' (diagnostic work-up as part of standard care). Susceptibility patterns were compared for 463 *Escherichia coli* isolates from UTIs (231 solicited; 232 routine) and 87 *Staphylococcus aureus* isolates from skin infections (35 solicited; 52 routine). Overall, *E. coli* showed higher susceptibility to ampicillin, amoxicillin–clavulanic acid and norfloxacin in solicited than in routine samples. Among 15–45-year-old patients, susceptibility rates were comparable between solicited and routine samples for all antibiotics except for amoxicillin–clavulanic acid. However, among patients >45 years old, isolates from routine samples showed lower susceptibility to all β-lactams tested and quinolones than those from solicited samples. Extended-spectrum β-lactamase (ESBL)-producing *E. coli* isolates were rare (solicited, 0.4%; routine, 1.7%; p 0.4). Susceptibility patterns of *S. aureus* were comparable between solicited and routine samples. Therefore, in the outpatient setting, susceptibility rates for *E. coli* isolates differ by indication for urinary culture and age. Surveillance based on samples taken during standard care may underestimate susceptibility rates for uncomplicated infections, especially among the elderly. Reports of resistance data should include age stratification.

Keywords: Active, multiresistance, skin infection, surveillance, Switzerland, urinary tract infection
Original Submission: 6 January 2011; **Revised Submission:** 3 March 2011; **Accepted:** 5 March 2011
Editor: F. Allerberger
Article published online: 23 March 2011
Clin Microbiol Infect 2011; **17:** 1845–1851
10.1111/j.1469-0691.2011.03519.x

Corresponding author: K. Mühlemann, Institute for Infectious Diseases, University of Bern, Friedbühlstrasse 51, 3010 Bern, Switzerland
E-mail: kathrin.mühlemann@ifik.unibe.ch

Introduction

Antibiotic resistance is increasing worldwide in developed and developing countries [1]. Multidrug resistance in important human pathogens is no longer restricted to high-risk settings such as acute-care hospitals, but is now spreading in the population at large [2]. Community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) and extended spectrum β-lactamase (ESBL)-producing *Escherichia coli* are timely examples of multidrug-resistant organisms causing community-acquired infections [3]. Increasing resistance trends introduce uncertainty about the correct choice of empirical antibiotic treatment if information about the local resistance epidemiology is lacking. This applies to the outpatient setting, in which microbiological diagnosis in individual patients is not recommended in standard care for common non-invasive infections.

Enormous effort and progress have been made in the establishment of large-scale resistance surveillance systems around the globe [4]. There are now several databases available, many of which also provide resistance information for the community setting. For economic reasons, such surveillance programmes usually rely on passive collection of routine microbiological data, and some programmes are based mainly on data from invasive isolates. Therefore, the resistance information represents a selection of clinical situations, such as severe infections and infections associated with high-risk populations, and it may overestimate the resistance prevalence of mild community-acquired infections, such as

those of the upper respiratory tract, the lower urinary tract, and the skin. These infections account for the majority of prescribed antibiotics, and standard care does not require microbiological work-up. Changes of empirical treatment habits to broader regimens based on erroneous interpretation of surveillance data will introduce an unnecessary selection pressure and promote further resistance spread. An illustrative example is provided by uncomplicated lower urinary tract infections. Concerns about the rapid increase in resistance to trimethoprim–sulphamethoxazole in *E. coli* has started a vicious circle of increased use of quinolones followed by raising quinolone resistance rates and the emergence of ESBL-producing clones [5,6].

In this study, we present the resistance rates observed in an active surveillance study conducted in ambulatory-care patients presenting with acute uncomplicated urinary tract infections (UTIs) or purulent skin infections. We compare the resistance results of samples that would not have been sent for analysis outside this study (solicited samples) with those of routine samples.

Patients and Methods

Study population and definitions

This study fulfilled the ethical requirements of the Canton of Bern. In August 2008, all general practitioners and dermatologists practising in the Canton of Bern, Switzerland, were asked by the Department of Public Health to participate in this prevalence study. Patients were recruited between 1 September 2008 and 28 February 2009. Consecutive patients >15 years of age were included in the study if they fulfilled the following criteria: (i) residing in the Canton of Bern; and (ii) first visit with a purulent wound infection or with a new episode of a UTI, defined as the presence of typical symptoms and a positive dipstick test result. Patients with wound infections were recruited only once. Patients with UTIs could be recruited twice, if the time interval between the current and the last episode was longer than 30 days. Physicians filled in a short questionnaire for each patient about the clinical diagnosis, living conditions (at home vs. long-term care), antibiotic consumption during the last 3 months, and history of colonization with a multiresistant microorganism. Physicians stated for each patient whether microbiological diagnosis would have been performed independently of this study. Physician residence was categorized into rural or non-rural, according to the definition of the Swiss Federal Office of Statistics (http://www.bfs.admin.ch). Microbiological diagnosis included a wound swab for skin infection and a mid-stream urine sample for UTI. All microbiological analyses were performed at the Institute for Infectious Diseases, University of Bern. Wound swabs were placed in Amies transport medium without charcoal (Venturi Transystem; Copan, Brescia, Italy). Urine samples were transported in containers prefilled with boric acid preservative (Becton Dickinson, Franklin Lakes, NJ, USA). Susceptibility testing was performed with the Kirby–Bauer disk diffusion test, and the results were interpreted according to CLSI (formerly NCCLS) standards [7]. Testing of *E. coli* isolates for susceptibility to nitrofurantoin and fosfomycin was introduced in January 2009. All wound swabs were screened for MRSA, with a biplate consisting of mannitol salt agar 4% (Oxoid, Hampshire, UK) and oxacillin screen agar containing 6 μg of oxacillin/mL (BioMérieux, Croponne, France). Cefuroxime-resistant *Enterobacteriaceae* were screened for ESBL according to the CLSI ESBL recommendations for disk diffusion, including ceftriaxone, ceftazidime, and aztreonam. The second screening criterion was visible inhibition by clavulanic acid (amoxicillin–clavulanic acid placed between aztreonam and ceftazidime on screening plates). The presence of ESBL was confirmed by the double-disk test [8]. Significant bacteriuria was defined as a concentration of ≥1000 CFU/mL for *E. coli* and *Staphylococcus saprophyticus*, and a concentration of ≥10 000 CFU/mL for all other microorganisms, according to the European guidelines [9].

Statistical analysis

Samples that would have been collected by physicians for diagnostic purposes independently of the study were designated as 'routine samples', and all others as 'solicited samples'. In *E. coli*, 'dual resistance' was defined as resistance to norfloxacin and trimethoprim–sulphamethoxazole, and 'multi-resistance' was defined as resistance to three or more of norfloxacin, trimethoprim–sulphamethoxazole, amoxicillin–clavulanic acid, and cefuroxime axetil.

Data were analysed with Epi info Version 3.4.3 (CDC, Atlanta, GA, USA). Proportions were compared by use of the chi-square test or Fisher's exact test as appropriate.

Results

Antimicrobial resistance prevalence in urinary tract isolates

In total, 1018 urine samples were provided by a total of 124 physicians, who account for 13% of all practising physicians in the ambulatory setting in the Canton of Berne (http://www.fmh.ch). Each physician recruited a median number of three patients. Of the 1018 urine samples, about half (n = 525, 51.6%) represented 'routine samples' and 428 (42.0%) 'solicited samples' (information was missing for 65

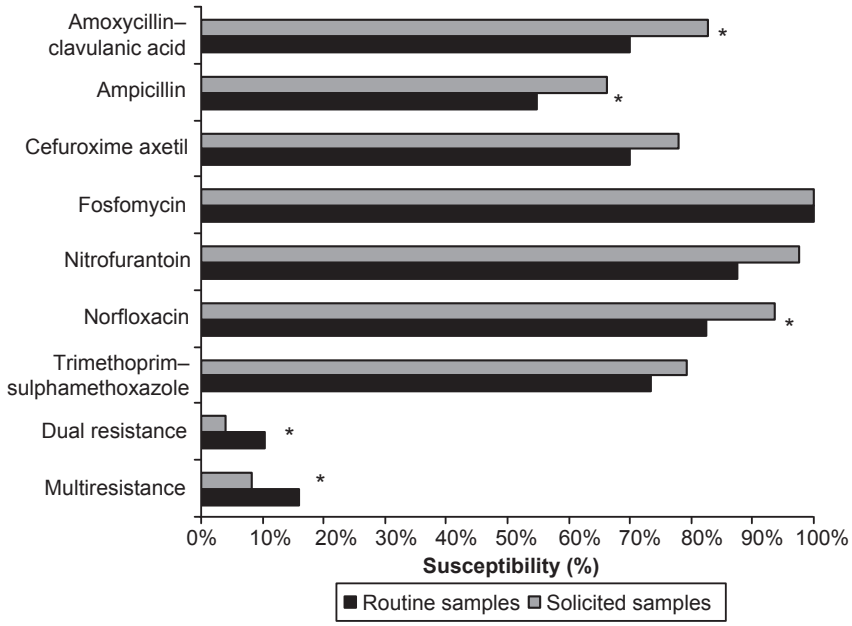

FIG. 1. Susceptibility rates (%) of *Escherichia coli* urinary tract isolates in routine vs. solicited samples. The numbers of isolates tested were 231 for solicited samples and 232 for routine samples, except for fosfomycin (31 for each) and nitrofurantoin (40 for solicited samples and 48 for routine samples). Significant differences between solicited and routine samples are indicated by an asterisk (*p <0.05).

samples (6.4%); Fig. 1). Assuming that the participating physicians cared for 13% of the population of the Canton of Bern (*n* = 969 299; http://www.be.ch), the annual incidence rate of UTIs amounted to 1.6 episodes per 100 population per year.

Table 1 shows socio-demographic, clinical and microbiological characteristics for solicited and routine samples. Solicited samples were more often from patients of younger age, of female gender, residing in urban regions, and living at home. Also, patients with solicited samples less often had a history of antibiotic treatment.

About two-thirds (68.5%) of urine samples showed significant bacteriuria. Significant bacteriuria with a single microorganism was more frequent in routine samples (87.9%) than in solicited samples (81.3%, p <0.001). *E. coli* was the most prevalent microorganism, and the proportion of *E. coli* was higher among solicited samples. The distribution of other microorganisms was comparable between routine and solicited samples.

Antimicrobial susceptibility rates for *E. coli* are shown in Fig. 1. Susceptibility rates were significantly higher among the solicited samples for ampicillin, amoxicillin–clavulanic acid, and norfloxacin. Also, *E. coli* isolates from solicited samples were less often multidrug-resistant. After stratification for age, susceptibility rates differed between solicited and routine samples for ampicillin, amoxicillin–clavulanic acid, cefuroxime and norfloxacin in patients >45 years old, but differed only for amoxicillin–clavulanic acid in patients between the ages of 15 and 45 years (Table 1). Susceptibility rates for norfloxacin were significantly higher among younger patients (95.7%) than among older patients (82.9%, p <0.001), whereas susceptibility rates for other antibiotics were comparable between the two age groups (Table 1).

Prior antimicrobial treatment was associated with significantly higher resistance rates for all antibiotics tested except for fosfomycin, for which no resistance was observed (Table 2).

ESBLs were detected in five (1.1%) *E. coli* isolates or in 0.8% of all culture-positive urine samples (0.4% in solicited and 1.7% in routine samples, p 0.4). ESBL carriers were not known previously in any of these patients. All were females, and their age ranged between 16 and 80 years. Four of the five ESBL carriers had a history of recurrent UTI and antimicrobial exposure during the past 3 months. Two of the five ESBL isolates were multiresistant (to gentamicin, trimethoprim–sulphamethoxazole, and norfloxacin).

Antimicrobial resistance prevalence in skin and soft tissue infections

A total of 213 samples from skin and soft tissue infections were provided by a total of 72 physicians. More than half of these samples (*n* = 113, 53.1%) were routine samples, and 84 (39.4%) were collected explicitly for the study (information was missing for 16 samples (7.5%)). Table 3 shows socio-demographic and clinical data, and microbiological results. Solicited samples differed from routine samples by

TABLE 1. Socio-demographic, clinical and microbiological characteristics of patients with urinary tract infections[a]

	Solicited samples, *n* = 428	Routine samples, *n* = 525	p
Demographic and clinical characteristics			
Age (years), mean (SD)	48.3 (22.3)	55.7 (23.0)	<0.001
Female gender, *n* (%)	358 (83.6)	409 (77.9)	0.006
Rural, *n* (%)	128 (29.2)	212 (40.4)	0.001
Antimicrobial treatment during the last 3 months, *n* (%)	48 (11.2)	228 (43.4)	<0.001
Bladder catheter, *n* (%)	21 (4.9)	36 (6.9)	>0.05
ESBL carriage known, *n* (%)	2 (0.5)	8 (1.5)	>0.05
Long-term care, *n* (%)	11 (2.6)	38 (7.2)	0.002
Bacteriology			
Bacteriuria, *n* (%)[b]	305 (71.3)	348 (66.3)	>0.05
Single microorganism	248 (81.3)	323 (87.9)	<0.001
Escherichia coli	231 (75.7)	232 (66.7)	0.01
Klebsiella spp.	13 (4.3)	22 (6.3)	>0.05
Proteus mirabilis	10 (3.3)	14 (4.0)	>0.05
Other *Enterobacteriaceae*	16 (5.2)	17 (4.9)	>0.05
Pseudomonas aeruginosa	2 (0.7)	6 (1.7)	>0.05
Enterococcus spp.	61 (20.0)	52 (14.9)	>0.05
Staphylococcus aureus	3 (1.0)	5 (1.4)	>0.05
Staphylococcus saprophyticus	10 (3.3)	17 (4.9)	>0.05
Streptococcus agalactiae	6 (2.0)	6 (1.7)	>0.05
Other	5 (1.6)	17 (4.9)	0.04
Susceptibility rates for *Escherichia coli*, *n* (%)			
Age 15–45 years			
Ampicillin	107 (67.3)	78 (57.7)	>0.05
Amoxicillin–clavulanic acid	107 (85)	78 (69.2)	0.016
Cefuroxime axetil	107 (76.6)	78 (73.1)	>0.05
Fosfomycin	16 (100.0)	11 (100.0)	>0.05
Nitrofurantoin	21 (95.2)	15 (93.3)	>0.05
Norfloxacin[c]	107 (98.1)	78 (92.3)	>0.05
TMP-SMX	107 (79.4)	78 (75.6)	>0.05
Dual resistance	107 (1.9)	78 (5.1)	>0.05
Multiresistance	107 (6.5)	78 (10.3)	>0.05
Age >45 years			
Ampicillin	112 (66.1)	133 (51.1)	0.026
Amoxicillin–clavulanic acid	112 (80.4)	133 (68.4)	0.049
Cefuroxime axetil	112 (81.3)	133 (64.7)	0.006
Fosfomycin	14 (100)	19 (100.0)	>0.05
Nitrofurantoin	18 (100)	32 (84.4)	>0.05
Norfloxacin[c]	112 (90.2)	133 (76.7)	0.009
TMP-SMX	112 (79.5)	133 (71.4)	>0.05
Dual resistance	112 (5.4)	133 (12.8)	>0.05
Multiresistance	112 (8.9)	133 (20.3)	0.022

ESBL, extended-spectrum β-lactamase; SD, standard deviation; TMP-SMX, trimethoprim–sulphamethoxazole.
[a]Missing data: age, *n* = 77; gender, *n* = 65; rural/urban, *n* = 10; missing data were equally distributed between solicited and routine samples (data not shown).
[b]Number and percentage of urinary samples with significant bacterial growth. The total sum of microorganisms exceeds 100%, because some samples contained more than one pathogen.
[c]Comparison of susceptibility to norfloxacin between the two age groups: p 0.028 for solicited samples; p 0.007 for routine samples.

TABLE 2. Susceptibility rates (%) and number tested (*n*) of *Escherichia coli* urinary tract isolates[a] stratified according to antimicrobial exposure during the last 3 months

	Antimicrobial treatment in the last 3 months				
	Yes		No		
	%	*n*	%	*n*	p
Ampicillin	46.4	110	66.5	316	<0.001
Amoxycillin–clavulanic acid	61.8	110	81.6	316	<0.001
Cefuroxime axetil	60.9	110	78.5	316	<0.001
Fosfomycin	100.0	16	100.0	40	>0.05
Nitrofurantoin	79.2	24	98.2	55	0.009
Norfloxacin	70.9	110	94.6	316	<0.001
TMP-SMX	57.3	110	83.9	316	<0.001

TMP-SMX, trimethoprim–sulphamethoxazole.
[a]Solicited and routine samples combined.

younger age, lower rate of chronic ulcers and lower rate of antimicrobial treatment during the preceding 3 months.

In 64.5% of all samples, at least one established human pathogen was detected. Mixed flora was reported in 27.9% of cultures, and in 7.6% there was no bacterial growth. The microbial spectra were similar for routine and solicited samples, with *S. aureus* being the most prevalent pathogen isolated. Antibiotic susceptibility rates for *S. aureus* are shown in Fig. 2. Susceptibility rates were comparable for all antibiotics tested in both solicited and routine samples.

MRSA isolates were rare, with a prevalence of 2.1% (two of 94, one in a routine sample and one in a solicited samples). One of the two patients had been known to carry MRSA, and he had a history of polytrauma with prolonged hospitalization and multiple antibiotic treatments. The MRSA isolate from

TABLE 3. Socio-demographic, clinical and microbiological characteristics of patients with skin infections[a]

	Solicited samples, *n* = 84	Routine samples, *n* = 113	p
Demographic and clinical characteristics			
Age (years), mean (SD)	37.5 (20.8)	50.3 (23.0)	<0.001
Male gender, *n* (%)	36 (42.9)	58 (51.3)	NS
Rural, *n* (%)	20 (23.8)	28 (24.8)	NS
Type of infection			
Abscess/folliculitis, *n* (%)	47 (56.0)	51 (45.1)	>0.05
Wound infection, *n* (%)	22 (26.2)	27 (23.9)	>0.05
Chronic ulcer, *n* (%)	3 (3.6)	17 (15.0)	0.016
Impetigo, *n* (%)	7 (8.3)	10 (8.8)	>0.05
Antimicrobial treatment during the last 3 months, *n* (%)	6 (7.1)	29 (25.7)	0.002
MRSA carriage known, *n* (%)	1 (1.2)	3 (2.7)	>0.05
Long-term care, *n* (%)	3 (3.6)	6 (5.3)	>0.05
Bacteriology			
Culture-positive, *n* (%)[b]	54 (64.3)	73 (64.6)	>0.05
Staphylococcus aureus	35 (64.8)	52 (71.2)	>0.05
Streptococcus pyogenes	5 (9.3)	3 (4.1)	>0.05
Coagulase-negative staphylococci	1 (1.9)	2 (2.7)	>0.05
Other Gram-positive cocci	7 (13.0)	11 (15.1)	>0.05
Enterobacteriaceae	8 (12.5)	9 (12.3)	>0.05
Other Gram-negative rods	7 (14.8)	7 (9.6)	>0.05
Anaerobes	1 (1.9)	1 (1.4)	>0.05

MRSA, methicillin-resistant *Staphylococcus aureus*; NS, not significant; SD, standard deviation.
[a]Missing data: age, *n* = 16; gender, *n* = 6; rural vs. urban, *n* = 8; missing data were equally distributed between solicited and routine samples (data not shown).
[b]Number and percentage of samples with bacterial growth. The total sum of microorganisms exceeds 100%, because some samples contained more than one pathogen.

the solicited sample was obtained from a 35-year-old women with an axillary abscess, whose father carried a community-acquired MRSA isolate. MRSA infection or carriage was not suspected in this patient before testing. Both MRSA isolates were susceptible to trimethoprim–sulphamethoxazole, ciprofloxacin, tetracycline, and clindamycin; in addition, the isolate of the polytrauma patient was susceptible to gentamicin.

Discussion

Standard care for prevalent infections, such as uncomplicated UTIs, respiratory tract infections, and skin infections, does not require microbiological work-up [10–12]. If indicated, the choice of empirical antimicrobial treatment is based on epidemiological data for (local) antibiotic resistance prevalence. Active surveillance for antimicrobial susceptibility is expensive, and is therefore often substituted for by passive surveillance based on data from routine clinical microbiology laboratories. By virtue of the standards of care, such passive surveillance tends to over-represent complicated clinical situations, such as infectious episodes in patients with comorbidity or recent antimicrobial exposure, or infections with signs of invasiveness. All of these factors may be associated with higher antimicrobial resistance prevalence. In order to correct for such potential bias, laboratory-based surveillance data should be validated against active surveillance data [10].

Surveillance of antibiotic resistance in urinary tract isolates

The estimated annual incidence rate of lower UTI in our population was 1.6 episodes per 100 population, which is slightly above the rate of 1.3 episodes per 100 population reported by a laboratory-based passive surveillance study performed in the Calgary area between 2004 and 2005 [13]. The higher incidence observed in our study is probably a consequence of soliciting samples from non-complicated UTIs during the active surveillance study.

Significant bacteriuria was observed in about two-thirds (68.5%) of urinary samples, which is slightly lower than the rate of 74.6% observed in the large international survey

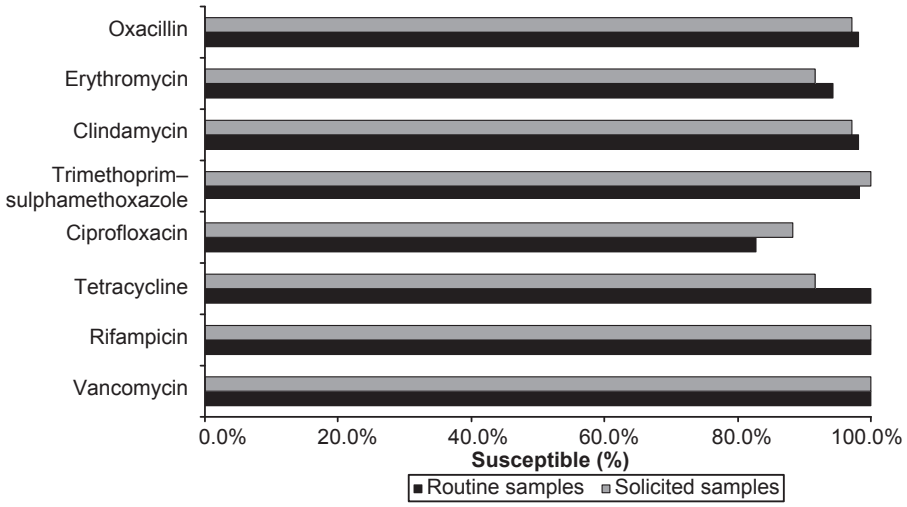

FIG. 2. Susceptibility rates (%) of *Staphylococcus aureus* skin infection isolates in routine vs. solicited samples. The numbers of isolates tested were 36 for solicited samples, except for ciprofloxacin and rifampicin with 34 isolates each, and 52 for routine samples. There were no significant differences between solicited and routine samples.

ARESC [14]. As expected, *E. coli* was the most common uropathogen [14,15]. However, the proportion of *E. coli* was significantly higher in solicited samples, probably because these samples were from young, healthy women. Naber *et al.* described a lower prevalence of *E. coli* in recurrent UTIs and in UTIs in pregnant or young diabetic patients [14,15].

In this study, susceptibility rates for *E. coli* were significantly higher in clinical situations for which microbiological work-up is not a standard (solicited samples) than in situations for which urine culture is recommended (routine samples). This difference was, however, mainly observed in patients older than 45 years.

For trimethoprim–sulphamethoxazole, susceptibility rates tended to be higher in solicited samples (79.2%) than in routine samples (73.3%, p 0.16). It has been argued that trimethoprim–sulphamethoxazole should be maintained as a valuable option for first-line therapy of uncomplicated cystitis, given the high clinical success rate (85%), even at a resistance prevalence of 30% [16]. Therefore, trimethoprim–sulphamethoxazole remains a therapeutic option in our region. However, trimethoprim–sulphamethoxazole susceptibility varies widely between different European countries, from 59.6% in Hungary to 87.7% in France [15]. Therefore, local active surveillance is important in order to evaluate the appropriateness of this drug for empirical treatment.

Susceptibility rates for norfloxacin were higher than those for trimethoprim–sulphamethoxazole, and were significantly higher in solicited (93.5%) than in routine samples (82.3%, p <0.001). Higher susceptibility rates for ciprofloxacin than for trimethoprim–sulphamethoxazole are observed in all European countries participating in the ARESC study [15]. However, rising trends in fluoroquinolone resistance have been shown over the past 7 years all over Europe [17], and also for ambulatory *E. coli* isolates in Switzerland between 2004 and 2007 [18]. This correlates with increased consumption of fluoroquinolones in most European countries [19]. High resistance levels threaten the safety of empirical treatment of invasive UTIs with a quinolone. Our study shows that empirical use of quinolones in invasive UTIs may still be correct in patient populations at low risk of resistance, despite high overall resistance levels. However, this information might be missed if surveillance is based on passive surveillance only.

Susceptibility patterns for the β-lactam antibiotics amoxicillin–clavulanic acid and cefuroxime axetil were comparable. For both antibiotics, we observed significantly higher susceptibility rates in solicited than in routine samples. The susceptibility rates of approximately 80% for amoxicillin–clavulanic acid and for cefuroxime observed in this study compare well with the average results from the ARESC study, although susceptibility rates for these antibiotics vary widely between different European countries [15].

Susceptibility rates for nitrofurantoin and fosfomycin were generally high, in accordance with the overall situation in Europe [15]. However, these drugs may be increasingly used in populations at risk for UTI not responding to standard treatment because of rising resistance rates. As shown in our study, multiresistance is significantly more prevalent in routine samples.

This prevalence study showed that ESBL-producing *E. coli* isolates are still rare in our region (0.4% in solicited samples; 1.1% in routine samples; p 0.4). Across Europe, ESBL rates in community-acquired UTIs vary between 0.9% in France in 2006 [20], 1.9% in Italy in 2003 [21], 5.2% in Spain in 2006 [22], and 20.2% in Turkey in 2007 [23]. We did not perform molecular typing of our ESBL-producing isolates, but a previous Swiss study showed a predominance of CTX-M [24], as has been described for Europe in general [15]. Most of the ESBL carriers identified in our study had at least one of the described risk factors, such as older age [3,25–28], diabetes mellitus [3,27], prostatic disease [29], recurrent UTI [3,27,29], previous antimicrobial use [28,29], residence in a long-term-care facility [28], and recent hospital admission [26–28].

Surveillance of antibiotic resistance in skin and soft tissue infections

As expected, *S. aureus* was the most prevalent microorganism found in skin and soft tissue infections in our population. Neither the microbial spectrum nor *S. aureus* susceptibility rates differed meaningfully between solicited and routine samples. MRSA rates were low (2.1%), and did not differ significantly between routine and solicited samples. This was also shown in another study conducted recently in Switzerland [30].

In conclusion, in the outpatient setting, susceptibility rates for *E. coli* isolates differ by age and indication for urinary culture. Surveillance based on samples taken during standard care (routine samples) may underestimate susceptibility rates for uncomplicated infections, especially among the elderly. Reports of resistance data should include age stratification. However, surveillance based on routine samples predicts susceptibility rates of *S. aureus* from skin infections well. As this study applies to UTIs and skin infections diagnosed in general practice, extrapolation of the observed results to other settings, such as inpatients or specialized outpatient clinics, may not be possible.

Acknowledgements

We would like to thank the health office of the Canton of Bern for its support in the organization of this study, and all physicians for participating.

Funding

There was no external funding.

Transparency Declarations

There are no conflicts of interest to declare.

References

1. Zhang R, Eggleston K, Rotimi V, Zeckhauser RJ. Antibiotic resistance as a global threat: evidence from China, Kuwait and the United States. *Global Health* 2006; 2: 6.
2. Livermore DM, Woodford N. The beta-lactamase threat in Enterobacteriaceae, Pseudomonas and Acinetobacter. *Trends Microbiol* 2006; 14: 413–420.
3. Rodriguez-Bano J, Alcala JC, Cisneros JM *et al.* Community infections caused by extended-spectrum beta-lactamase-producing *Escherichia coli*. *Arch Intern Med* 2008; 168: 1897–1902.
4. Harbarth S, Emonet S. Navigating the world wide web in search of resources on antimicrobial resistance. *Clin Infect Dis* 2006; 43: 72–78.
5. Durham LK, Ge M, Cuccia AJ, Quinn JP. Modeling antibiotic resistance to project future rates: quinolone resistance in *Escherichia coli*. *Eur J Clin Microbiol Infect Dis* 2010; 29: 353–356.
6. Pitout JD, Gregson DB, Campbell L, Laupland KB. Molecular characteristics of extended-spectrum-beta-lactamase-producing *Escherichia coli* isolates causing bacteremia in the Calgary health region from 2000 to 2007: emergence of clone st131 as a cause of community-acquired infections. *Antimicrob Agents Chemother* 2009; 53: 2846–2851.
7. Clinical and Laboratory Standards Institute. *Performance standards for antimicrobial susceptibility testing*. Wayne, PA: CLSI, 2008.
8. Coudron PE, Moland ES, Sanders CC. Occurrence and detection of extended-spectrum beta-lactamases in members of the family Enterobacteriaceae at a Veterans Medical Center: seek and you may find. *J Clin Microbiol* 1997; 35: 2593–2597.
9. Aspevall O, Hallander H, Gant V, Kouri T. European guidelines for urinalysis: a collaborative document produced by European clinical microbiologists and clinical chemists under ECLM in collaboration with ESCMID. *Clin Microbiol Infect* 2001; 7: 173–178.
10. Scottish intercollegiate guidelines network. *Management of suspected bacterial urinary tract infection in adults. A national clinical guideline. Scottish intercollegiate guidelines network*. 2006. Available at: www.sign.ac.uk.
11. Grabe M, Bishop MC, Bjerklund-Johansen TE *et al. Guidelines on urological infections*. European Association of Urology 2009. Available at: www.ur.web.org.
12. Gradwohl SE, Chenoweth CE, Fondue RK, Van Harrison R, Zoschnick LB. *Guidelines for clinical care. Urinary tract infection*. University of Michigan Health System, 2005. Available at: http:/cme.mcd.umich.edu.
13. Laupland KB, Ross T, Pitout JD, Church DL, Gregson DB. Community-onset urinary tract infections: a population-based assessment. *Infection* 2007; 35: 150–153.
14. Schito GC, Naber KG, Botto H *et al.* The ARESC study: an international survey on the antimicrobial resistance of pathogens involved in uncomplicated urinary tract infections. *Int J Antimicrob Agents* 2009; 34: 407–413.
15. Naber KG, Schito G, Botto H, Palou J, Mazzei T. Surveillance study in Europe and Brazil on clinical aspects and antimicrobial resistance epidemiology in females with cystitis (ARESC): implications for empiric therapy. *Eur Urol* 2008; 54: 1164–1175.
16. Hooton TM, Besser R, Foxman B, Fritsche TR, Nicolle LE. Acute uncomplicated cystitis in an era of increasing antibiotic resistance: a proposed approach to empirical therapy. *Clin Infect Dis* 2004; 39: 75–80.
17. EARSS annual report 2008. Available at: http://www.Rivm.Nl/earss/images/earss%202008_final_tcm61-65020.Pdf (last accessed 1 October 2010).
18. Kronenberg AZG, Piffaretti JC, Mühlemann K. Antibiotikaresistenzdaten der schweiz: Jetzt online. *Schweiz Med Forum* 2008; 8: 415–418.
19. Ferech M, Coenen S, Malhotra-Kumar S *et al.* European surveillance of antimicrobial consumption (ESAC): outpatient quinolone use in Europe. *J Antimicrob Chemother* 2006; 58: 423–427.
20. Arpin C, Quentin C, Grobost F *et al.* Nationwide survey of extended-spectrum {beta}-lactamase-producing Enterobacteriaceae in the French community setting. *J Antimicrob Chemother* 2009; 63: 1205–1214.
21. Luzzaro F, Mezzatesta M, Mugnaioli C *et al.* Trends in production of extended-spectrum beta-lactamases among enterobacteria of medical interest: report of the second Italian nationwide survey. *J Clin Microbiol* 2006; 44: 1659–1664.
22. Andreu A, Planells I. Etiology of community-acquired lower urinary infections and antimicrobial resistance of *Escherichia coli*: a national surveillance study. *Med Clin (Barc)* 2008; 130: 481–486.
23. Yilmaz N, Agus N, Yurtsever SG *et al.* Prevalence and antimicrobial susceptibility of *Escherichia coli* in outpatient urinary isolates in Izmir, Turkey. *Med Sci Monit* 2009; 15: PI61–PI65.
24. Lartigue MF, Zinsius C, Wenger A, Bille J, Poirel L, Nordmann P. Extended-spectrum beta-lactamases of the CTX-M type now in Switzerland. *Antimicrob Agents Chemother* 2007; 51: 2855–2860.
25. Pitout JD, Hanson ND, Church DL, Laupland KB. Population-based laboratory surveillance for *Escherichia coli* producing extended-spectrum beta-lactamases: importance of community isolates with blactx-m genes. *Clin Infect Dis* 2004; 38: 1736–1741.
26. Colodner R, Rock W, Chazan B *et al.* Risk factors for the development of extended-spectrum beta-lactamase-producing bacteria in nonhospitalized patients. *Eur J Clin Microbiol Infect Dis* 2004; 23: 163–167.
27. Rodriguez-Bano J, Navarro MD, Romero L *et al.* Epidemiology and clinical features of infections caused by extended-spectrum beta-lactamase-producing *Escherichia coli* in nonhospitalized patients. *J Clin Microbiol* 2004; 42: 1089–1094.
28. Ben-Ami R, Rodriguez-Bano J, Arslan H *et al.* A multinational survey of risk factors for infection with extended-spectrum beta-lactamase-producing enterobacteriaceae in nonhospitalized patients. *Clin Infect Dis* 2009; 49: 682–690.
29. Azap OK, Arslan H, Serefhanoglu K *et al.* Risk factors for extended-spectrum beta-lactamase positivity in uropathogenic *Escherichia coli* isolated from community-acquired urinary tract infections. *Clin Microbiol Infect* 2009; 16: 147–151.
30. Aramburu C, Harbarth S, Liassine N *et al.* Community-acquired methicillin-resistant *Staphylococcus aureus* in Switzerland: first surveillance report. *Euro Surveill* 2006; 11: 42–43.