Epidemiology of bloodstream infections caused by extended-spectrum cephalosporin-resistant *Escherichia coli* and *Klebsiella pneumoniae* in Switzerland, 2015–2022: secular trends and association with the COVID-19 pandemic

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A R T I C L E   I N F O

S U M M A R Y

Background: The association between the COVID-19 pandemic and the incidence of invasive infections caused by multidrug-resistant organisms remains a topic of debate.
Aim: To analyse the national incidence rates of bloodstream infections (BSI) caused by *Escherichia coli* (EC) and *Klebsiella pneumoniae* (KP) with extended-spectrum cephalosporin resistance (ESCR) in two distinct regions in Switzerland, each exhibiting varying antimicrobial resistance patterns and that were impacted differently by the pandemic.
Methods: Data was analysed from positive blood cultures prospectively collected by the nationwide surveillance system (ANRESIS) from January 1st, 2015, to August 31st, 2022. To explore the potential relationship between COVID-19 patient occupancy and ESCR incidence rates, an in-depth analysis was conducted over the two-year pandemic period from April 1st, 2020, to March 30th, 2022, using Quasi-Poisson and logistic regression analyses.
Findings: During the study period, 40,997 EC-BSI and 8537 KP-BSI episodes were collected and reported to ANRESIS by the participating hospitals. ESCR was observed in 11% (*N* = 4313) of *E. coli* and 8% (*N* = 664) of *K. pneumoniae*, respectively. A significant reduction in ESCR-EC BSI incidence occurred during the pandemic in the region with the highest COVID-19 incidence. Conversely, ESCR-KP BSI incidence initially fell considerably and then increased during the pandemic in both regions, though this effect was not statistically significant. No association between hospital occupancy from COVID-19 patients and these trends was observed.

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Conclusion: In the early phase of the COVID-19 pandemic, a decrease in ESCR rates was observed, particularly in ESCR-EC BSI within the most heavily impacted region.

Introduction

The pandemic of COVID-19 has affected healthcare systems worldwide, significantly influencing various aspects of infection control and prevention. This impact includes antimicrobial prescribing and consumption as well as healthcare-associated infections (HAIs), including bloodstream infections (HA-BSI) [1—4]. The effect of COVID-19 on antimicrobial resistance (AMR), a leading cause of mortality, has also been the subject of study, with heterogeneous findings [5—8]. Recently, a report has explored the role of multidrug-resistant organisms (MDROs) in causing invasive infections such as bloodstream infections (BSIs) during the pandemic, resulting in conflicting outcomes [9]. Overall, our understanding of the pandemic's influence on clinically relevant infections, such as BSI, caused by MDRO, remains limited, with most studies focusing on the impact of the initial pandemic wave and investigations into national and long-term trends being rare.

Despite efforts to overcome AMR, rates of extended-spectrum cephalosporin-resistant (ESCR, i.e. with resistance to third- and fourth-generation cephalosporins) and extended-spectrum β-lactamase (ESBL) producing Enterobacterales are increasing across several regions globally in both the healthcare and the community settings [10,11]. The World Health Organization lists these MDROs as critical priority pathogens for research and development of new antibiotics [12]. *Escherichia coli* and *Klebsiella pneumoniae* are the two most common and clinically relevant Enterobacterales and are the main drivers of these trends.

In this study, our primary objective was to analyse the long-term national AMR trends of BSI caused by ESCR *Escherichia coli* (ESCR-EC) and *Klebsiella pneumoniae* (ESCR-KP) in Switzerland, and identify any deviations during the pandemic. Given the distinct AMR patterns observed across various linguistic regions and the notably higher impact of the pandemic, particularly during the first wave in the Latin part, we examined trends at a regional level, using the regions as proxy for the pandemic's burden [13]. Our secondary objective was to investigate the reasons for the observed results using more detailed and comprehensive models, aiming to better understand the patterns during the pandemic. Specifically, we wanted to determine whether there was an association between regional monthly COVID-19 patient occupancy rates and the endpoints.

Methods

Study setting and design

This was a retrospective analysis of national epidemiological and microbiological data on positive blood cultures (BSIs) prospectively collected by the Swiss Centre for Antibiotic Resistance (ANRESIS) and COVID-19-related hospital occupancy data provided by the Swiss Federal Office of Public Health (FOPH).

Hypotheses

These were: (i) that the COVID-19 pandemic may be associated with changes in the epidemiology of ESCR-KP and ESCR-EC BDIs in Switzerland and that these changes may vary over time in two distinct Swiss regions, which had diverse pre-pandemic antimicrobial resistance patterns and were differentially affected by the pandemic; (ii) that calculated regional monthly COVID-19 patient occupancy rates may be associated with the incidence of ESCR-KP and ESCR-EC BSI and extended-spectrum cephalosporin resistance rates.

Data sources, collection, and definitions

Microbiological surveillance data

ANRESIS regularly receives information on all positive blood cultures from more than 30 Swiss microbiology laboratories, some of them collecting data from multiple hospitals. Hospitals are distributed across the country and represented 66% of annual hospitalization days in 2015 and 90% in 2020. Species identification and antimicrobial susceptibility testing are based on tests performed in the local laboratories, which apply either European Committee on Antimicrobial Susceptibility Testing (EUCAST, https://eucast.org) or Clinical and Laboratory Standards Institute (CLSI, https://clsi.org) guidelines. For the present study, data were collected on blood cultures positive for *Escherichia coli* and *Klebsiella pneumoniae*. In case of multiple positive blood cultures, only the first blood culture per micro-organism, patient, and calendar year was considered. For consistency over the study period we included for the current analyses only data from those Swiss hospitals that were included in the ANRESIS surveillance in the first year of the study (January 1st, 2015 for the first objective and April 1st, 2020 for the second objective) and that sent information during the entire study period.

Variables collected and baseline data

Variables routinely collected by ANRESIS and used in part in aggregated forms for this study include age group (0—2, 3—15, 16—45, 46—65, and >65 years), sex (male, female), year, month as well as the exact date of detection of the episode, detected micro-organism species, hospital type (non-university versus university), department (i.e. intensive care unit (ICU) vs non-ICU) and region of residency (as defined below). Extended-spectrum cephalosporin-resistant *Escherichia coli* (ESCR-EC) and *Klebsiella pneumoniae* (ESCR-KP) were defined as resistant to at least one of all third- or fourth-generation cephalosporins tested.

Study periods

To investigate the association between the COVID-19 pandemic and the occurrence of ESCR-EC and ESCR-KP, two distinct periods were analysed: the pre-pandemic phase spanning from January 1st, 2015, to February 29th, 2020, and the pandemic

phase from March 1st, 2020 to August 31st, 2022. Furthermore, to assess the association between COVID-19 patient occupancy and the incidence of BSI as well as the resistance rates, we specifically examined the two-year period from April 1st, 2020, to March 30th, 2022, as data collection by the FOPH commenced on March 30th, 2020.

Regions

The associations between the COVID-19 pandemic and the level and the changes of ESCR-KP and ESCR-EC incidence rates were analysed in two distinct linguistic and sociocultural regions of Switzerland, which experienced varying effects from different pandemic waves. The first region (Latin-languages-speaking region, hereinafter referred to as 'Latin region'), includes the Italian-speaking and French-speaking parts of Switzerland. This region was significantly affected by the first wave of COVID-19. The second region, the German-speaking region (hereinafter referred to as 'German region'), was largely spared from the first wave. Subsequently, the pandemic had a more homogeneous impact on the country as a whole.

Denominators

Incidence rates were calculated using corrected population data as denominator. Data were provided by the Swiss Federal Statistical Office (FSO); these are freely available online (https://www.bfs.admin.ch/bfs/en/home/statistics/population.html), and were corrected for the population covered by ANRESIS. For the years 2021 and 2022, a corrected reference scenario from the FSO was used [14]. COVID-19 occupancy rates (percent of beds occupied by COVID-19 patients) were calculated for each geographic region on a monthly (quasi-Poisson regression) and daily (for the logistic regression) basis. Data on Swiss hospital occupancy regarding patients with and without COVID-19 were freely available from the FOPH (https://www.covid19.admin.ch).

Government response to the COVID-19 pandemic

The Swiss government enacted measures under the Federal Law of Epidemics, and an 'extraordinary situation' was declared nationwide on March 16th, 2020. These included restrictions such as limiting gatherings, closing schools and non-essential stores, and urging people to stay at home. These measures were mandatory for the entire country; however, in line with the cited law, cantonal authorities could implement more strict measures locally, if needed. Restrictions were gradually eased from late April to June 2020 but were reinstated in October 2020 due to a rise in cases. The vaccination campaign started in December 2021. A second lockdown occurred from January to February 2021. After that, restrictions were gradually eased and, by the end of March 2022, all COVID-19 prevention measures were lifted, ending the 'extraordinary situation'.

Statistical analyses

The statistical analysis included two steps. First, to investigate the association between the COVID-19 pandemic and the incidence rates of ESCR-KP and ESCR-EC BSIs in the German and Latin regions, a quasi-Poisson regression was performed. Two separate models were built for each linguistic region to examine potential effect of COVID-19 on the levels (model A)

and the changes (model B) of ESCR-KP and ESCR-EC incidence rates. In these models, the COVID-19 pandemic was coded as a binary variable as described by Bernal *et al.* [15]. A harmonic wave with a 12-month period was included in this model to test for seasonality and the coverage-corrected population, as defined above, was included as offset. *F*-Tests were performed for each predictor. Since four models were fitted for each pathogen, the P-values were Bonferroni-corrected. Besides the models that were built for statistical inference testing, additional comprehensive exploratory quasi-Poisson models were developed (i.e. backward reduction was applied) to explore the potential influence of higher-level interactions on the AMR count [16].

Second, to evaluate whether the incidence of ESCR-KP and ESCR-EC would be affected by the occupancy of hospital beds by COVID-19 patients during the pandemic months (from April 1st, 2020, to March 30th, 2022), quasi-Poisson models were fitted, similarly to the first analysis. However, instead of using a binary variable for the pandemic, the COVID-19 occupancy rate was included in these models. Moreover, in order to investigate whether the ESCR-KP and ESCR-EC resistance rates were affected by COVID-19 patient occupancy rates, logistic regression models were fitted. These models also included hospital (type, department) and patient (age group, sex) specific predictors. Likelihood-ratio tests were used to test for significance.

All analyses were performed with R (version 4.2.2). $P < 0.05$ was considered statistically significant. The analysis complied with the STROBE guidelines for observational studies [17].

Results

During the study period, 49,534 blood cultures positive for *E. coli* or *K. pneumoniae* were collected and reported to ANRESIS by the participating hospitals, the majority of these episodes (83%) being caused by *E. coli*. ESCR was observed in 11% ($N = 4313$) of *E. coli* and 8% ($N = 664$) of *K. pneumoniae*, respectively (see Supplementary Figure S1). Baseline characteristics of the patients with BSI are provided in Table I. The population in the German part was 5,905,544 (3,865,769 coverage-corrected) and 2,421,582 (1,682,273 coverage-corrected) in the Latin part in 2015 and 6,275,027 (4,107,633 coverage corrected) in the German part and 2,560,028 (1,778,451 coverage corrected) in the Latin part in 2022.

In the second part of the analysis including only data from the pandemic period, the association of the hospital occupancy resulting from COVID-19 patients with incidence rates and percentages of ESCR-KP and ESCR-EC was investigated. This analysis was based on a total of 13,875 positive blood cultures (see Supplementary Figure S1 and, for the baseline characteristics of the included patients, Supplementary Table S1). Similar to the previous analysis, ESCR was observed in 10% ($N = 1173$) of *E. coli* and 8% ($N = 199$) of *K. pneumoniae*.

E. coli *and ESCR-EC*

The main findings are summarized in Figure 1 and Table II. Overall, the incidence rates of ESCR-EC were higher in the Latin region compared to the German region. These rates displayed an overall upward trend throughout the entire study period, although this increase did not reach statistical

Table I
Baseline characteristics of the included patients (January 1st, 2015 to August 31st, 2022)

Baseline characteristics	*E. coli*		*K. pneumoniae*	
	ESCR	ESCS	ESCR	ESCS
	$N = 4313$	$N = 36,684$	$N = 664$	$N = 7873$
Female	2050 (48%)	20,641 (56%)	227 (34%)	3173 (40%)
Age (median, IQR)	70 (60, 80)	75 (60, 80)	70 (55, 75)	70 (60, 80)
Latin region	1728 (40%)	12,418 (34%)	305 (46%)	2603 (33%)
Department				
ICU	226 (5.2%)	1254 (3.4%)	73 (11%)	526 (6.7%)
Interdisciplinary	877 (20%)	8909 (24%)	92 (14%)	1684 (21%)
Medicine	705 (16%)	5462 (15%)	148 (22%)	1456 (19%)
Surgery	441 (10%)	2300 (6.3%)	103 (16%)	751 (9.5%)
Other	231 (5.4%)	1708 (4.7%)	44 (6.6%)	378 (4.8%)
Outpatient	1833 (43%)	17,051 (46%)	204 (31%)	3078 (39%)

IQR, interquartile range; ESCR, extended-spectrum cephalosporin-resistant; ESCS, extended-spectrum cephalosporin-susceptible; ICU, intensive care unit.

significance following Bonferroni correction. However, a noteworthy and statistically significant decrease in ESCR-EC incidence was observed for the pandemic period in the Latin region ($P < 0.001$). Conversely, in the German region, there were no significant alterations in both the level and the slope of ESCR-EC incidence rates. Seasonality was not significant in either linguistic region for both the models. The decrease in the Latin region during the pandemic can also be observed in the fit of the exploratory model (Figure 1 and Supplementary Table S2).

When considering the models containing data from the pandemic only, increasing incidence rates were confirmed but a dependence from the COVID-19 patient occupancy rates was not observed (Supplementary Table S3). Similarly, the logistic regression model revealed no significant association between COVID-19 occupancy rates and resistance rates. Nevertheless, this model did identify significant predictors for the resistance rates, including time, linguistic region, hospital type, and sex. These same predictors persisted in the final exploratory model (Supplementary Table S4).
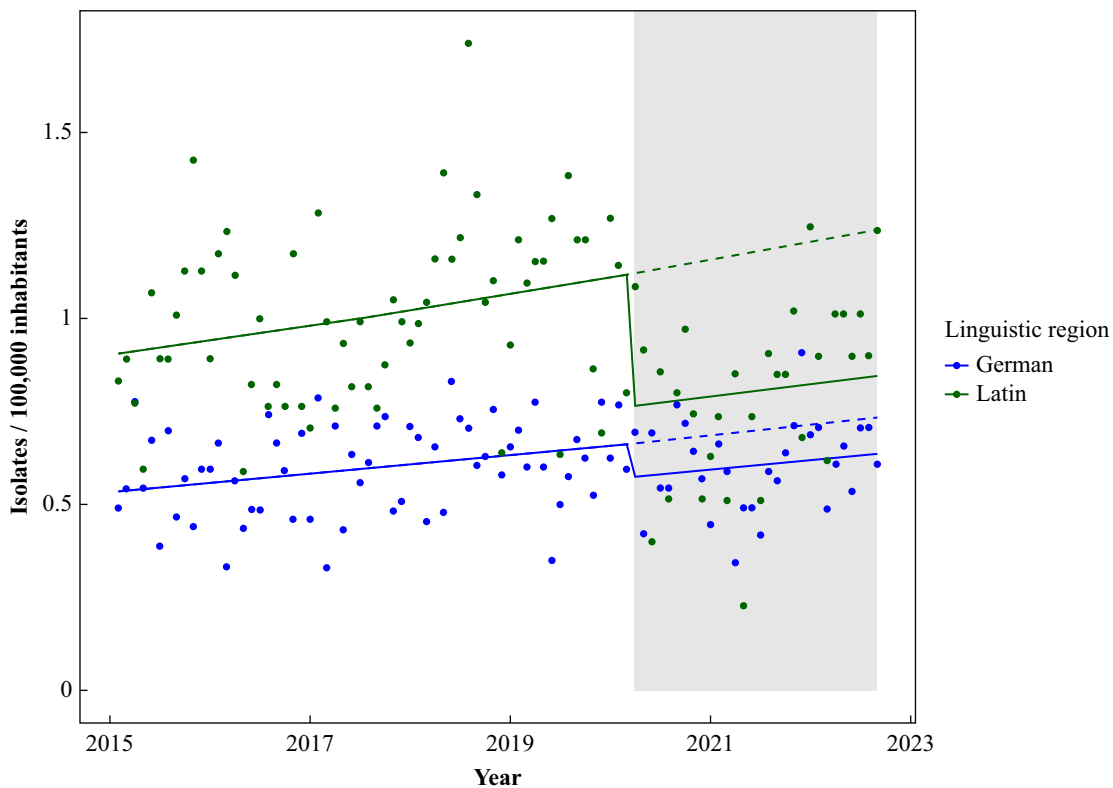

Figure 1. ESCR-EC incidence in the two different linguistic regions of Switzerland and estimates from the exploratory quasi-Poisson model (see Supplementary Appendix for more information). The dashed line shows a counterfactual scenario in which the COVID-19 pandemic had not occurred. The pandemic phase is highlighted in grey.

Table II
Changes in the ESCR-EC bloodstream infection incidence rates in the German and Latin regions of Switzerland during the COVID-19 pandemic

Model	German region			Latin region		
	Estimate	95% CI	P-value[a]	Estimate	95% CI	P-value[a]
Model A: incidence rate changes						
COVID-19	−0.11	−0.25 to −0.04	0.68	−0.41	−0.59 to −0.23	<0.001
Time[b]	0.00	−0.00 to 0.01	0.19	0.00	0.00 to 0.01	0.06
Seasonality[c]						
Term 1	−0.05	−0.11 to 0.01	0.49	−0.02	−0.09 to 0.05	1
Term 2	0.03	−0.03 to 0.09		−0.01	−0.08 to 0.06	
Model B: slope of incidence rate changes						
COVID-19[d]	−0.12	−0.29 to 0.05	1	−0.52	−0.75 to −0.30	0.36
Time	−0.00	0.00 to 0.01		0.00	−0.00 to 0.01	
Interaction	−0.00	−0.01 to 0.01		0.01	−0.00 to 0.02	
Seasonality[c]						
Term 1	−0.05	−0.11 to 0.00	0.50	−0.02	−0.09 to 0.05	1
Term 2	0.03	−0.03 to 0.01		−0.01	−0.08 to 0.06	

ESCR, extended-spectrum cephalosporin-resistant; EC, *E. coli*; CI, confidence interval.
Residual deviance and degrees of freedom illustrate the goodness-of-fit of different models: Model A, German: residual deviance 82.6 on 87 df; Model A, Latin: residual deviance, 88.0 on 87 df; Model B, German: residual deviance, 82.6 on 86 df; Model B, Latin: residual deviance, 85.1 on 86 df.
[a] Bonferroni correction was applied (multiplication of P-values by 4, as for each region models were fitted with and without interaction).
[b] The study month was included as a numeric predictor.
[c] Seasonality: amplitudes of a sine (Term 1) and a cosine (Term 2) component were estimated. The wavelength was set to 12 months.
[d] The COVID-19—time interaction was fitted to detect a change in the slope during the COVID-19 pandemic.

K. pneumoniae *and ESCR-KP*

The main findings are summarized in Figure 2 and Table III. Throughout the entire study period, the incidence rates of ESCR-KP were consistently higher in the Latin region when compared to the German region. Over time, these rates showed an upward trend in both regions, with a statistically significant long-term increase observed only in the German
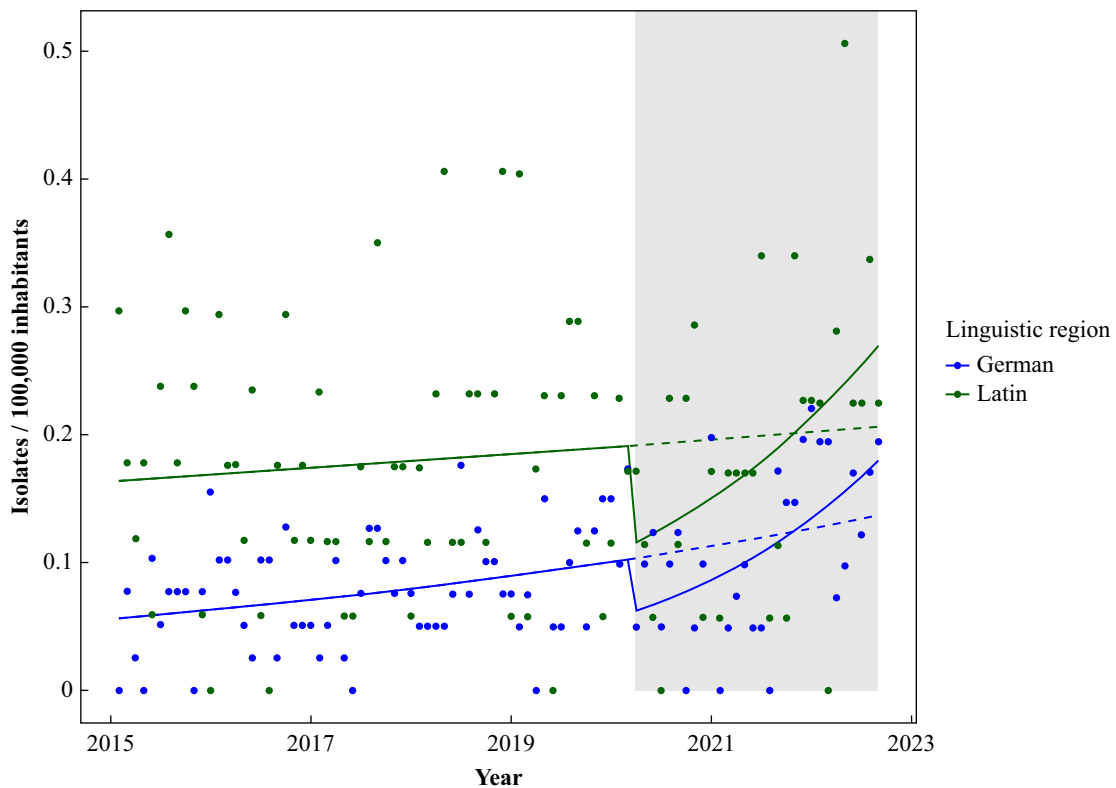

Figure 2. ESCR-KP incidence in the two different linguistic regions of Switzerland and estimates from the exploratory quasi-Poisson model (see Supplementary Appendix for more information). The dashed line shows a counterfactual scenario in which the COVID-19 pandemic had not occurred. The pandemic phase is highlighted in grey.

Table III
Changes in the ESCR-KP bloodstream infection incidence rates in the German and Latin regions of Switzerland

Model	German region			Latin region		
	Estimate	95% CI	P-value[a]	Estimate	95% CI	P-value[a]
Model A: ESCR-KP BSI incidence rate changes						
COVID-19	−0.24	−0.63 to 0.15	1	−0.15	−0.58 to 0.29	1
Time[b]	0.01	0.01 to 0.02	0.007	0.00	−0.00 to 0.01	1
Seasonality[c]						
Term 1	−0.16	−0.32 to −0.00	0.55	−0.07	−0.24 to 0.10	1
Term 2	0.08	−0.07 to 0.24		−0.02	−0.20 to 0.15	
Model B: ESCR-KP BSI slope of the incidence rates						
Increase/decrease during COVID-19[d]						
COVID-19	−0.51	−0.98 to −0.05	0.14	−0.46	−1.00 to 0.06	0.12
Time	0.01	0.00 to 0.02		0.01	−0.01 to 0.01	
Interaction	0.03	0.00 to 0.05		0.03	0.05 to 0.05	
Seasonality[c]						
Term 1	−0.16	−0.32 to −0.01	0.4	−0.07	−0.23 to 0.09	1
Term 2	0.10	−0.06 to 0.25		−0.01	−0.17 to 0.15	

ESCR, extended-spectrum cephalosporin-resistant; KP, *Klebsiella pneumoniae*; CI, confidence interval.
Residual deviance and degrees of freedom illustrate the goodness-of-fit of different models: Model A, German: residual deviance 108.7 on 87 df; Model A, Latin: residual deviance 104.3 on 87 df; Model B, German: residual deviance 103.3 on 86 df; Model B, Latin: residual deviance 98.7 on 86 df.
[a] Bonferroni correction was applied (multiplication of P-values by 4, as for each region models were fitted with and without interaction).
[b] The study month was included as a numeric predictor.
[c] Seasonality: amplitudes of a sine (Term 1) and a cosine (Term 2) component were estimated. The wavelength was set to 12 months.
[d] The COVID-19—time interaction was fitted to detect a change in the slope during the COVID-19 pandemic.

region. A more noticeable increase was observed in both linguistic regions during the COVID-19 pandemic; however, this change in slope did not retain statistical significance after applying Bonferroni correction. Seasonal variations were not found to be statistically significant in either linguistic region. The exploratory model incorporating data from both regions indicated region- and pandemic-specific increases (Figure 2 and Supplementary Table S2).

When focusing on models containing data solely from the pandemic period, a significant increase in ESCR-KP rates during this timeframe was observed, but this increase did not appear to be dependent on the COVID-19 patient occupancy rates, with time and linguistic region being the only predictors in the final exploratory model (Supplementary Table S5). No significant association was observed between the COVID-19 occupancy and the resistance rates in the logistic regression model; by contrast, the predictors time, patient age, hospital type (university vs non-university hospital) and department (ICU vs non-ICU) were significant and retained their significance in the final model of our exploratory analysis, which initially included seasonality and higher-order interactions (Supplementary Table S6).

Discussion

In this comprehensive nationwide study, we have identified a reduction in ESCR-EC rates during the COVID-19 pandemic, with the most notable decline occurring in the region most severely affected by the pandemic. Conversely, an initial non-significant decrease in ESCR-KP BSI incidence was followed by an upward trajectory over time, eventually reverting to and even surpassing pre-pandemic levels.

Overall, knowledge on the influence of the pandemic on clinically relevant infections caused by MDR is limited. Data on ESCR-EC- and ESCR-KP-associated BSI are scarce, conflicting, and mostly limited to the first wave of the pandemic [18—21]. A French multicentre study found a significant increase in the rate of ESCR Enterobacterales BSIs, including ESBL-producing *K. pneumoniae*, during March—April 2020 compared to 2019, accompanied by higher blood culture sampling and antibiotic usage [21]. In a tertiary hospital in Rome, Italy, there was no overall difference in the incidence of ESCR Enterobacterales BSI between the COVID-19 period and a pre-COVID period [18]. A study conducted in a reference centre in Jakarta found similar results, with no increase in the frequency of ESCR-KP and ESCR-EC between 2019 and 2020 [19]. By contrast, a significant decrease was found in the rate of various infections (including BSI) caused by ESBL-producing Enterobacterales during the first and second quarters of 2020 in an American study [22]. Noteworthy, these data need to be interpreted with caution, due to the limited reporting and the fact that more studies are likely to be published in this area in the near future. This reflects conflicting findings from studies on the impact of COVID-19 on AMR (not necessarily invasive infections). In a recent systematic review of 12 studies, it was observed that ESBL-producing *E. coli* and *K. pneumoniae* infections decreased during the COVID-19 pandemic (in contrast with the previous upward trend) while a meta-analysis pooling several resistant Gram-negative organisms did not find a significant effect [6,7]. Even more recently, a Canadian study investigating the ESBL rates in urine cultures showed decreased rates for *E. coli* in both the community and long-term care facilities, but increasing rates for ESBL *K. pneumoniae* rates in the latter [23].

Collectively these observations, along with our own, underscore the intricate interplay between the COVID-19 pandemic and AMR: as far as our knowledge extends, no study has addressed this matter by accounting for the impact of the entire pandemic on distinct regions differentially hit by the

pandemic within an entire country. Furthermore, our findings highlighted how the significance of local circumstances may elucidate the divergent findings reported previously. The reason behind the significant decrease in ESCR-EC — a predominantly community-acquired pathogen — can likely be attributed to the introduction of community preventive measures and the restrictions imposed by the federal government (culminating in the national lockdown on March 16th, 2020) [24]. These measures led to a reduction in travel, movement, and overall interpersonal contacts, subsequently resulting in a decrease in the transmission of pathogens, and, secondarily, in the observed reduction in the use of antibiotics, the main driver of MDR [25,26].

Conversely, the rise of ESCR-KP, primarily a pathogen acquired within healthcare settings, might be linked to the heightened usage of empirical broad-spectrum antibiotics in inpatients, to the occurrence of hospital outbreaks, as reported in several studies, and to challenges such as patient overflow and understaffing [21,25,27,28].

Notably, our in-depth analysis did not reveal any discernible association between the increase in hospital occupancy due to COVID-19 patients and the incidence or the resistance rates of the bacteria included. Conversely, university hospitals and ICUs (where the usage of broad-spectrum antibiotics is more prominent and where outbreaks were most often described) were found to be predictors for ESCR-KP. Nevertheless, more nuanced and challenging-to-attribute factors might have contributed. For instance, the latter phase of the study was characterized by a substantial upsurge in migration from regions characterized by higher rates of AMR [29].

Our study has several limitations. Clinical individual patient data, including baseline comorbidities, reasons for hospital admission, source of BSI and presence of risk factors (e.g. indwelling urinary catheters), COVID-19 status at individual level, and antibiotic exposure information were not available in the datasets used for our study. Second, information on the site of acquisition of BSI (community vs hospital-acquired) was incomplete and an analysis was not possible. Roughly, 40% of the blood cultures were collected from outpatients, with a substantial majority likely being obtained in emergency rooms from patients who were subsequently hospitalized. Third, if the burden of hospitalized COVID-19 patients does not seem to significantly impact the outcome, we could only hypothesize the reasons behind the presented results, and we might not have been able to account for certain relevant confounders, such as migration patterns and government-imposed measures/restrictions in response to the pandemic. A more intricate model featuring additional predictors and, perhaps, shorter time intervals could have better represented the data, yet such complexity might elevate the risk of overfitting. Switzerland is a country with relatively low incidences, especially concerning ESCR-KP. It is conceivable that higher incidences would have resulted in more statistical power. Finally, we focused on ESCR rather than ESBL because the focus of ANRESIS is on phenotypic rather than genotypic data. Notably, a previous ANRESIS study analysed a subset of isolates in Switzerland, suggesting that 93–96% of ESCR isolates in Switzerland were true ESBL [30]. ESCR may therefore be used as a proxy for ESBL.

One of the key strengths of our study is the comprehensive nationwide data collection, spanning five years before and during the COVID-19 pandemic. This extensive dataset includes information from all university and tertiary hospitals, enabling us to stratify the data according to different linguistic and sociocultural regions. This is particularly valuable due to the country's heterogeneity, as different regions were impacted differently by the pandemic. Another strength is the statistical methodological approach used here. The separation of inference testing models from exploratory models allowed hypotheses to be tested without a bias that might be introduced during model development, while still providing evidence of further complex relationships that were not considered when the original hypotheses were formulated. Such evidence may then lead to new hypotheses that can be tested with new independent data (e.g. from other countries).

In conclusion, in the early phase of the COVID-19 pandemic, a decrease in ESCR rates was observed, particularly in ESCR-EC BSI within the most heavily impacted region.

Author contributions

Study conception: L.D., M.G., N.B.; data collection: A.K.; data processing, modelling and statistical analyses: L.D., M.G.; data interpretation: L.D., M.G., N.B., A.K.; drafting the manuscript: L.D., M.G.; approving the final version: L.D., M.G., N.B., A.K.

Conflict of interest statement
None declared.

Ethics statement
This study was based on national surveillance data submitted to the Swiss Centre for Antibiotic Resistance ANRESIS. Because of the anonymous nature of the data, neither ethical approval nor written informed consent from patients was required.

Data availability
All data can be made available upon request to the corresponding author.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2024.05.013.

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