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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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Background
The COVID-19 pandemics has influenced several aspects of infection control and prevention, such as antimicrobial prescribing and consumption or the epidemiology of healthcare-associated infections. Its association with the incidence of clinically relevant infections caused by multidrug-resistant organisms remains, however, a topic of debate.

Objectives
The aim of this study was 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 (German and Latin, respectively), each exhibiting varying pre-pandemic antimicrobial resistance patterns and that were impacted differently by the pandemic. Subsequently, to better understand the reasons for the observed results, we investigated the potential association between regional monthly COVID-19 patient occupancy rates and these incidence rates.

Methods
We analysed data of positive blood cultures prospectively collected by the nationwide surveillance system (ANRESIS) from January 1, 2015, to August 31, 2022. Incidence rates of BSI were calculated using corrected population data provided by the Swiss Federal Statistical Office as denominator. To explore the potential relationship between COVID-19 patient occupancy and ESCR incidence rates, we conducted an in-depth analysis over the two-year pandemic period from April 1, 2020, to March 30, 2022, using the data provided by the Swiss Federal Office of Public Health as denominator. We employed Quasi-Poisson and logistic regression analyses to investigate these associations.

Results
During the study period, a total of 40997 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. Overall, ESCR incidence rates were higher in the Latin region compared to the German region and showed an upward trend in both regions. A significant ($p<0.001$) reduction in ESCR-EC BSI incidence occurred during the pandemic in the Latin region, which exhibited the highest COVID-19 incidence (Fig.1). Conversely, ESCR-KP BSI incidence initially fell considerably and then increased during the pandemic in both regions, however, this effect was not statistically significant (Fig.2). No association between hospital occupancy from COVID-19 patients and these trends was observed.

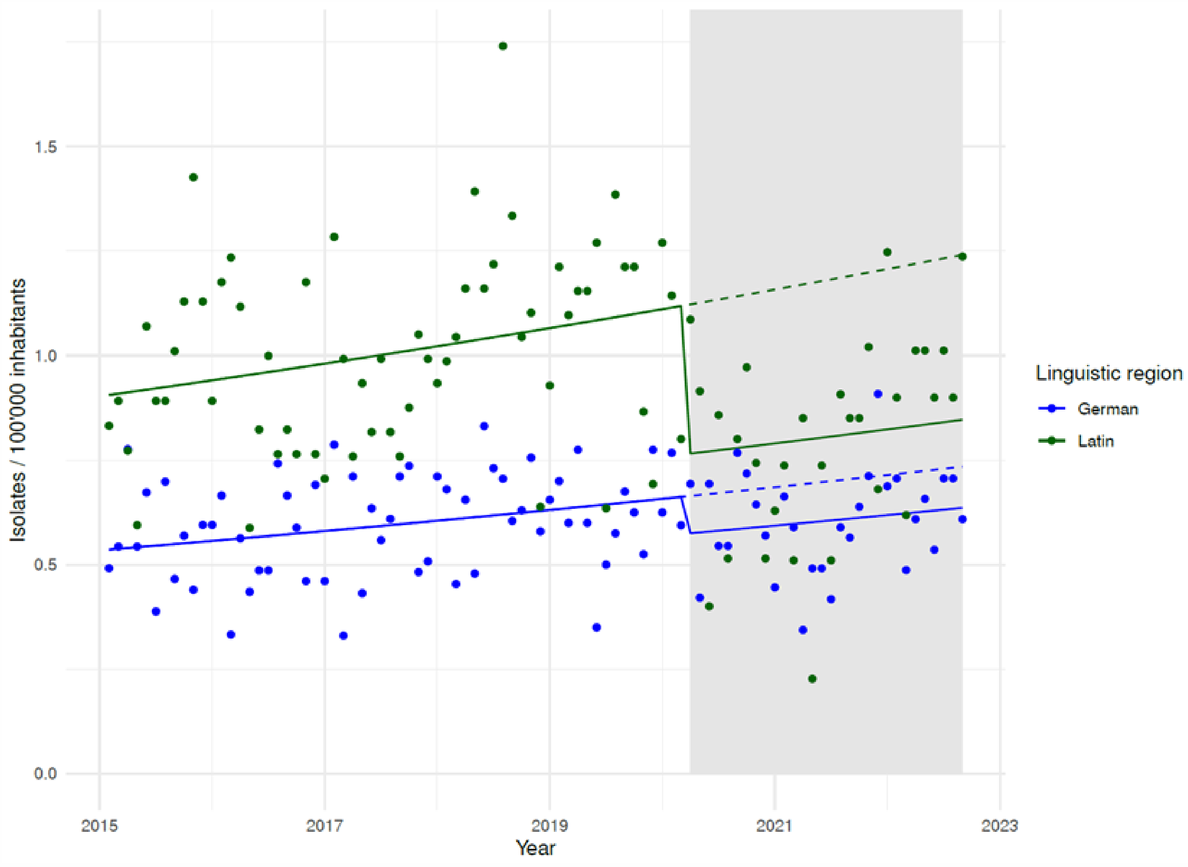

Figure 1: ESCR-EC incidence in the two different linguistic regions of Switzerland and estimates from a quasi-Poisson model. The dashed line shows a counterfactual scenario in which the COVID-19 pandemic had not occurred. The pandemic phase is highlighted in grey.

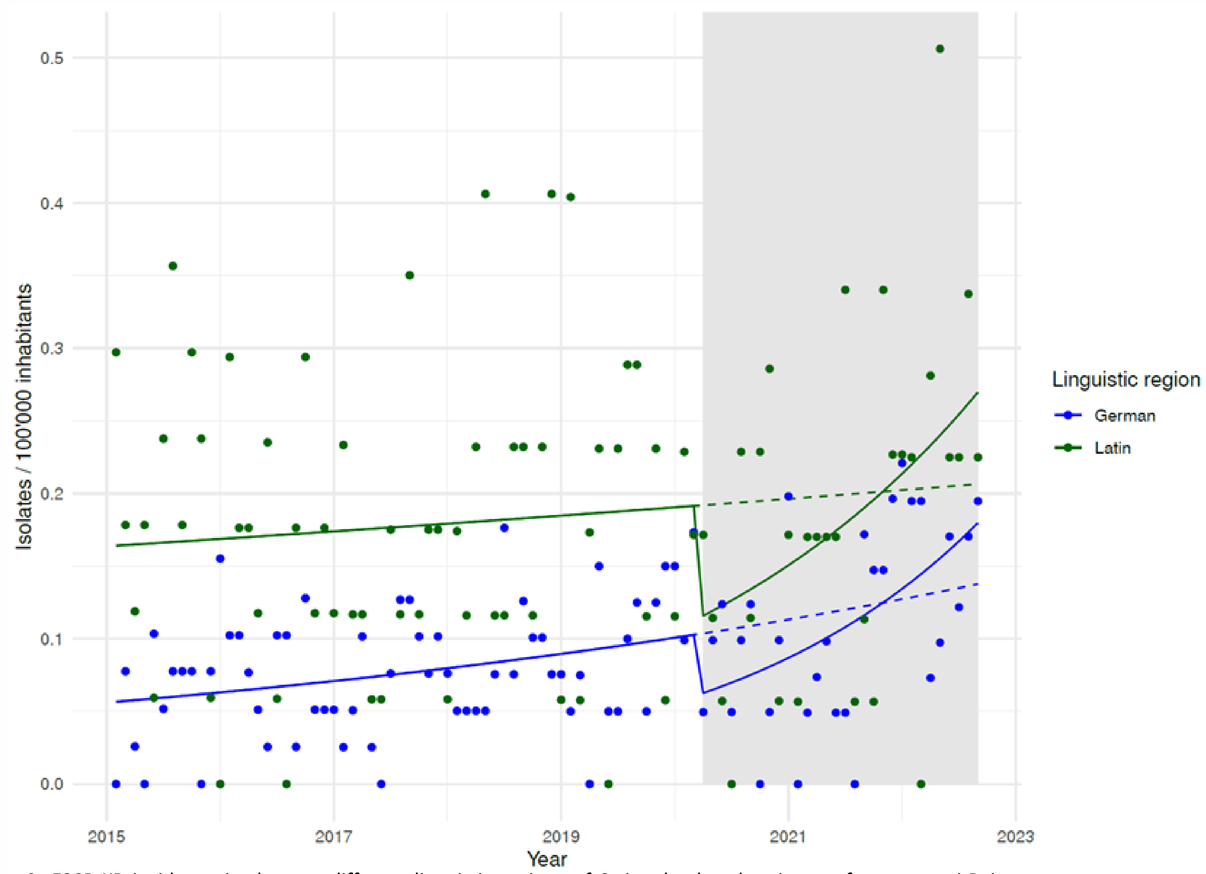

Figure 2: ESCR-KP incidence in the two different linguistic regions of Switzerland and estimates from a quasi-Poisson model. The dashed line shows a counterfactual scenario in which the COVID-19 pandemic had not occurred. The pandemic phase is highlighted in grey.

Discussion and conclusions
In this comprehensive nationwide study, we have identified a reduction in ESCR-EC BSI incidence 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 rates was followed by an upward trajectory over time, eventually reverting to and even surpassing pre-pandemic levels. The in-depth analysis did not reveal any discernible association with the hospital occupancy due to COVID-19 patients.