P0096

Association of fluoroquinolone consumption and ciprofloxacin resistance rates in *Escherichia coli* of urinary tract infections in the outpatient sector, Switzerland 2004 – 2021

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Background

- Antibiotic resistance is a major public health threat, with antibiotic use in outpatient settings contributing to the development of community resistance patterns (1,2).
- In Switzerland, more than 80% of antibiotics are used in outpatient settings. Despite concerns regarding their overuse and the emergence of fluoroquinolone-resistant *E. coli,* fluoroquinolones still accounted for 20% of prescriptions for lower urinary-tract infections in Switzerland in 2021 (5).
- The excessive use of fluoroquinolones in Switzerland has paralleled with the increase in the prevalence of quinolone-resistant *E. coli* (3,5).
- As fluoroquinolones play a crucial role in treating non-urinary infections, they are no longer recommended as the first-line antimicrobial agent for uncomplicated UTIs (4).

Objective

- The objective of this study is to examine the trends and relationship between fluoroquinolone consumption and ciprofloxacin resistance among urinary *E. coli* isolates in the outpatient setting from 2004 to 2021 in Switzerland.

Methods

- A retrospective observational study spanning 18 years (2004-2021) was conducted to investigate the correlation between antibiotic consumption and resistance rates of *E. coli* from outpatient urine specimens in Switzerland.
- Fluoroquinolone (ciprofloxacin, norfloxacin, levofloxacin, moxifloxacin) consumption and ciprofloxacin-resistance data were obtained from the Swiss Centre for Antibiotic Resistance (ANRESIS) database.
- A total of 450'799 urine sample isolates were included in the study. The isolates were collected from general practitioners and gynecologists across the French-speaking (45.0%), German-speaking (48.5%), and Italian-speaking (6.5%) parts of Switzerland. To remove duplicate entries for patients from the dataset, only the isolate with the highest resistance level per year was selected and included in the analysis.
- Pearson correlation analyses and mixed logistic regression models were used to analyze the data and investigate the potential correlation between antibiotic consumption and resistance rates of *E. coli*.

Results

- Outpatient fluoroquinolone consumption in Switzerland peaked in 2007, then declined significantly over the years, with an overall downward trend (Figure 1A).
- The ciprofloxacin resistance rate for *E.coli* urine sample isolates initially increased from 12.5% in 2004 to a peak of 16.9% in 2011. Subsequently, there was a general trend of decline in resistance rates, reaching a low of 10.2% in 2021 (Figure 1B).
- The results of the Pearson correlation coefficient analysis demonstrated a statistically significant positive correlation between fluoroquinolone consumption and the ciprofloxacin *E.coli* resistance rate (R2 = 0.65, p < 0.01) (Figure 1C).
- Regional differences can be observed. According to the correlation analysis, there is no correlation in the French-speaking region, a strong positive correlation in the German-speaking region, and a weak positive correlation in the Italian-speaking region (Figure 1D).
- Age- and sex-dependent effects were observed in *E. coli* resistance rates (Figure 2). These findings were supported by a mixed-effects logistic regression model, which, in addition to the correlation, indicates that males have 1.4 times higher odds of carrying resistant *E. coli* than females (p < 0.01), while younger individuals have lower odds of carrying a resistant isolate (16-45 years: 0.4; 46-65 years: 0.58, p < 0.01).

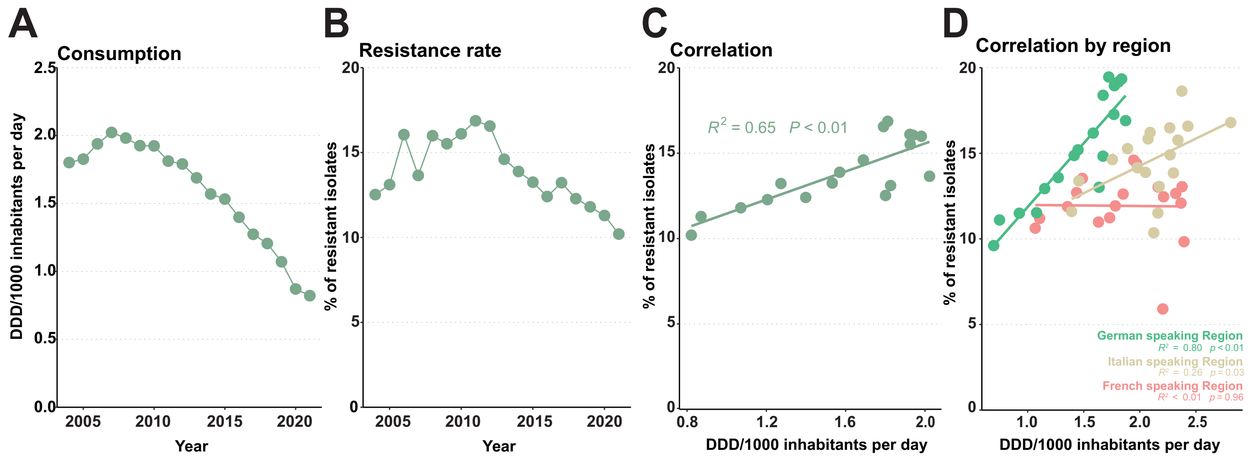

Figure 1. Trends in Outpatient Fluoroquinolone Consumption and E. coli Resistance Rates in Switzerland from 2004 to 2021. This figure displays the temporal changes in outpatient fluoroquinolone consumption and E. coli resistance rates in Switzerland. Panels A and B show the patterns of consumption and resistance rates, respectively, while Panel C depicts the association between these variables for the entire country. Panel D extends the analysis to the linguistic regions of Switzerland.

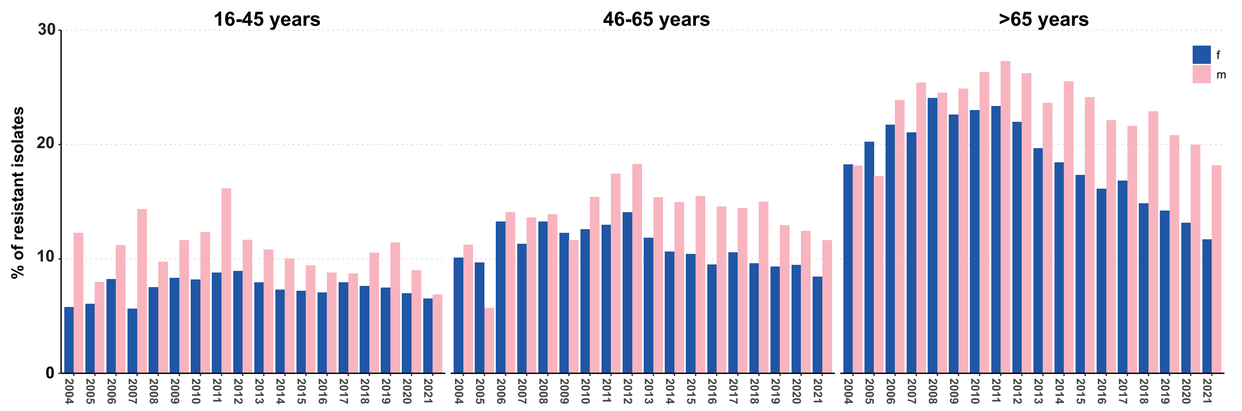

Figure 2. Sex and Age-Dependent Trends in E. coli Resistance Rates in Switzerland from 2004 to 2021. Barplots illustrating the trends in *E. coli* resistance rates for males and females, as well as age categories (16-45 years, 46-65 years, and over 65 years), from 2004 to 2021 in Switzerland.

Conclusions

- This study found a significant correlation between outpatient fluoroquinolone consumption and fluoroquinolone resistance in *E. coli* in outpatient urine samples in Switzerland, with regional and demographic differences.
- These findings suggest that changes in therapy guidelines have resulted in reduced fluoroquinolone consumption and a subsequent decline in resistance rates, although this impact may be delayed. The observed trend highlights the effectiveness of adapting guidelines to reduce inappropriate use of antibiotics in the outpatient setting.

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