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Original Study

Molecular Epidemiology and Risk Factors for Extended-Spectrum β-Lactamase–Producing *Enterobacterales* in Long-Term Care Residents

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A B S T R A C T

Objectives: We aimed to assess the burden of extended-spectrum β-lactamase (ESBL)-producing *Enterobacterales* in Swiss long-term care facilities (LTCFs) to describe the molecular epidemiology, describe the intrainstitutional and regional clusters of resistant pathogens, and identify independent institution- and resident-level factors associated with colonization.
Design: Cross-sectional study.
Setting and Participants: From August to October 2019, we performed a point prevalence study among residents from 16 LTCFs in Western and Eastern Switzerland (8 per region).
Methods: Residents underwent screening for ESBL-producing *Enterobacterales* (ESBL-E); whole-genome sequencing (WGS) was performed. We gathered institution-level (eg, number of beds, staff-resident ratio, alcoholic hand rub consumption) and resident-level [eg, anthropometric data, time in facility, dependency, health care exposure, antibiotic treatment, proton-pump inhibitor (PPI) use] characteristics. Factors associated with colonization were identified using a generalized linear model.
Results: Among 1185 eligible residents, 606 (51%) consented to the study. ESBL-E prevalence was 11.6% (70/606), ranging from 1.9% to 33.3% between institutions, with a median of 12.5% in the West and 6.9% in the East ($P = .03$). Among 59 *Escherichia coli* (from 58 residents), multilocus sequence type (ST) 131 was most common (n = 43/59, 73%), predominantly its subclone *H*30R1 (n = 37/43, 86%). WGS data identified multiple intrainstitutional and regional clusters. Independent risk factors for ESBL carriage were previous ESBL colonization [adjusted odds ratio (aOR) 23.5, 95% confidence interval (CI) 6.6-83.8, $P < .001$), male gender (aOR 2.6, 95% CI 1.5-4.6, $P = .002$), and use of PPIs (aOR 2.2, 95% CI 1.2-3.8, $P = .01$).
Conclusions and Implications: Overall ESBL-E prevalence in Swiss LTCF residents is low. Yet, we identified several clusters of residents with identical pathogens within the same institution. This implies that particularly affected institutions might benefit from targeted infection control interventions. PPI use was the only modifiable factor associated with carriage of ESBL producers. This study adds to the growing list

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of adverse outcomes associated with PPIs, calling for action to restrict their use in the long-term care setting.

Residents of long-term care facilities (LTCFs) are at particular risk of being colonized and developing infections with antibiotic-resistant pathogens.[1,2] Given the constant patient transfer between acute care facilities and LTCFs, these institutions are considered as potential catalysts for the dissemination of resistant pathogens within health care networks.[3] Notably, hyperendemic clones, often carrying plasmids encoding for extended-spectrum β-lactamases such as *Escherichia coli* ST131 or *Klebsiella pneumoniae* ST258, have a propensity to spread within the older population and within residents of LTCFs.[4,5] As a consequence, these high-risk clones are often responsible for so-called clustering of cases (ie, detection of identical pathogens within different residents in a particular institution) within LTCFs.[6]

In general, compared to infections with their sensitive counterparts, infections due to resistant pathogens are associated with prolonged length of hospital stay and even with increased mortality in some studies.[7–9] One factor complicating the management of these infections is that identified pathogens often remain susceptible to only intravenously administered substances.[10] Particularly in long-term care, the need for a venous catheter poses additional challenges for both the caregiver and the patient.

Understanding factors promoting antibiotic resistance is important to inform best practices and to reduce the burden of resistance. Risk factors for colonization with resistant pathogens in long-term care residents include recurrent exposure to health care and antibiotic substances,[11] being bedridden,[12] high dependency or physical inability,[13] and presence of medical devices.[14] Another potentially modifiable factor, which has been suggested to increase the risk of colonization with resistant pathogens, is the use of proton-pump inhibitors (PPIs).[15] Institution-level factors associated with increased risk include low staffing,[14] low adherence to hand hygiene and use of PPE,[16] and less stringent implementation of infection prevention guidelines.[17,18]

The burden of antimicrobial resistance (AMR) in Swiss LTCFs remains largely unknown.[19] Previous studies in this setting have focused on methicillin-resistant *Staphylococcus aureus* (MRSA).[20] Data on extended-spectrum β-lactamase (ESBL)-producing *Enterobacterales* (ESBL-E) are lacking, although laboratory-based surveillance data suggest a substantial increase of ESBL-E over the past decade.[10,19] We aimed to assess the prevalence and describe the molecular epidemiology of ESBL-E among LTCF residents from 2 geographic regions in Switzerland. We also aimed to identify intra- and interinstitutional clusters of pathogens based on next-generation sequencing (NGS) and to assess institution- and resident-level risk factors for carriage of resistant pathogens.

Methods

Selection of Institutions and Residents, and Ethical Approval

LTCFs in the cantons of Vaud (VD), Western Switzerland, and St Gallen (SG), Eastern Switzerland, with ≥40 residents were invited to participate. Residents with a life expectancy of >7 days were eligible. Local staff contacted the residents (or their next of kin in case of dementia) for participation and obtained oral informed consent. Consenting residents, who showed obvious discomfort during the screening procedure, were excluded. The study was approved by the local ethic commissions (#2019-00087).

Study Design and Procedures

This multicenter point prevalence study was performed between August and October 2019. Every institution was visited by at least 2 study team members; data were collected within 1-2 days. Institutional characteristics were collected according to the HALT protocol.[21] Resident characteristics included age, sex, presence of urinary/vascular catheters, dementia, disorientation, immobility (ie, wheelchair or bedbound), presence of wounds or decubital ulcers, Katz index,[22] day of admission, hospital admissions, endoscopic examinations and antibiotic treatment (all within 6 months before the study), use of PPIs at the time of the study, and previous (timely unrestricted) documentation of ESBL-E. Residents underwent rectal (all), urine (in case of urine catheters), or wound (if applicable) screening for ESBL-E. Screenings were performed using eSwabs (rectal and wound) or by collecting catheter urine, either by the study team or the institutional care teams. Samples from both geographic regions were sent to the same microbiology laboratory for further processing.

Microbiology Processing

For ESBL-E screening, 10 μL of the preservation liquid of an eSwab (or urine) were inoculated into enrichment broth (trypticase soy broth). Following 24-hour incubation, chromID ESBL (enabling growth of ESBL-producing gram-negatives) were inoculated with 10 μL enriched trypticase soy broth. In case of bacterial growth after 19-hour incubation at 36° C, identification at the species level was done with MALDI-ToF mass spectrometry (MALDI Biotyper Smart System, Bruker Daltonics, Bremen, Germany), using the BDAL 9.0 database. Depending on the actual susceptibility test patterns reported by the BD Phoenix M50 (Becton Dickinson, Sparks, MD), further confirmation tests were performed (E-test ESBL confirmation with specific E-test stripes, purchased from bioMérieux, Marcy l'Etoile, France).

Whole Genome Sequencing and Definition of Clusters

For further molecular characterization, isolates identified as ESBL-E were sent to the Clinical Bacteriology Laboratory of the University Hospital Basel. DNA was extracted using the EZ1, Qiacube robotic system (Qiagen, Hilden, Germany) followed by library preparation using Nexteraflex (Illumina, San Diego, CA) and sequencing on a NextSeq500 platform (Illumina) in the ISO 17025–accredited facility. All were sequenced to a mean coverage over 20×, and following assembly with Unicycler v0.3.0 b,[23] all genomes passed the Ridom Seqsphere+ (Jünemann, Updating benchtop sequencing performance comparison) criterion of possessing >90% of the core genome MLST targets (https://www.cgmlst.org/ncs/schema/5064703/). Clusters were defined as ≥2 isolates from different patients with a genetic difference of ≤10 cgMLST alleles. We assessed patient clusters within institutions, but also clusters between institutions of the same geographic region (ie, regional clusters). MLST sequence types were determined within Ridom Seqsphere + according to the Warwick scheme. FimH typing of ST131 genomes was performed using FimTyper,[24] and H30Rx isolates were defined according to previously published criteria.[25]

Table 1
Baseline Characteristics of Long-Term Care Residents Undergoing and Those Not Undergoing Screening (Factor Present/Not Present at Time of the Study if Not Specified Otherwise)

Characteristics	Screening (n = 606)	No Screening (n = 579)	*P* Value
West (canton of Vaud)	265 (43.7)	320 (55.3)	**<.001**
Age, y, mean (SD)	84.1 (11)	84.9 (33)	.57
Female	411 (67.8)	426 (73.6)	**.035**
Urinary catheter	83 (13.7)	28 (4.8)	**<.001**
Incontinence	396 (65.3)	364 (62.9)	.41
Decubitus	22 (3.6)	17 (2.9)	.61
Other wound	52 (8.6)	43 (7.4)	.53
Disoriented	325 (53.6)	303 (52.3)	.70
Dementia	270 (44.6)	275 (47.5)	.34
Wheelchair or bedbound	225 (37.1)	185 (32.0)	.07
Surgery previous 30 d	7 (1.2)	4 (0.7)	.60
Proton-pump inhibitor	210 (34.6)	206 (35.6)	.79
Antibiotic treatment	16 (2.6)	18 (3.1)	.76

SD, standard deviation.
Values are n (%) if not stated otherwise.
P values <.05 are given in bold.

Data Analysis and Statistics

Baseline characteristics of screened and nonscreened residents were compared using descriptive statistics. Categorical variables were compared using chi-square or Fisher exact test, as appropriate; continuous variables were compared with the Mann-Whitney *U* test. The prevalence of positive screenings was calculated for every institution, with the number of screened individuals as denominator.

For univariable analysis, institutional characteristics were compared between institutions with high (above median) and low (below median) ESBL-E prevalence. Resident-level characteristics were analyzed regarding their association with ESBL-E colonization using logistic regression. For both institution- and resident-level variables, those reaching statistical significance in univariable analyses were entered into a multivariable model. Collinearity was tested calculating the variance inflation factor (cut off >5). We used a generalized linear mixed model adjusting for random effects on the institutional level. In a subgroup analysis, resident-level characteristics between those colonized with *E coli* ST131 vs other sequence types were compared using descriptive statistics. Two-sided *P* values ≤ .05 were considered statistically significant; statistical analyses were performed using R, version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Institutions and Residents

We included 8 LTCFs in Western and 8 in Eastern Switzerland with a mean of 73 and 75 residents, respectively (Supplementary Figure 1, Supplementary Table 1). Among 1185 eligible residents, 606 (51.1%) underwent screening for resistant pathogens (Table 1). The mean number of screened residents across LTCFs was 38 (range 16-56). Screened residents were more likely to be male (32% vs 26%, $P = .04$), to have a urinary catheter (14% vs 5%, $P < .001$), and to be located in the East (55% vs 44% in the West, $P < .001$). Of note, 35% and 36%, respectively, of screened and nonscreened residents were treated with a PPI on the day of the survey ($P = .79$).

Prevalence, Coresistances, and Molecular Epidemiology

Among 606 screened residents, 70 (11.6%) had at least 1 positive screening result for ESBL-E. Among the 70 residents, 68 had positive rectal screening, 1 had a positive urine (declined rectal screening), and 1 a positive wound swab (negative rectal screening). Most residents with ESBL-E were colonized with *E coli* (n = 62; 89%), followed by *K pneumoniae* (n = 5; 7%). One resident was colonized with 2 different *E*

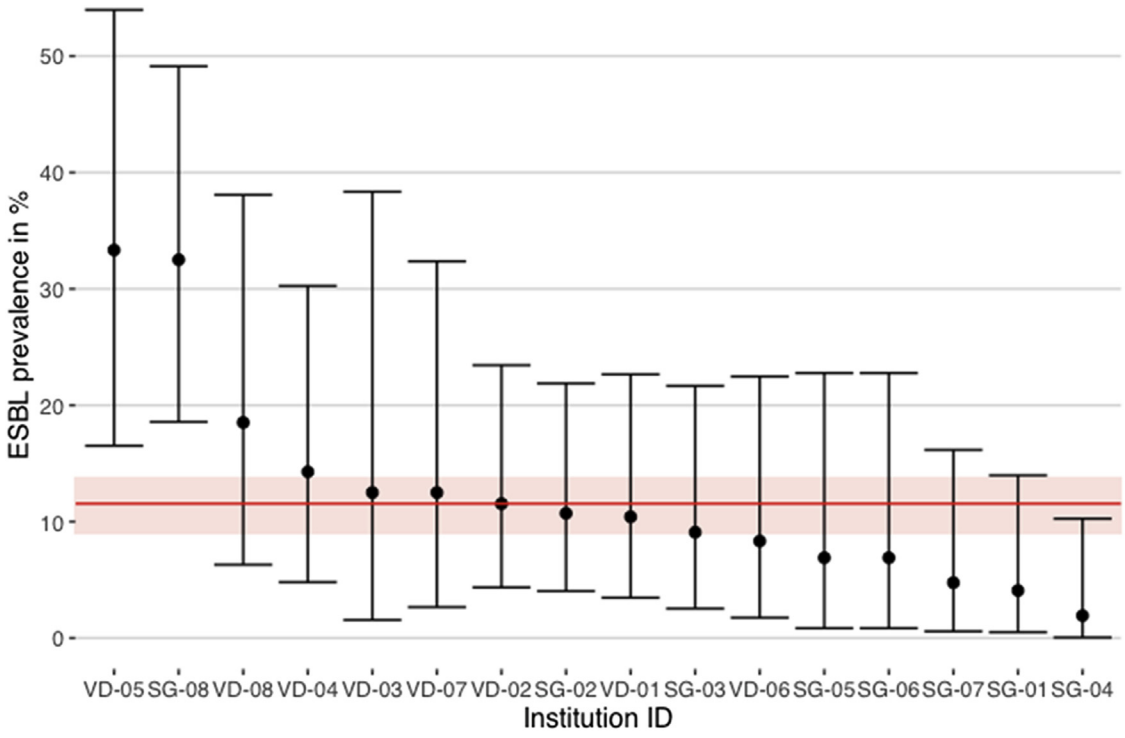

Fig. 1. ESBL prevalence (*y* axis) among residents in 16 Swiss long-term care facilities (dots represent institutional prevalence; bars, 95% CIs) and overall prevalence (red line represents overall prevalence; red band, 95% CI). *x* axis: Long-term care facilities from the West start with the abbreviation VD (Vaud), those from the East with SG (St Gallen); 2-digit numbers denote the different facilities. ID, identifier.

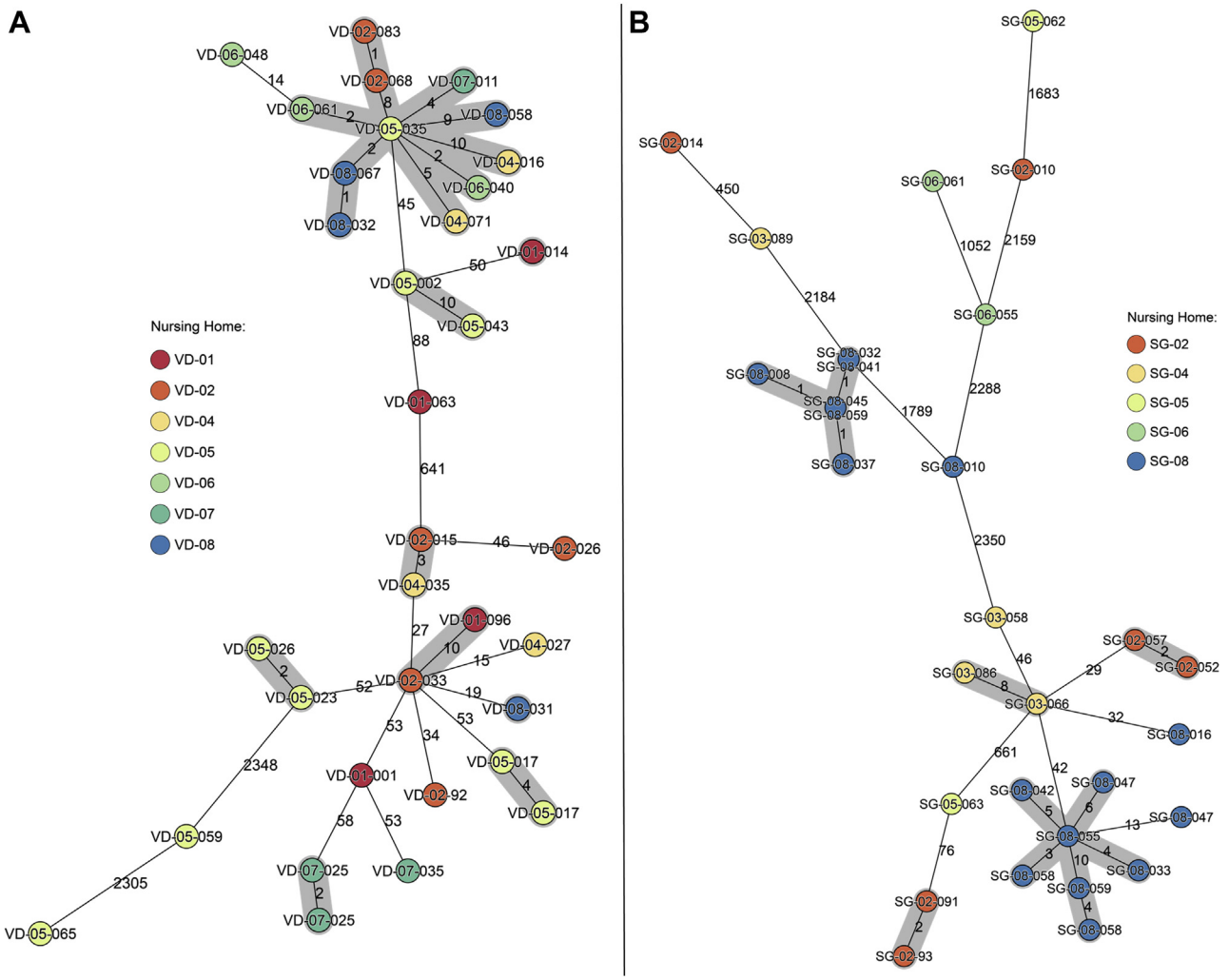

Fig. 2. Results of next-generation sequencing showing extended spectrum β-lactamase producing *Escherichia coli* isolates from (A) the Western and (B) the Eastern part of Switzerland. Colors followed by 2-digit numbers denote long-term care facilities for each region; facilities from the West start with the abbreviation VD (Vaud), those from the East with SG (St Gallen); the 3-digit number at the end stands for individual residents. Numbers on lines between colored circles show number of single-nucleotide polymorphisms (ie, genetic distance between isolates). Cluster defined as distance of 10 single-nucleotide polymorphisms or less.

coli STs (Supplementary Table 2). On the institutional level, ESBL-E prevalence ranged from 1.9% to 33.3% (Figure 1), with a median of 12.5% in the West and 6.9% in the East ($P = .03$). Institutional characteristics were similar between facilities with high and those with low prevalence (Supplementary Table 1).

NGS was performed on 67 nonduplicated ESBL-E (59 E coli and 8 non-*E coli*) from 66 residents. Of the 59 *E coli*, the most commonly detected ST was ST131 (n = 43, 73%), with a higher proportion in the West (91%) than in the East (54%) (Supplementary Table 2, Supplementary Figure 2). All the isolates possessing the type 1 fimbriae FimH30 allele (n = 24/43, 56%) were resistant to ciprofloxacin (*H*30R). ST131 most commonly harbored $bla_{\text{CTX-M-14}}$ (n = 23/43; 53%) or $bla_{\text{CTX-M-27}}$ (n = 14/43, 33%) (*H*30R1), and 4 (9%) carried $bla_{\text{CTX-M-15}}$ (*H*30Rx). Among the 4 *K pneumoniae* isolates sequenced, 3 different STs were found, none of them belonging to any high-risk clone (Supplementary Table 2).

Clustering of ESBL-E Within and Between LTCFs

We identified 7 (2 in VD, 5 in SG) intrainstitutional ESBL–*E coli* clusters (range of 2-7 residents); 2 large clusters caused by ST131 (6 residents) and ST69 (6 residents) (with 1 resident being colonized with both ST131 and ST69) were detected in 1 single LTCF in SG. We detected 3 (all in VD) interinstitutional clusters (2 with 2 patients, respectively, and 1 with 11 patients from 6 institutions). This large cluster was caused by $bla_{\text{CTX-M-14}}$-producing *E coli* ST131 (*H*30R1), and no common link (eg, spatiotemporal overlap in acute care hospital or endoscopy at the same center) was evident for these residents (Figure 2). No clustering between geographic regions was observed. For ESBL–*K pneumoniae*, we found 1 putative intrainstitutional cluster involving 2 patients.

Risk Factors for ESBL-E and for ESBL–E coli ST131

In univariable analysis, previous ESBL-E colonization was the strongest risk factor for ESBL-E [odds ratio (OR) 29.6, 95% confidence interval (CI) 9.0-97.2, $P < .001$]. PPI use was documented for 175 of 536 (32.6%) of ESBL-negative, and for 35 of 70 (50%) ESBL-positive residents, translating into an OR of 2.2 (95% CI 1.3-3.6, $P = .003$). No collinearity was detected between variables entered in multivariable analysis. Independent risk factors for ESBL-E were previous ESBL colonization with an adjusted OR (aOR) of 23.5 and a 95% CI of 6.6-83.8 ($P < .001$), male gender (aOR = 2.6, 95% CI 1.5-4.6,

Table 2
Univariable and Multivariable Analysis of Risk Factors Between ESBL-E-Negative and ESBL-E-Positive Residents

Characteristics	ESBL Negative (n = 536)	ESBL Positive (n = 70)	Univariable Logistic Regression		Multivariable Logistic Regression	
			OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Western Switzerland	227 (42.4)	38 (54.3)	1.8 (0.8-3.9)	.13	NA	NA
Age, y, median (IQR)	87 (80-92)	84.5 (70-89)	**0.97 (0.95-0.99)**	**.006**	0.99 (0.96-1.00)	.46
Male sex	157 (29.3)	38 (54.3)	**3.0 (1.8-5.0)**	**<.001**	**2.6 (1.5-4.6)**	**.001**
Urinary catheter	67 (12.5)	16 (22.9)	1.7 (0.9-3.3)	.10	NA	NA
Decubitus	18 (3.4)	4 (5.7)	1.5 (0.5-4.6)	.53	NA	NA
Wound	47 (8.8)	5 (7.1)	0.8 (0.3-2.1)	.66	NA	NA
Wheelchair or bedbound	193 (36.0)	32 (45.7)	1.4 (0.8-2.4)	.22	NA	NA
Incontinence	346 (64.6)	50 (70.4)	1.4 (0.8-2.4)	.27	NA	NA
Disorientation	291 (54.3)	34 (47.9)	0.9 (0.5-1.5)	.64	NA	NA
Dementia	240 (44.8)	30 (42.3)	1.0 (0.6-1.7)	.91	NA	NA
Years in facility, median (IQR)	2 (1-5)	2.5 (1-5)	1.0 (0.9-1.1)	.66	NA	NA
Katz-Score, median (IQR)	16 (10-20)	17 (13-21)	1.03 (0.98-1.08)	.21	NA	NA
Proton-pump inhibitor	175 (32.6)	35 (50.0)	**2.2 (1.3-3.6)**	**.003**	**2.2 (1.2-3.8)**	**.007**
Previous ESBL detection	5 (0.9)	12 (17.1)	**29.6 (9.0-97.2)**	**<.001**	**23.5 (6.6-83.8)**	**<.001**
Previous hospital admission	88 (16.4)	17 (24.3)	1.6 (0.9-3.0)	.13	NA	NA
Previous endoscopy	8 (1.5)	1 (1.4)	1.3 (0.2-10.8)	.84	NA	NA
Previous antibiotic treatment	175 (32.6)	33 (47.1)	**1.7 (1.0-2.9)**	**.04**	1.2 (0.7-2.1)	.57

IQR, interquartile range; NA, not available.
Values are n (%) if not stated otherwise. OR, 95% CI, and *P* values are from logistic regression analysis.
P values <.05 are given in bold.

$P = .001$), and current PPI use (aOR = 2.2, 95% CI 1.2-3.8, $P = .007$) (Table 2).

In the subgroup of residents colonized with ESBL-E, the only risk factor associated with ESBL–*E coli* ST131 was residence in Western Switzerland (Supplementary Table 3).

Discussion

In this multicenter point prevalence study among 606 residents from 16 Swiss LTCFs, we found an ESBL-E prevalence of 11.6%. ESBL–*E coli* ST131 (mostly *H*30R1) was the most common ST. The only modifiable risk factor for ESBL-E carriage was treatment with a PPI. The large sample size, inclusion of institutions from 2 geographical areas, and the use of NGS are particular strengths of the study.

The ESBL-E prevalence of 11.6% is similar to other Middle European countries. Data from LTCFs in Germany and Austria have shown an ESBL-E prevalence of 15% and 13%, respectively.[26,27] In a systematic review from 2017, global ESBL-E prevalence among LTCF residents was estimated at 18% (range 5%-70% between countries).[28] These results suggest that Swiss LTCFs are not (yet) a hotspot of antibiotic resistance. However, we observed multiple clusters of ESBL-E in several LTCFs, which suggests that basic infection prevention measures are not rigorously followed. For example, almost one-third of residents in an LTCF from Eastern Switzerland were colonized with ESBL-E. In this institution, a workshop was held after communication of the results, and potential breaches in hygiene were discussed with the local infection control and prevention nurse. This example suggests that if infection prevention measures are to be improved in the long-term care setting, a customized approach considering the epidemiology of the respective institution could be the most efficient strategy.

NGS has been shown to be an extraordinarily valuable tool in the detection of outbreaks and transmission of resistant gram-negative pathogens.[29,30] NGS allows detailed characterization of resistant bacterial strains, rapid differentiation of related and nonrelated strains within the same sequence type at high resolution, as well as determination of the underlying resistance mechanisms by identification of specific genes associated with resistance.[29] NGS results showed that *E coli* ST131 was the most common ST in our study. Spread of ESBL–*E coli* ST131 in LTCFs has been described from many countries.[6,31] Its success has been partly attributed to the longer carriage time compared to other STs.[32] Worryingly, carbapenemase-producing *E coli* ST131 (mostly bla_{KPC} and $bla_{OXA-48-like}$) have recently been reported from England and Germany.[33,34] In our study, ST131 strain *H*30R was most common, carrying predominantly $bla_{CTX-M-14}$ and $bla_{CTX-M-27}$ (ie, *H*30R1), whereas $bla_{CTX-M-15}$ (associated with *H*30Rx strains) was less common.[25] Indeed, ST131 carrying $bla_{CTX-M-27}$ has been suggested to be more transmissible than those with $bla_{CTX-M-15}$, which might explain its successful spread.[35] Of note, the interfacility spread of ST131 among residents without any common epidemiologic link in the Western part of Switzerland was caused by *H*30R1-carrying $bla_{CTX-M-14}$, which suggests that this subclone is not confined to health care settings but is endemic in the region. The scarcity of data on the molecular epidemiology of ESBL-producing *E coli* in Switzerland makes it difficult to put our data into context. However, an analysis of acute care patient isolates from Geneva (Western Switzerland) has shown an ST131 prevalence of 38% among ESBL *E coli*, most of them belonging to the $bla_{CTX-M-27}$-carrying C1/*H*30R1 subclone,[36] which was also the second most common subclone in our study. To increase our rather limited knowledge about the molecular epidemiology of antibiotic-resistant pathogens in community and health care settings, NGS should be performed more broadly and more systematically in Switzerland.

We identified PPI use to be independently associated with ESBL-E carriage. Similar findings have been published before, mostly from studies performed in acute care patients,[37] but also from a Belgian LTCF,[38] and from the general population.[39] In a recent meta-analysis, the OR for ESBL colonization was estimated at 1.7 for patients under gastric acid–suppressive treatment,[15] which is perfectly in line with our data. Owing to potential residual confounding, causality cannot be inferred between PPI use and risk for ESBL-E colonization based on our cross-sectional study design. However, the purported mechanism—which is that PPI might facilitate the colonization of the gastrointestinal tract by *Enterobacterales* through disruption of the gastric acid barrier—seems plausible. Of note, PPIs have also been associated with recurrent *Clostridioides difficile* infection,[40] health care–acquired pneumonia,[41] and even increased mortality.[42]

The proportion of residents being treated with a PPI was 35% in our study, which is almost as high as the 45% reported from a Belgian study.[38] Although we did not evaluate if PPIs were indeed indicated, these high numbers suggest that PPIs are being overprescribed in this population, as shown by others.[43] In a previous study in 22 LTCFs from the United States, almost 80% of residents were given a PPI at the time

of admission, more than half without an indicated diagnosis.[44] Based on these data, we think that antibiotic stewardship programs should not only focus on reducing antibiotic use but also on reducing acid suppression therapy.[45] Previous efforts to do so have shown that reducing PPI use is challenging. Although PPI usage declined after implementation of a PPI deprescribing guideline in LTCFs in Ontario, Canada, the effect could not be maintained over time.[46]

This study has several limitations. First, the selection of LTCF might not be representative for all institutions in Switzerland. LTCF with a particular interest in the topic are probably overrepresented, which could lead to both over- and underestimation of the prevalence. Second, only about 50% of residents consented to participate in the study. Men and those with urinary catheters were more likely to consent, which might have led to an overestimation of the prevalence. Third, the frequency of ESBL–*E coli* STs and subtypes, as described in our study, is determined by the epidemiology in the participating LTCFs. Nevertheless, the overall predominance of ST131 *H*30 and the interfacility spread of $bla_{\text{CTX-M-14}}$-carrying ST131 in Western Switzerland give us valuable insights into this hitherto surprisingly understudied area. Fourth, previous antibiotic use was not independently associated with ESBL-E detection. Although collinearity was formally not detected, adjustment for the variable "previous ESBL detection," which might itself be associated with higher antibiotic exposure, could account for the nonsignificant effect of antibiotic use in multivariable analysis. However, because antibiotic use has been found as a risk factor for antibiotic resistance in many other studies, we still believe that antibiotic use plays an important role in the promotion of AMR in LTCFs. Fifth, as outlined above, residual confounding is possible. For instance, variables not captured in our questionnaires include adherence to hand hygiene and use of PPE at the institution level and duration of previous hospital stays or exposure to ESBL-colonized roommates at the resident level.

Conclusion and Implications

The prevalence of ESBL-E in Swiss LTCFs is comparable to other middle European countries; *E coli* ST131, and its subclone *H*30R1, is the predominant ST, as shown in many other long-term care settings across the globe. We observed multiple clusters of residents with identical pathogens in certain institutions, calling for targeted interventions to revise and improve infection control policies in affected institutions. Such interventions may include efforts to increase adherence to hand hygiene, instructions for the correct use of personal protective equipment, and strategies to reduce prescription of antibiotics. Use of PPI represents an independent risk factor for ESBL-E carriage, which is why reducing PPI use should be considered as part of any antibiotic stewardship programs in long-term care.

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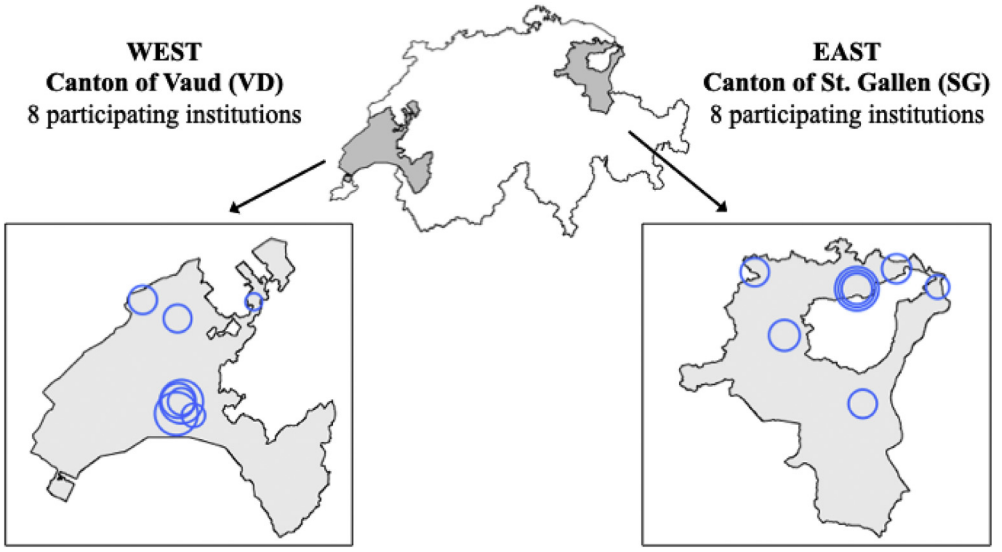
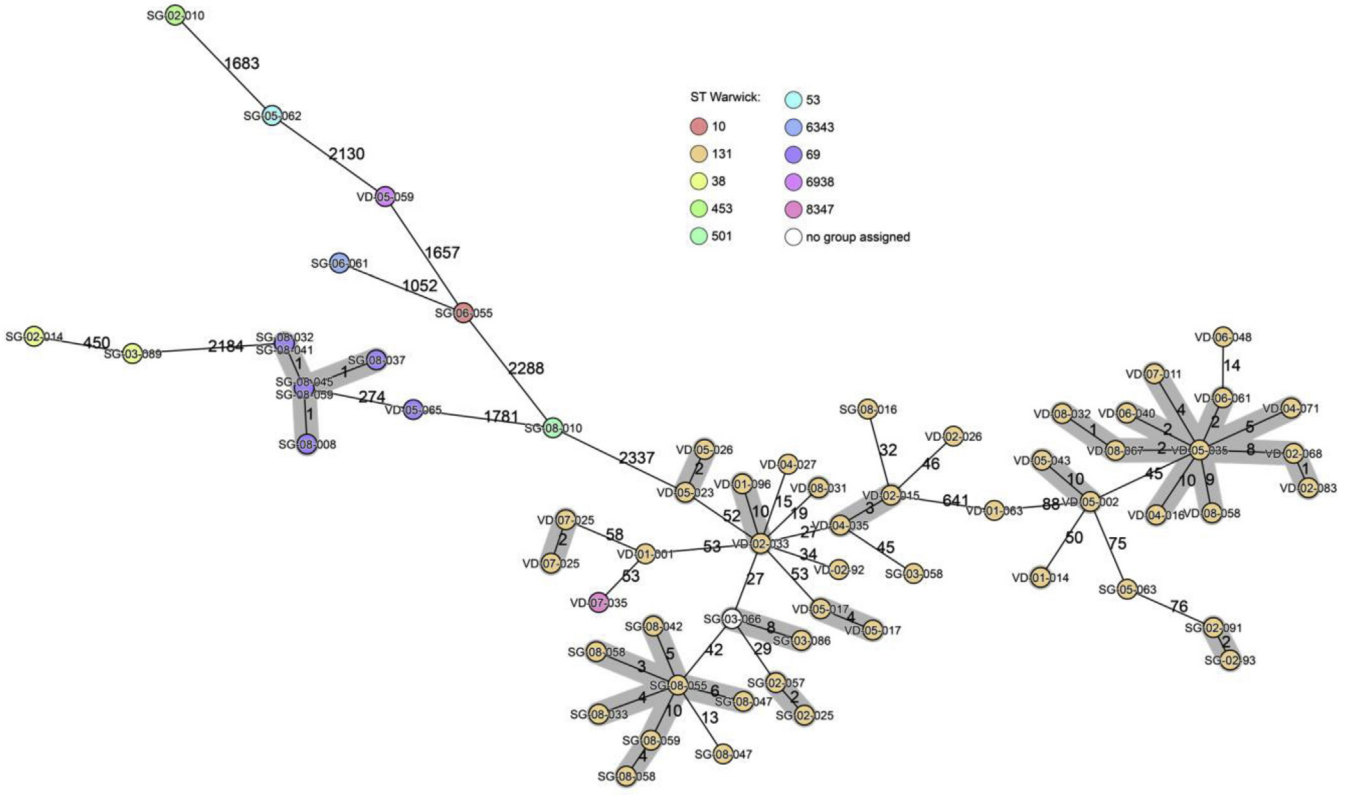


Supplementary Figure 1. Geographical location of participating institutions in the west and in the east of Switzerland.



Supplementary Figure 2. Results of next-generation sequencing of extended spectrum β-lactamase producing *Escherichia coli* from Swiss nursing home residents by sequence type. SG isolates are from Eastern Switzerland and VD isolates from Western Switzerland.

Supplementary Table 1
Organizational Characteristics of Included Long-Term Care Facilities Stratified by Those With High and Low Prevalence of ESBL-Producing *Escherichia coli*

Characteristics	High Prevalence (Median 13.4%) (n = 8)	Low Prevalence (Median 6.9%) (n = 8)	*P* Value
General information			
Western Switzerland	6 (75.0)	2 (25.0)	.13
Ownership			.80
Public	1 (12.5)	2 (25.0)	
Not for profit	5 (62.5)	4 (50.0)	
For profit	2 (25.0)	2 (25.0)	
Occupied beds at time of survey	73.50 (21.99)	75.00 (14.71)	.88
Qualified nursing care available 24 h	3 (37.5)	1 (12.5)	.56
FTE nursing assistants, %, mean (SD)	44.13 (11.70)	50.08 (11.43)	.32
FTE per occupied bed, mean (SD)	0.36 (0.20)	0.55 (0.24)	.11
Single beds, %, mean (SD)	76.39 (23.63)	64.58 (23.97)	.34
Medical care			.27
Both	5 (62.5)	3 (37.5)	
Personal general practitioners (GPs)	1 (12.5)	4 (50.0)	
Medical staff employed by the facility	2 (25.0)	1 (12.5)	
Residents			
Katz score, median (IQR)	16.50 (3.04)	15.12 (2.63)	.35
Age >85 y, %, mean (SD)	55.58 (25.87)	55.44 (13.95)	.99
Consent for screening, %, mean (SD)	46.71 (10.54)	55.28 (10.17)	.12
Infection control practice			
Trained persons in infection control and prevention	8 (100.0)	8 (100.0)	NA
Infection prevention training for nurses	1 (12.5)	1 (12.5)	>.99
Infection prevention training for non-nurses	6 (75.0)	2 (25.0)	.13
Infection control committee	6 (75.0)	3 (37.5)	.31
Hand hygiene training	2 (25.0)	0 (0.0)	.45
Liters of alcohol rub solution in 2018/bed, mean (SD)	3.70 (2.15)	6.94 (5.39)	.17
Antimicrobial policy			
Therapeutic guidelines available	2 (25.0)	5 (62.5)	.31
Pharmacist advice for antimicrobials	5 (62.5)	7 (87.5)	.56
Microbiology laboratory in charge of institution			.14
One	5 (62.5)	4 (50.0)	
More than 1	2 (25.0)	0 (0.0)	
None, this is done directly by the GP	1 (12.5)	4 (50.0)	

FTE, full-time equivalent; GP, general practitioner; IQR, interquartile range; NA, not available; SD, standard deviation.
Values are n (%) if not stated otherwise.

Supplementary Table 2
Phenotypic Resistance (n = 71) and Next-Generation Sequencing (n = 67) Results of ESBL-Producing *Enterobacterales* (From 70 Residents)

ID	Species	AMC	TZP	CAZ	FEP	ATM	IMI	MER	AM	TBM	NOR	CIP	LVX	FOS	NF	SXT	ST	β-Lactamase-Gene	bla-Class A Genes (I)	bla-Class A Gene (II)	bla-Class D Gene	bla-misc. Groups	fim Type
SG-01-007	*Proteus mirabilis*	R	S	R	R	S	R	R	S	S	R	R	R	S	n.a.	R	35		blaCTX-M-36				
SG-01-046	*Klebsiella pneumoniae*	R	S	R	R	R	S	S	S	S	R	R	I	S	n.a.	R	1190		blaCTX-M-15	blaSHV-106		blaTEM-1	
SG-02-012	*Citrobacter farmeri*	R	S	S	S	R	S	S	S	S	S	S	S	S	n.a.	S						blaSED	
SG-02-014	*Escherichia coli*	R	S	I	R	R	S	S	S	S	S	S	S	S	S	R	38	blaEC-8	blaCTX-M-9				
SG-02-052	*E coli*	S	S	I	I	I	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH30
SG-02-057	*E coli*	S	S	I	I	I	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH30
SG-02-091	*E coli*	S	S	I	I	I	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH41
SG-02-093	*E coli*	S	S	I	I	I	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH41
SG-03-058	*E coli*	R	S	I	R	R	S	S	S	R	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30
SG-03-066	*E coli*	S	S	R	I	R	S	S	S	S	R	R	R	S	S	R	unk	blaEC-5	blaCTX-M-27				
SG-03-086	*E coli*	S	S	I	R	R	S	S	S	R	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH30
SG-03-089	*E coli*	S	S	I	R	R	S	S	S	S	I	S	S	S	S	S	38	blaEC-8	blaCTX-M-15				
SG-04-028	*Klebsiella oxytoca*	S	S	R	S	R	S	S	S	S	S	S	S	S	n.a.	S	224		blaOXY-6-1	blaSHV-12			
SG-05-062	*E coli*	R	S	I	R	R	S	S	S	S	S	S	S	S	S	S	53	blaEC-18	blaCTX-M-1				
SG-05-063	*E coli*	R	S	I	I	I	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-1			blaTEM-1	fimH412
SG-06-055	*E coli*	R	S	S	I	I	S	S	S	S	I	I	I	S	S	R	10	blaEC	blaCTX-M-14				
SG-06-061	*E coli*	R	I	R	R	R	S	S	S	R	R	R	R	S	S	R	3643	blaEC-15		blaTEM-40			
SG-07-030	*K pneumoniae*	R	S	R	R	R	S	S	S	R	R	R	R	R	n.a.	S	307		blaCTX-M-15	blaSHV-106	blaOXA-1	blaTEM-1	
SG-07-034	*K pneumoniae*	R	S	R	I	R	S	S	S	R	R	R	R	R	n.a.	S	307		blaCTX-M-15	blaSHV-106	blaOXA-1	blaTEM-1	
SG-08-008	*E coli*	S	S	I	I	R	S	S	S	S	S	S	S	S	S	S	69	blaEC-8	blaCTX-M-15				
SG-08-010	*E coli*	S	S	R	R	R	S	S	S	S	R	R	R	S	S	R	501	blaEC-8	blaCTX-M-15				
SG-08-016	*E coli*	S	S	I	R	R	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH30
SG-08-032	*E coli*	R	S	I	R	R	S	S	S	S	S	S	S	S	S	S	69	blaEC-8	blaCTX-M-15				
SG-08-033	*E coli*	R	S	S	R	I	S	S	S	R	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30
SG-08-037	*E coli*	R	S	I	R	R	S	S	S	S	S	S	S	S	S	S	69	blaEC-8	blaCTX-M-15				
SG-08-041	*E coli*	R	S	I	R	R	S	S	S	S	S	S	S	S	S	S	69	blaEC-8	blaCTX-M-15				
SG-08-042	*E coli*	R	S	I	R	I	S	S	S	R	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30
SG-08-045	*E coli*	S	S	R	R	R	S	S	S	S	S	S	S	S	S	S	69	blaEC-8	blaCTX-M-15				
SG-08-047	*E coli*	R	S	I	R	R	S	S	S	R	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30
SG-08-055	*E coli*	R	S	S	I	I	S	S	S	R	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30
SG-08-058	*E coli*	R	S	I	R	I	S	S	S	R	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-14				fimH30
SG-08-059*	*E coli*	R	S	I	R	I	S	S	S	R	R	R	R	S	S	S	69	blaEC-5	blaCTX-M-14				
SG-08-059*	*E coli*	R	S	I	R	I	S	S	S	R	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-14				fimH30
VD-01-001	*E coli*	R	S	R	R	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-15			blaTEM-1	fimH30
VD-01-014	*E coli*	R	S	R	R	R	S	S	S	S	I	I	I	S	S	S	131	blaEC-5	blaCTX-M-55				fimH41
VD-01-063	*E coli*	R	S	R	R	R	S	S	S	R	R	R	R	S	n.d.	R	131	blaEC-5	blaCTX-M-15			blaTEM-1	fimH41
VD-01-078	*K pneumoniae*	R	S	R	S	R	S	S	S	S	R	R	R	S	n.a.	S				blaSHV-33			
VD-01-096	*E coli*	S	S	R	R	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-27				fimH30
VD-02-015	*E coli*	R	S	R	I	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-27				fimH30
VD-02-026	*E coli*	S	S	R	I	R	S	S	S	S	R	R	R	S	R	R	131	blaEC-5	blaCTX-M-27				fimH30
VD-02-033	*E coli*	S	S	I	I	R	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH30
VD-02-068	*E coli*	R	S	I	I	R	S	S	S	R	I	I	S	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-02-083	*E coli*	R	S	I	R	R	S	S	S	R	I	I	S	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-02-092	*E coli*	S	S	I	I	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-27				fimH30
VD-03-042	*E coli*	S	S	I	R	R	S	S	S	S	R	R	R	S	S	S	nd	nd					
VD-03-050	*E coli*	S	S	I	I	R	S	S	S	S	R	R	R	S	S	R	nd	nd					
VD-04-008	*E coli*	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	nd	nd					
VD-04-016	*E coli*	R	S	I	I	R	S	S	S	R	I	I	S	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-04-027	*E coli*	S	S	R	I	R	S	S	S	S	R	R	R	S	S	R	131	blaEC-5	blaCTX-M-27				fimH30
VD-04-035	*E coli*	S	S	R	I	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-27				fimH30
VD-04-071	*E coli*	R	S	I	I	R	S	S	S	R	I	I	I	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-05-002	*E coli*	R	S	I	R	I	S	S	S	S	S	S	S	S	S	S	131	blaEC-5	blaCTX-M-14				fimH41-like
VD-05-017	*E coli*	R	S	R	R	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-15			blaTEM-1	fimH30
VD-05-023	*E coli*	R	S	S	R	I	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30
VD-05-026	*E coli*	R	S	S	R	I	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH30

VD-05-035	*E coli*	R	S	I	I	R	S	S	S	R	I	I	I	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-05-042	*K pneumoniae*	R	I	R	R	R	S	S	S	R	R	R	R	S	n.a.	R	235	blaLAP-2	blaCTX-M-15	blaSHV-145	blaOXA-1		
VD-05-043	*E coli*	S	S	S	I	I	S	S	S	R	S	S	S	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH41-like
VD-05-059	*E coli*	R	I	R	R	R	S	S	S	R	R	R	R	S	R	R	6938	blaEC-15	blaCTX-M-15			blaTEM-1	
VD-05-065	*E coli*	S	S	R	R	R	S	S	S	S	I	I	S	S	S	R	69	blaEC-8	blaCTX-M-15			blaTEM-1?	
VD-06-040	*E coli*	R	S	I	R	R	S	S	S	S	R	I	I	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-06-048	*E coli*	R	S	I	I	R	S	S	S	R	I	I	I	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-06-061	*E coli*	R	S	I	I	R	S	S	S	R	I	I	S	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-07-011	*E coli*	R	S	I	R	R	S	S	S	S	I	S	S	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-07-025	*E coli*	R	S	R	R	R	S	S	S	R	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-15		blaOXA-1		fimH30
VD-07-035	*E coli*	R	S	R	R	R	S	S	S	R	R	R	R	S	S	R	8347	blaEC-5	blaCTX-M-15		blaOXA-1	blaTEM-1	
VD-08-031	*E coli*	S	S	R	R	R	S	S	S	S	R	R	R	S	S	S	131	blaEC-5	blaCTX-M-27				fimH30
VD-08-032	*E coli*	R	S	I	I	R	S	S	S	R	I	I	S	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-08-058	*E coli*	R	S	I	R	R	S	S	S	R	I	I	S	S	S	R	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-08-067	*E coli*	R	S	I	I	R	S	S	S	R	I	I	S	S	S	S	131	blaEC-5	blaCTX-M-14			blaTEM-1	fimH89
VD-08-068	*E coli*	R	S	I	I	R	S	S	S	S	I	I	S	S	S	R	nd	nd					

AM, amikacin; AMC, amoxicillin; ATM, aztreonam; CAZ, ceftazidime; CIP, ciprofloxacin; FEP, cefepime; FOS, fosfomycin; ID, identifier; IMI, imipenem; LVX, levofloxacin; MER, meropenem; NF, nitrofurantoin; NOR, norfloxacin; ST, sequence type; SXT, sulfamethoxazole; TBM, tobramycin; TZP, tazobactam; unk, unknown.

*Same patient with 2 different STs.

Supplementary Table 3
Risk Factors Compared Between Residents* With Extended Spectrum β-Lactamase (ESBL)–Producing *Escherichia coli* ST131 and ESBL *E coli* of Other STs

Characteristics	ST131 (n = 42)	Other ST (n = 14)	*P* Value
Western Switzerland	29 (69.0)	2 (14.3)	**.001**
Age, median (IQR)	85 (69-91)	84 (75-87)	.59
Female sex	17 (40.5)	9 (64.3)	.22
Urinary catheter	10 (23.8)	2 (14.3)	.71
Incontinence	32 (76.2)	9 (64.3)	.60
Decubitus	4 (9.5)	0 (0.0)	.55
Wound	4 (9.5)	0 (0.0)	.55
Disorientation	23 (54.8)	4 (28.6)	.17
Dementia	18 (42.9)	5 (35.7)	.88
Wheelchair or bedbound	21 (50.0)	5 (35.7)	.54
Proton-pump inhibitor	22 (52.4)	8 (57.1)	>.99
Previous endoscopy	0 (0.0)	0 (0.0)	NA
Previous hospital admission	9 (21.4)	3 (21.4)	>.99
Previous ESBL	8 (19.0)	0 (0.0)	.19
Previous antibiotic treatment	19 (45.2)	4 (28.6)	>.99
Years in facility, median (IQR)	3 (1-4)	1.5 (1.5-7.5)	.88
Katz-score, median (IQR)	18 (16-21)	18 (8-21)	.34

ESBL, extended-spectrum β-lactamase; IQR, interquartile range.
Values are n (%) if not indicated otherwise.
P values <.05 are given in bold.
*Resident with co-colonization (ST131 and ST69) excluded from analysis.