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Prevalence, genetic diversity of- and factors associated with ESBL-producing Enterobacteriaceae carriage in residents of French Nursing Homes

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Abstract

Objective: To determine the prevalence and genotypic characteristics of extended-spectrum β -lactamase-producing *Enterobacteriaceae* (ESBLE) and Carbapenemase-producing *Enterobacteriaceae* (CPE) in Nursing Homes (NHs) in a French region. Risk factors associated with their carriage were also investigated.

Methods: A point-prevalence survey was proposed from November 2017 to June 2018 to NHs of our region. Volunteer residents were screened for ESBLE and CPE carriage. We genotyped *E. coli* and *K. pneumoniae* isolates using, MLST, PFGE and phylogrouping (only for *E. coli*). Collective and individual data were analyzed by random-effects logistic regression.

Results: The study was conducted in 18 nursing homes and included 262 patients. Fifty-two of them (19.8%) carried at least one ESBLE, corresponding to 56 isolates (42 *E. coli*, 11 *K. pneumoniae*, and 3 others) while no CPE was detected. A majority (27/42) of ESBL-*E. coli* belonged to phylogroup B2 and ST131 was overrepresented in this subset (21/27). PFGE analysis revealed ST131 cross-transmission within NHs. Regarding ESBL-*K. pneumoniae*, 9 out of 11 isolates belonged to ST663 and PFGE suggested the diffusion of the clone in six NHs. Significant individual risk factors for colonization by ESBLE were: use of non-private toilettes, previous antibiotic use and recent history of hospitalization. Significant collective protective factors were proper compliance with gloves use and support of the NH by a healthcare facility.

Conclusion: This study shows that NHs within our region are an important reservoir of ESBLE, whereas no residents were CPE carrier. ESBLE control in NHs should focus on antibiotic stewardship and excreta management policies.

Introduction

Antimicrobial resistance is a worldwide problem and is projected to surpass cancer as the leading cause of death by 2050 [1]. Of particular interest, extended-spectrum β -lactamase-producing *Enterobacteriaceae* (ESBLE) has become a major European public health concern in the last two decades [2]. For instance, the incidence of infections caused by ESBLE has increased dramatically in French hospitals, and *Escherichia coli* has become the most frequent species among ESBLE (60%), before *Klebsiella pneumoniae* (25%) [3]. There is rising concern regarding Nursing Homes (NHs) which are considered as reservoirs of ESBLE, because the residents frequently require medical care and antimicrobial treatments [4]. In addition, the recent emergence of carbapenemase-producing *Enterobacteriaceae* (CPE) also represents a significant worldwide threat to public health and some studies from Southern Europe have reported significant prevalence of CPE carriage in NH or long-term-care facilities residents [5, 6]. However, the prevalence of ESBLE and CPE carriage among residents of French NHs remains poorly described. In this context, the objective of our study was to assess the prevalence of ESBLE and CPE carriage in residents of NHs of Franche-Comté, a region in eastern France. We further investigated the molecular characteristics of these multi-drug-resistant isolates as well as collective and individual risk factors associated with their carriage.

Methods

Study design, setting and participants

A cross-sectional prevalence survey was performed one day from November 2017 to June 2018, in NHs from Franche-Comté (France). A two stage random sampling method was used. We randomly selected 50 NHs out of 135 eligible to participate in the study. In NHs volunteered to participate, from 20 to 35 residents per NH, depending on the housing capacity, were also randomly selected. Residents with inability to express their participation agreement were excluded. Individual residents elected to participate in the study were appropriately informed of the study protocol by the medical coordinator. Their oral approval was noticed in their medical record. The study was approved by the ethical committee 'Comité d'Etude Clinique' of the Besançon university hospital, Besançon, France, Reference: 2017-A00276-47.

Microbiological analysis

Rectal bacterial samples were collected using a rectal swab or with fresh stool (Fecal swab, Copan Diagnostics, Brescia, Italy). Samples were all analyzed in hygiene laboratory of Besançon University hospital within 72 hours after collection. Samples were streaked onto ChromiD ESBL and ChromID® CARBA SMART agar (Biomérieux, Marcy-l'Etoile, France) and incubated aerobically at $35 \pm 2^\circ\text{C}$ for 24h, in accordance with the manufacturer's instructions. Isolates obtained were identified to the species level using a MALDI-TOF mass spectrometry (Microflex LT; Bruker Daltonik GmbH, Bremen, Germany) according to the manufacturer's recommendations. For all ESBL-suspected *Enterobacteriaceae* isolates, the presence of ESBL was confirmed using a double-disk synergy test according to the EUCAST recommendations (http://www.eucast.org/clinical_breakpoints/). ESBL

genes were identified by PCR and sequencing. After screening all samples with consensus primers targeting *bla*_{CTX-M}, we carried out more specific amplifications, beginning with primers targeting different groups of CTX-M (*bla*_{CTX-M} group 1 *bla*_{CTX-M} group 9, *bla*_{CTX-M} group 2). Then, we tested for the presence of *bla*_{SHV} or *bla*_{TEM} genes [7]. All ESBL-producing *E. coli* isolates were typed by phylogrouping as previously described [8]. MLST was performed on all ESBL-producing *E. coli* and *K. pneumoniae* isolates according to protocols previously described [9]. The MLST website (<http://pubmlst.org/>) was used for the assignment of allele numbers and ST. PFGE was used to assess the clonal diversity within each ST using *Xba*I digestion. Pulsotypes (PTs) were defined according to international recommendations [10]. For a given bacteria, isolates which shared similar PT, and recovered from the same NH, were thought to be cross-transmitted.

Data collection

Two trained infection control practitioners collected all data using standardized questionnaires for collective and individual variables.

Facility questionnaire

Numerical variables collected included: a French index to evaluate the average level of dependency of NH residents (GMP), housing capacity and number of physicians participating to care of the residents. Categorical variables collected included: sectorization (specific staff allocated to units of the NH during day and night shifts), whether physicians had a list of recommended antibiotics and antimicrobial stewardship guidelines, whether the NH was linked to larger healthcare institution, existence of an in-house pharmacy, hygiene protocols regarding ESBL and CPE or

route for waste disposal, whether the NH benefit intervention of an infection control nurse of the regional mobile team, availability of items related to hygiene (bedpan washer disinfectors, near patient alcohol-based hand-rub, single-use gloves and aprons) and frequency of use, staff training in standard precautions and hand hygiene and information to residents regarding hand hygiene.

Resident questionnaire

Individual data collected were: age, sex, a French index to evaluate the level of dependency (GIR varying from 1 to 6, an index close to 1 indicates a high level of dependency), duration of stay, single or shared bedroom, bed rest, how urine and feces were eliminated (their own bathroom, shared bathroom, commode chair, use of incontinence products), medical history including diabetes, immunodeficiency, urinary and fecal incontinence, presence of invasive medical devices, antibiotic treatment in the previous 6 months and hospitalization in the past 12 months.

Statistical analysis

Descriptive statistics were displayed for both nursing homes and individual residents. Univariate comparison between groups was done using Pearson's Chi-square test or Fisher's exact test for categorical variables. We compared numerical variables by carrying out Student's t-test or the Mann-Whitney U test, as appropriate. Multivariate analysis was conducted using random-effects logistic regression model taking into account the clustered structure of data (residents nested within NHs). The binary outcome variable was ESBL positivity on stool sample. Explanatory variables were selected using stepwise regression through backward elimination procedure. All explanatory variables that showed a p value of less than 0.10 in the univariate

analysis were considered for the multivariate analysis. Analyses were conducted using the software package Stata, version 14.1 (Stata Corp., College Station, TX, USA). A p value of less than 0.05 was considered significant.

Results

Participation

Out of the 50 NHs randomized, 18 (36.0%) volunteered to participate to the study. In these NH, 776 residents met the inclusion criteria. After randomization and record of participation agreement, 262 residents, with complete data and sample, were included, representing an average of 14.5 residents per NH (range: 3 to 33). The flow chart of the study is presented in the Figure 1. Data collected on NHs and residents are displayed in Table I and Table II, respectively.

Microbiological analysis

Fifty-two of the residents (19.8% [CI: 12.5-27.1]) carried at least one ESBLE, corresponding to 56 isolates (42 *E. coli*, 11 *K. pneumoniae*, 2 *Citrobacter farmeri* and 1 *Morganella morganii*) while no CPE was detected. The overall ESBLE prevalence in NHs varied from 0 to 43.8%, four of them had no ESBLE carriers amongst the 5 to 17 residents tested, while one had seven carriers amongst 16 residents tested.

Four residents carried 2 ESBLE (3 *E. coli* and *K. pneumoniae*, 1 *E. coli* and *M. morganii*). A majority (27/42) of ESBL *E. coli* belonged to phylogroup B2, the others were distributed in phylogroup D (n=8), phylogroup A (n=4) and phylogroup B1 (n=3). ST131 was overrepresented in the phylogroup B2 (21 out of the 27 isolates). The 21 ST131 isolates were recovered in only five NHs (from one to nine cases per NH) and PFGE analysis revealed ST131 cross-transmission within NHs. In two NHs, all of the isolates (n=4 and n=6 respectively) belonged to the same PFGE pattern. In the NH where nine ST131 isolates were identified, isolates clustered in four PFGE patterns (with six isolates sharing the same PFGE pattern). It should be noted that no PFGE

patterns of ST131 were shared by residents from different NHs. All the ESBLs identified in ST131 isolates were of CTX-M type with a predominance of CTX-M-27 (n=9) and CTX-M-15 (n=8). In phylogroup D, CC69 and ST362 were identified for three and two isolates, respectively with no evidence of cross-transmission. Regarding ESBL producing *K. pneumoniae*, 9 out of 11 belong to ST663; were CTX-M-15 producers and belonged to the same PFGE pattern, but were detected in residents from six different NHs. Genotyping data are summarized in Table III.

Statistical analysis

The results of univariate and multivariate analysis are presented in Table IV. The risk of carrying ESBL was increased by not using the resident's own bathroom (OR = 2.32, CI [1.17-4.57], p = 0.015) and history of antibiotic use in the past 6 months (OR = 2.32, CI [1.20-4.49], p = 0.012) or hospitalization in the past 12 months (OR = 2.04, CI [1.03-4.03], p = 0.041). Protective factors were systematic use of single-use gloves whenever expected (OR = 0.25, CI [0.11-0.58], p = 0.001) and the nursing home being linked to a larger healthcare institution (OR = 0.41, CI [0.19-0.87], p = 0.020).

Discussion

This study shows that NHs in our region are an important reservoir of ESBLE with almost 20% carriage amongst residents. This figure is in line with the pooled prevalence of ESBLE reported by Flokas and colleagues in their systematic review (i.e. 18% in European NHs) despite considerable geographical variability [11]. We also observed huge variability within NHs included in this study mainly due to intra-NHs outbreaks of the pandemic clonal group ST131. Indeed, our survey reveals occult outbreaks of ST131 specific pulsotypes in 3 NHs; involving C1-CTX-M-27 and C2-CTX-M-15 clades. The latter is the predominant ST131 cluster, responsible for the worldwide spread of CTX-M-15 [12] and has been first detected in our region in 2006 [13]. C1-CTX-M-27 clade emerged in 2010 in our university hospital [13]. This cluster initially described in Japan in 2004 [14], has spread secondarily in Europe where it has been notably identified in children [15] and in adult inpatients [16]. To the best of our knowledge, this report is the first to detect C1-CTX-M-27 cluster in French NHs.

ST131 clonal group, for which we observed a carriage rate of 8% in that study, has been frequently associated to elderly and NHs with carriage rates varying from 4 to 20% of the residents [17, 18]. The specific success of ESBL ST131 over other ESBL producing *E. coli* clones in NHs may be due to prolonged colonization. Indeed, Overdeest and colleagues demonstrated in Dutch NHs that half-time carriage was significantly longer for ESBL ST131 (13 months) than for other ESBL producing *E. coli* (2-3 months) [19].

PFGE results of ESBL producing *K. pneumoniae* strongly suggest spread of isolates of ST663 in NHs from a common reservoir. This ST has been only reported in Spanish hospitals associated to OXA-48 production [20]; it is a single-locus variant of ST405, which was responsible for an outbreak in the university hospital of our region (Personal data X Bertrand). Consequently, it is very likely that this strain originated from the university hospital and imported in NHs via colonized patients. It should be noticed that one of the residents was carrier of the emerging pandemic ST307 lineage. A recent phylogenetic analysis using whole genome sequencing showed that this has emerged in the 1990s, has spread globally intimately associated with a conserved plasmid containing the *bla*_{CTX-M-15} ESBL gene and several other resistance genes [21]. ST307 can also acquire and disseminate carbapénémases [21]. None of the residents were CPE carrier, this reflects that our region remains an area with very low incidence of CPE, to date [22].

Risk analysis in the current study indicated that previous hospitalization, previous antibiotic exposure and the use of non-private toilettes were associated with high probability of ESBLE carriage. Acute care hospitals and NHs seem to act as communicating vessels for ESBLE as mentioned by Latour and colleagues [23] and history of previous hospitalization as well as previous antibiotic use were frequently identified as risk factors for ESBLE carriage in NHs [11]. Excreta management had also been identified in person-to-person transmission of ESBLE [24]. Our analysis stresses the importance of individualized toilets for residents who are able to use it. This study revealed a significant protective impact of proper observance of single-use gloves too, underlining the need of proper practices for excreta management. However, the relevance of the use of gloves was not evaluated and misuse of gloves,

like overuse, can increase the risk of cross transmission via contaminated gloved hands [25]. Other risk factors such as history of invasive devices, underlying comorbidities that are frequently reported in the literature [11] to be associated with ESBLE carriage in NH residents were not found in our study, probably due to insufficient number of residents included in the present surveillance. In accordance to previous studies [16], level of mobility and gender were not associated to ESBLE carriage.

We do acknowledge that this study had several limitations. First, the study design (point prevalence survey) did not take into account the dynamics of ESBLE epidemiology. Second, the low proportion of NHs that agreed to participate to the study limits the number of residents included and potentially hinder the identification of risk factors associated to ESBLE carriage.

Conclusion

This study shows that NHs within our region are an important reservoir of ESBLE, that special attention should be given to pandemic ST131 *E. coli* and *K. pneumoniae* clones and that ESBLE control in NHs should focus on antibiotic stewardship and excreta management policies.

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Performed the experiments: MB, CBS, FB. Analysed the data: CBS, HGH, XB, MB.
Wrote the paper: CBS, XB.

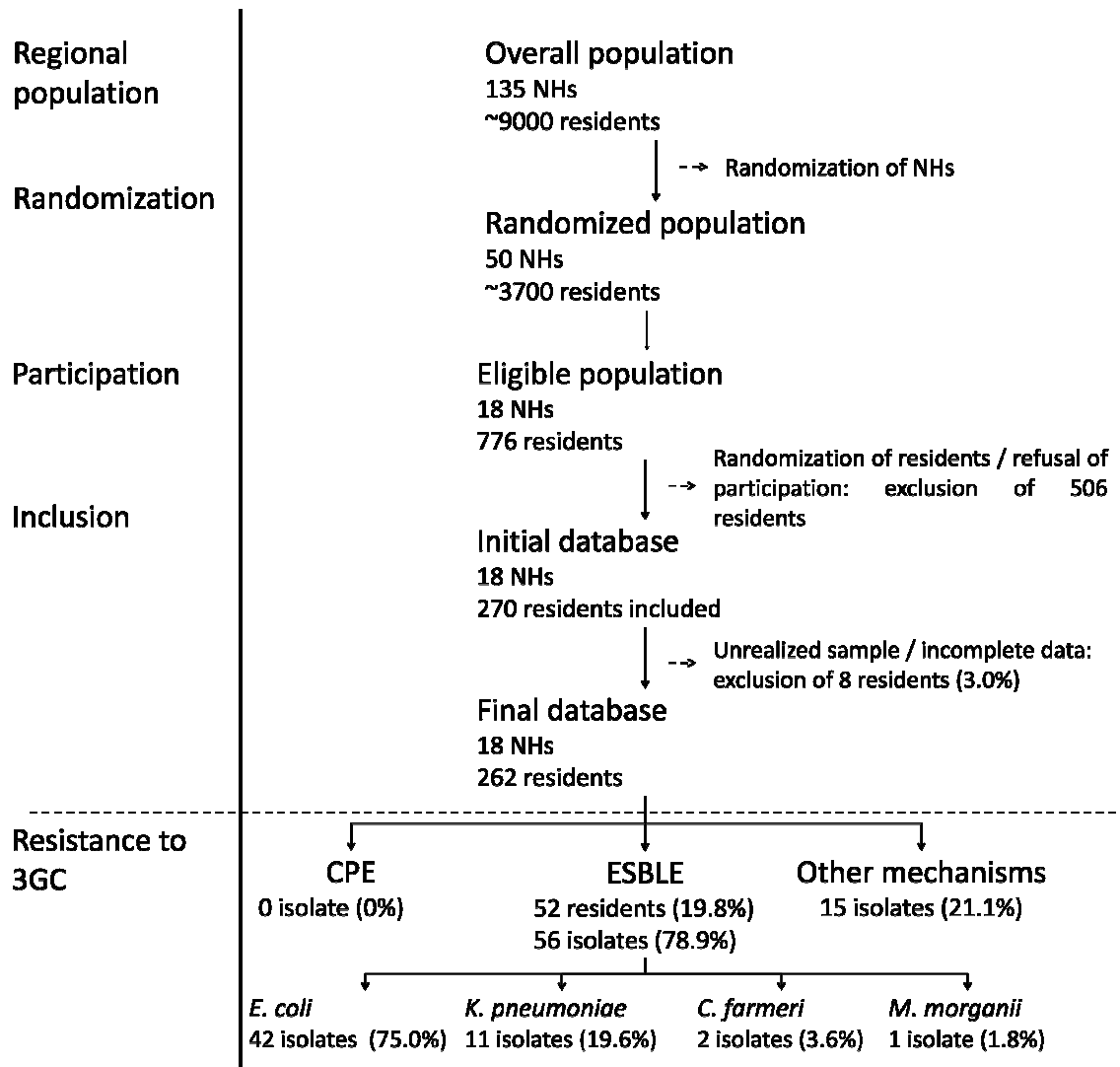
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Figure 1. Flow chart of the study.



NH: nursing home; 3GC: third generation cephalosporin; ESBLE: extended-spectrum-beta-lactamase-producing *Enterobacteriaceae*; CPE: carbapénémase-producing *Enterobacteriaceae*.

Table I. Characteristics of nursing homes (N=18)

	N (%)	Median (min-max)
GMP		729.5 (568-840)
Housing capacity		78.9 (24-236)
Number of eligible residents per NH		30.0 (9-197)
Number of volunteer residents per NH		15.5 (3-33)
Number of physicians		9.5 (1-31)
Sectorisation of care during the day	11 (61.1)	
Sectorisation of care during the night	6 (33.3)	
Existence of a preferential list of ATB	8 (44.4)	
Existence of an institutional ATB policy	13 (72.2)	
NH linked to a larger healthcare institution	8 (44.4)	
Existence of an in-house pharmacy	9 (50.0)	
Intervention of a hygienist nurse of the regional mobile team	13 (72.2)	
Existence of a route for waste disposal	18 (100)	
Existence of protocols regarding ESBLE	11 (61.1)	
Existence of protocols regarding CPE	11 (61.1)	
Bedpan washer disinfectant	6 (33.3)	
ABHR available close to the care	18 (100)	
Single-use gloves available	18 (100)	
Single-use apron available	18 (100)	
Staff training in universal hygiene precautions	15 (83.3)	
staff training in hand hygiene	16 (88.9)	
information to resident regarding hand hygiene	11 (61.1)	

GMP : a French index to assess the average level of dependence of NH residents; NH: nursing home; ATB : antibiotics; ESBLE: extended-spectrum-beta-lactamase producing *Enterobacteriaceae*; CPE: carbapenemase-producing *Enterobacteriaceae*; ABHR: alcohol-based hand-rub

Table II. Characteristics of patients according to their carrier statute (N=262)

		ESBLE carriers N=52 Proportion n (%) or Median (min-max)	Non-ESBLE carriers N=210 Proportion n (%) or Median (min-max)
Sex			
	Female	40 (76.9)	163 (77.6)
	Male	12 (23.1)	47 (22.4)
Age		88 (62-100)	89 (62-100)
GIR <3		37 (71.2)	118 (56.2)
Duration of stay (in days)		1030 (20-4802)	779.5 (19-5790)
Single bedroom		43 (82.7)	156 (74.3)
Way to excreta disposal			
	Private bathroom	27 (51.9)	143 (68.1)
	Shared bathroom	8 (15.4)	56 (26.7)
	Commode chair	15 (28.9)	54 (25.7)
	Incontinence pad	47 (90.4)	170 (81.0)
Medical history			
	Immunodeficiency	4 (7.7)	12 (5.7)
	Diabetes	6 (11.5)	29 (13.8)
	Urinary incontinence	46 (88.5)	153 (72.9)
	Fecal incontinence	31 (59.6)	100 (47.6)
	Bed rest	5 (9.6)	16 (7.6)
Previous carriage of ESBLE or CPE (n=206)		4/37 (10.8)	5/169 (3.0)
Exposure to an invasive medical device		3 (5.8)	13 (6.2)
	Digestive tract device	0	1 (0.5)
	Urinary tract device	1 (3.1)	7 (3.3)
Previous exposure to ATB within 6 months (n=253)		30/50 (60.0)	76/203 (37.4)
	Fluoroquinolones	2 (4.0)	8 (3.9)
	Amoxicillin	10 (20.0)	18 (8.9)
	Amoxicillin-clavulanate	5 (10.0)	19 (9.4)
	3GC	10 (20.0)	21 (10.3)
	Carbapenems	0	0

	Other	10 (20.0)	31 (15.3)
Previous hospitalization within 12 months		24 (46.2)	50 (23.8)

GIR: level of dependency French index; ESBLE: extended-spectrum-beta-lactamase producing *Enterobacteriaceae*; CPE: carbapenemase-producing *Enterobacteriaceae*; ATB: antibiotics; 3GC: third generation cephalosporins.

Table III. Summary table of the genotypic and phenotypic characteristics of bacterial isolates

Isolate no	NH no	Resident no	Specie	Phylogroup	ST	CC	ESBL	PFGE no
1	1/19	1/19/002	<i>E. coli</i>	B2	1618	73	CTX-M-17	
2	6/01	6/01/007	<i>E. coli</i>	B2	131	131	CTX-M-27	5
3	6/01	6/01/008	<i>E. coli</i>	B2	131	131	CTX-M-27	5
4	6/01	6/01/015	<i>E. coli</i>	B2	131	131	CTX-M-27	5
5	6/01	6/01/016	<i>E. coli</i>	B2	131	131	CTX-M-27	5
6	7/63	7/63/004	<i>E. coli</i>	B2	141	141	CTX-M-14	
7	4/26	4/26/007	<i>E. coli</i>	B1	708	469	CTX-M-1	8
8	4/26	4/26/008	<i>E. coli</i>	B1	708	469	CTX-M-1	8
9	4/26	4/26/011	<i>E. coli</i>	D	362		CTX-M-1	
10	4/26	4/26/019	<i>E. coli</i>	B2	372		CTX-M-1	
11	7/64	7/64/002	<i>E. coli</i>	B2	73	73	CTX-M-3	
12	7/64	7/64/004	<i>E. coli</i>	B1	443		CTX-M-15	
13	8/1	8/01/086	<i>E. coli</i>	D	648		CTX-M-15	
14	8/2	8/02/001	<i>E. coli</i>	D	69	69	CTX-M-1	
15	8/2	8/02/007	<i>E. coli</i>	B2	131	131	CTX-M-1	6
16	9/1	9/01/003	<i>E. coli</i>	A	23	23	CTX-M-14	
17	9/1	9/01/006	<i>E. coli</i>	D	362		CTX-M-14	
18	9/1	9/01/007	<i>E. coli</i>	A	23	23	CTX-M-14	
19	8/3	8/03/004	<i>E. coli</i>	B2	131	131	CTX-M-1	
20	8/3	8/03/005	<i>E. coli</i>	D	69	69	CTX-M-1	
21	8/3	8/03/010	<i>E. coli</i>	D	106	69	CTX-M-1	
22	9/3	9/03/001	<i>E. coli</i>	B2	131	131	CTX-M-27	3
23	9/3	9/03/002	<i>E. coli</i>	B2	131	131	CTX-M-27	3
24	9/3	9/03/005	<i>E. coli</i>	B2	131	131	CTX-M-15	4
25	9/3	9/03/008	<i>E. coli</i>	B2	131	131	CTX-M-27	3
26	9/3	9/03/013	<i>E. coli</i>	B2	131	131	CTX-M-27	3
27	9/3	9/03/014	<i>E. coli</i>	B2	131	131	CTX-M-27	3
28	9/3	9/03/019	<i>E. coli</i>	B2	131	131	CTX-M-15	2
29	9/3	9/03/023	<i>E. coli</i>	B2	131	131	CTX-M-27	3
30	9/3	9/03/026	<i>E. coli</i>	B2	131	131	CTX-M-1	7
31	9/4	9/04/005	<i>E. coli</i>	B2	104		CTX-M-14	
32	9/4	9/04/008	<i>E. coli</i>	B2	127		CTX-M-15	
33	9/4	9/04/011	<i>E. coli</i>	D	59	59	CTX-M-14	
34	9/4	9/04/014	<i>E. coli</i>	A	23	23	CTX-M-14	
35	9/4	9/04/016	<i>E. coli</i>	A	23	23	CTX-M-14	
36	9/5	9/05/001	<i>E. coli</i>	D	38	38	CTX-M-15	
37	9/5	9/05/012	<i>E. coli</i>	B2	131	131	CTX-M-15	1
38	9/5	9/05/013	<i>E. coli</i>	B2	131	131	CTX-M-15	1
39	9/5	9/05/016	<i>E. coli</i>	B2	131	131	CTX-M-15	1
40	9/5	9/05/018	<i>E. coli</i>	B2	131	131	CTX-M-15	1
41	9/5	9/05/024	<i>E. coli</i>	B2	131	131	CTX-M-15	1
42	9/5	9/05/026	<i>E. coli</i>	B2	131	131	CTX-M-15	1
43	1/54	1/54/003	<i>K. pneumoniae</i>		663		CTX-M-15	2
44	1/54	1/54/008	<i>K. pneumoniae</i>		663		CTX-M-15	2
45	8/1	8/01/068	<i>K. pneumoniae</i>		663		CTX-M-15	2
46	8/2	8/02/001	<i>K. pneumoniae</i>		663		CTX-M-15	2
47	8/2	8/02/002	<i>K. pneumoniae</i>		663		CTX-M-15	2

Isolate no	NH no	Resident no	Specie	Phylogroup	ST	CC	ESBL	PFGE no
48	8/2	8/02/014	<i>K. pneumoniae</i>		663		CTX-M-15	2
49	9/3	9/03/023	<i>K. pneumoniae</i>		663		CTX-M-15	2
50	9/4	9/04/003	<i>K. pneumoniae</i>		663		CTX-M-15	2
51	9/4	9/04/016	<i>K. pneumoniae</i>		3455		CTX-M-14	3
52	9/5	9/05/018	<i>K. pneumoniae</i>		307		CTX-M-15	1
53	9/5	9/05/009	<i>K. pneumoniae</i>		663		CTX-M-15	2
54	9/2	9/02/004	<i>C. farmeri</i>					
55	9/2	9/02/016	<i>C. farmeri</i>					
56	9/4	9/04/006	<i>M. morgannii</i>					

NH: nursing home; ST: sequence type; CC: clonal complex; ESBL: extended spectrum beta-lactamase; PFGE: pulsed field gel electrophoresis.

Table IV. Factors associated with ESBLE carriage from random-effects logistic regression analysis

	Univariate analysis		Multivariate analysis	
	OR	95% CI	OR	95% CI
Collective variables				
Housing capacity 50-100 residents	4.71	1.00-22.29		
Sectorisation of care during the night	0.42	0.19-0.92		
NH linked to a larger healthcare institution	0.43	0.21-0.90	0.41	0.19-0.87
Existence of an in-house pharmacy	0.49	0.23-1.03		
Existence of a preferential list of ATB	0.47	0.22-1.02		
Systematic use of single-use gloves	0.39	0.16-0.96	0.25	0.11-0.58
Staff training in hand hygiene	4.59	0.93-22.6		
Individual variables				
GIR < 3	2.04	0.99-4.18		
Never use of private bathroom	2.06	1.05-4.04	2.32	1.18-4.57
Urinary incontinence	2.70	1.05-6.93		
Previous exposure to ATB within 6 months	2.38	1.25-4.52	2.32	1.20-4.49
Amoxicillin	2.40	1.00-5.79		
3GC	2.33	0.97-5.56		
Previous hospitalization within 12 months	2.56	1.31-4.98	2.04	1.03-4.03

HW: healthcare workers; GIR: level of dependency French index; ESBLE: extended-spectrum-beta-lactamase producing *Enterobacteriaceae*; CPE: carbapenemase-producing *Enterobacteriaceae*; ATB: antibiotics; 3GC: third generation cephalosporins; NH: nursing home; CI: confidence interval.