**University of Verona**

**Department of Diagnostic and Public Health, Infectious Diseases Section**

*Graduate School for Health and Life Sciences*

*PhD Program in Applied Life and Health Sciences*

Cycle XXXI Year 2015

**A POINT PREVALENCE SURVEY**

**OF HEALTHCARE-ASSOCIATED INFECTIONS,**

**ANTIMICROBIAL USE**

**AND RECTAL COLONISATION**

**WITH EXTENDED-SPECTRUM BETA-LACTAMASE**

**AND CARBAPENEMASE-PRODUCING GRAM-NEGATIVE BACTERIA**

**IN SEVEN LONG-TERM CARE FACILITIES**

S.S.D. MED/17

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**A POINT PREVALENCE SURVEY OF RECTAL COLONISATION**

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Fulvia Mazzaferri

PhD Thesis

Verona, May 2019

ISBN

**SOMMARIO**

**Introduzione**

Nonostante le strutture di lungodegenza siano gravate da un elevato rischio di colonizzazione/infezione da batteri multi-resistenti (MDR) agli antibiotici, i dati relativi alla prevalenza di colonizzazione da batteri Gram-negativi MDR sono esegui in questo specifico contesto, dove, peraltro, le misure di controllo e prevenzione delle infezioni atte a ridurre la diffusione di tali patogeni non sono ben definite. Lo studio si propone di valutare la prevalenza e le caratteristiche epidemiologiche della colonizzazione rettale da batteri Gram-negativi (GNB) produttori di beta-lattamasi a spettro-esteso (ESBL) e di carbapenemasi tra i degenti in sette lungodegenze della Provincia di Verona.

**Metodi**

Uno studio pilota, multicentrico, di prevalenza puntuale (PPS) è stato condotto in sette lungodegenze della Provincia di Verona. Un tampone rettale è stato raccolto per identificare isolati produttori di ESBL e carbapenemasi, utilizzando test rapidi fenotipici e, successivamente, genotipici (PCR). Nel giorno prescelto per l’esecuzione della PPS, sono state valutate variabili cliniche ed epidemiologiche, tra cui durata della degenza in LTCF, eventuale ospedalizzazione nei tre mesi precedenti, eventuale intervento chirurgico nel mese precedente, somministrazione di antibiotico-terapia nel mese precedente, grado di autonomia funzionale e capacità cognitive, presenza di dispositivi medici e lesioni cutanee croniche. Proporzioni ed intervalli di confidenza sono stati stimati considerando l’effetto cluster determinato dalla struttura gerarchica del campione (in base alla struttura in cui sono stati raccolti i dati). Le associazioni tra colonizzazione e fattori di rischio sono state stimate mediante un modello di regressione logistica multivariata multilivello, considerando la singola struttura come componente random. Sono state prese in considerazione le variabili caratterizzate da *p* < 0.05 nell’analisi bivariata. Le associazioni sono state valutate calcolando Odds Ratios (ORs) e CI95. *p* < 0.05 sono stati considerati significativi.

**Risultati**

Nello studio sono stati arruolati complessivamente 453 residenti nelle lungodegenze (74.6% di sesso femminile; età media, 83.7 anni [SD 10.4 anni]). La maggior parte dei soggetti reclutati era residente da più di un anno in LTCF (78.4%) ed era caratterizzato da incontinenza urinaria e/o fecale (81%) nonché da un considerevole deterioramento delle capacità cognitive (70.2%) e del grado di autonomia funzionale (65.8%). Complessivamente, era stato somministrato un antibiotico nel mese precedente al 27.1% dei residenti, in particolare nel 9.3% dei soggetti erano state somministrate penicilline associate ad inibitori delle ß-lattamasi, nel 4.2% cefalosporine di terza generazione, nell’8.6% fluorochinoloni e nel 9.7% cotrimossazolo. Il 16.6% dei soggetti reclutati aveva un catetere urinario, il 14.6% ulcere da decubito, il 15.7% lesioni cutanee; il 9.5% era stato ospedalizzato nei tre mesi precedenti, il 3.8% disponeva di un catetere vascolare e l’1.1% era stato sottoposto ad intervento chirurgico nel mese precedente.

Durante il giorno della rilevazione, il 7.7% (n = 35) era affetto da infezione ed il 4.6% (n = 21) stava assumendo terapia antibiotica.

I degenti colonizzati con ceppi produttori di ESBL (88.8% *Enterobacteriaceae* e 11.2% GNB non-fermentanti) e GNB produttori di carbapenemasi (77.8% *Enterobacteriaceae* e 22.2% GNB non-fermentanti) erano 39.5% (CI95, 32.5%-47%) e 4% (CI95, 2.8%-5.6%), rispettivamente. La prevalenza di colonizzazione a livello di singola struttura variava dal 14.3% al 57.1% per i ceppi produttori di ESBL e da 0 a 9.5% per i GNB produttori di carbapenemasi. I fattori di rischio significativamente associati alla colonizzazione da MDR-GNB differivano tra i residenti colonizzati con GNB produttori di ESBL e quelli colonizzati con ceppi produttori di carbapenemasi. L’appartenenza al genere maschile (OR, 2.2; CI95, 1.4-3.7; *p* = 0.002), una pregressa esposizione alle cefalosporine di terza generazione (OR, 3.9; CI95, 1.3-12; *p* = 0.016) e l’allettamento (OR, 1.7; CI95, 1-2.9; *p* = 0.04) erano indipendentemente associati con la colonizzazione da GNB produttori di ESBL, mentre la pregressa ospedalizzazione (OR, 4.1; CI95, 1.3- 13.1; *p* = 0.02) rappresentava l’unico fattore di rischio indipendentemente associato con la colonizzazione da ceppi produttori di carbapenemasi.

**Conclusioni**

Lo studio conferma un’elevata prevalenza di colonizzazione da GNB produttori di ESBL tra i residenti nelle LTCFs ed evidenzia un allarmante tasso di colonizzazione da GNB produttori di carbapenemasi. Da questi dati emerge la necessità urgente di promuovere e coordinare a livello nazionale un sistema di sorveglianza attiva di MDR-GNB in LTCF, che guidi le attività di prevenzione e controllo delle infezioni. Le differenze rilevate nell’associazione di specifici fattori di rischio suggeriscono che la diffusione di GNB produttori di ESBL e carbapenemasi segua percorsi differenti. Le misure di controllo e prevenzione delle infezioni dovrebbero, pertanto, essere mirate in funzione del tipo di GNB antibiotico-resistente.

**ABSTRACT**

**Background**

Although long-term care facility (LTCF) residents are at increased risk for colonisation/infection with multidrug-resistant (MDR) organisms, few data are available on the prevalence of colonisation due to MDR-gram negative bacteria (GNB) in this setting, where infection control and preventive measures to reduce the spread of MDR bacteria are not well defined. The study investigated the prevalence and differences in the epidemiology of rectal colonisation with extended-spectrum beta-lactamase (ESBL) and carbapenemase-producing GNB among residents in LTCFs.

**Methods**

A multicenter point prevalence survey (PPS) was conducted in seven LTCFs in Italy. A rectal swab was collected to identify ESBL and carbapenemase-producing isolates, using rapid phenotypic methods and, subsequently, multiplex and single PCR. Clinical and epidemiological variables were assessed on the day of the PPS, including LTCF length of stay, hospitalization within three months and surgery and antimicrobial therapy within one month, functional and mental status, presence of medical devices and chronic skin lesions. Proportions and 95% confidence interval (CI95) were estimated accounting for cluster effect of the sample hierarchical structure (data collection site). The associations between colonisation and risk factors were estimated with a multilevel multivariate logistic regression model, with the data collection site as random component, assessing variables with *p* < 0.05 from bivariate analysis. Odds ratios (ORs) and CI95 were calculated to evaluate the associations. A *p* value < 0.05 was considered significant.

**Results**

A total of 453 residents were enrolled (74.6% females; mean age 83.7 years, SD 10.4 years). The majority of residents had urinary and/or faecal incontinence (81%), had spent more than one year in LTCF (78.4%), and had a low mental (70.2%) and functional (65.8%) status. 9.3% residents were administered penicillins/ß-lactamase inhibitors within the previous month, 4.2% were administered third-generation cephalosporins, 8.6% fluoroquinolones, and 9.7% cotrimoxazole (27.1% had received an antibiotic within the previous month). 16.6% had a urinary catheter, 15.7% had skin lesions, 14.6% had pressure sores, 9.5% had been hospitalised within 3 months, 3.8% had a vascular catheter, and 1.1% underwent surgery within the previous month.

7.7% (n = 35) was the prevalence of active infections on the PPS day. 21 residents (4.6%) received at least one antibiotic on the PPS day.

Residents colonised with ESBL (88.8% *Enterobacteriaceae* and 11.2% non-fermenting GNB) and carbapenemase-producing GNB (77.8% *Enterobacteriaceae* and 22.2% non-fermenting GNB) were 39.5% (CI95, 32.5%-47%) and 4% (CI95, 2.8%-5.6%), respectively. Prevalence of colonisation at site level ranged from 14.3% to 57.1% for ESBL and from no detected cases to 9.5% for carbapenemase-producing GNB. Risk factors differed between residents colonised with ESBL and those with carbapenemase-producing strains. Male gender (OR, 2.2; CI95, 1.4-3.7; *p* = 0.002), previous exposure to third-generation cephalosporins (OR, 3.9; CI95, 1.3-12; *p* = 0.016) and bedridden status (OR, 1.7; CI95, 1-2.9; *p* = 0.04) were independently associated with ESBL colonisation, while previous hospitalization (OR, 4.1; CI95, 1.3-13.1; *p* = 0.02) was the only risk factor independently associated with carbapenemase-producing GNB colonisation.

**Conclusions**

The study confirms a high colonisation prevalence with ESBL-producing GNB among LTCFs residents and shows an alarming rate of residents colonised with carbapenemase-producing GNB. A national comprehensive effort is needed to promote and coordinate active surveillance of MDR-GNB in LTCFs to inform infection control teams. Differences in risk factors suggest that the spreading of ESBL and carbapenemase-producing GNB follows different routes. Infection control and preventive measures should be tailored on the type of antimicrobial-resistant GNB.

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**BACKGROUND**

Long-term care facilities (LTCFs) serve residents at increased risk for colonisation and infection with multidrug-resistant organisms, bear a disproportionate burden of multidrug resistant (MDR) bacteria, and have been shown to be a major contributor to the dissemination of resistances throughout a geographic region (1).In this setting, infections caused by MDR Gram-negative bacteria has been associated with increased morbidity, mortality, and cost, although the attributable morbidity, mortality, and cost of MDR bacteria has not yet been fully defined (2, 3). Moreover, LTCF residence has been frequently identified as a risk factor for antibiotic-resistant infections in hospitalized patients (4, 5).

Elderly and disabled residents are at increased risk for colonisation with resistant organisms, and colonisation may persist for long periods of time (months to years) (6-9). Both infected and colonised residents may serve as sources for the spread of MDR bacteria in the LTCF, most likely via cross-transmission after breaches in infection prevention measures, such as healthcare-worker hand hygiene and reduced compliance with basic hygiene measures because of the frequent cognitive impairment of residents (10, 11). Other relevant factors contribute to the promotion of MDR spread within these facilities, such as permanent living in a confined environment and challenging diagnosis of atypical infections. Moreover, antibiotics are among the most commonly prescribed classes of medications for LTCF residents, increasing the selective pressure for MDR bacteria (12).

As in other high-income countries worldwide, the aging population in Italy represents an increasing public health priority (13). Thus, coordinated regional active surveillance screenings have been promoted as necessary to achieve durable control.

**Demography**

There were 3.7 million residents of LTCFs in the European Union (EU) in 2010, according to the European Centre for Disease Prevention and Control (ECDC), and this number will certainly increase in the coming decades (2). The same is true beyond Europe: by 2030, 70 million people in the USA will be aged 65 years or more; given that nearly 4% of people aged 65 or older are nursing home residents, the need for LTCFs will increase (14).

According to the most recent (2013) national data (Istituto nazionale di Statistica, ISTAT), in Italy, residential care facilities were 12261 with 384450 beds (6.3/1000 residents). The majority of the residential care facilities provided both social and healthcare services (74%). They mainly provided services to care-dependent elderly. The rest of the facilities (26%) provided social care only. Huge geographical differences were detected: 66% of all residential care beds were located in the northern regions with a rate of 9 beds/1000 residents *versus* 3 beds/1000 residents in the southern regions. The greatest supply of both health and social residential care services was recorded in the northern regions with 7.4 beds/1,000 residents *versus* 2 beds/1000 residents in the southern regions. The residential care recipients were 367000. 76% were elderly people aged 65 and over, 19% were adults aged between 18 and 64. Half of the elderly recipients were aged over 85, 76% of them were care-dependent, and the ratio by sex was greatly unbalanced in favour of women (75%).

**Definitions**

**Long-term care facilities** (**LTCFs**) may be defined as institutions that provide healthcare to people who are unable to manage independently in the community. This care may be chronic care management or short-term rehabilitative services. A **resident** is a person living in the LTCF and receiving care. General nursing homes are facilities licensed with an organized professional staff and inpatient beds, that provide medical or skilled nursing and supervision 24h a day to residents who are not in the acute phase of an illness, mainly elderly with severe illnesses or injuries. Specialised LTCFs target one specific type of care (e.g. physical impairment, chronic diseases such as multiple sclerosis, dementia, psychiatric illnesses, rehabilitation care, palliative care, intensive care). Mixed LTCFs provide different types of care in the same facility (a mix of the above mentioned LTCF types).

**Health-care associated infections** (**HCAI**) include all the infections that are linked with the exposure to care procedures with a diagnostic or therapeutic purpose. The term nosocomial infection (NI) or hospital-acquired infection (HAI) includes all the infectious episodes that occur in a patient hospitalized for at least 48 hours, thus excluding all the infections clinically evident or incubating on admission. Friedman et al. have proposed to detach the NI from HCAI, specifying that the latter include all the infections that are clinically evident at admission or within 48 hours of hospitalization, arisen in an already-ill population of nursing-home residents, patients in LTCFs, patients undergoing same-day procedures (chemotherapy or dialysis), or recently (within 3 months) discharged from hospital or patients receiving home-based healthcare (among which intravenous therapy and wound dressing) (15). On the basis of this definition, this work will use the term HCAI to define infections in LTCFs.

**Extended-spectrum β-lactamases** (**ESBLs**) are a rapidly evolving group of β-lactamases capable of conferring bacterial (Gram-negative) resistance to the penicillins, first-, second-, and third-generation cephalosporins, and aztreonam (but not the cephamycins or carbapenems) by hydrolysis of these antibiotics, and which are inhibited by β-lactamase inhibitors such as clavulanic acid (16). Enzyme-mediated bacterial (Gram-negative) resistance to carbapenems is due to the production of beta-lactamases (**carbapenemases**) that are able to inactivate carbapenems together with other beta-lactam antibiotics, therefore hydrolyzing all or almost all beta-lactams (17). Both ESBL and carbapenemases are encoded by genes that are horizontally transferable by plasmids or transposons and are commonly associated with genes encoding for other resistance determinants (16, 17). Studies evaluating clinical outcomes in patients with infections sustained by bacteria producing ESBLs and, above all, carbapenemases have shown a trend toward higher mortality, longer hospital stay, greater hospital expenses, and reduced rates of clinical and microbiologic response (18). These beta-lactamases are harboured by both Enterobacteriaceae and non-fermenting Gram-negative rods, such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

**Epidemiology of HCAI**

In December 2008, ECDC initiated surveillance of HCAIs and antimicrobial use in European long-term care facilities (LTCFs) under the Healthcare-Associated Infections in Long-Term Care Facilities (HALT) project. The HALT project integrated variables from the European Surveillance of Antimicrobial Consumption in Nursing Homes (ESAC-NH) subproject into a protocol for repeated point prevalence surveys (PPSs) in LTCFs, thus providing an integrated methodology for continued assessment of the prevalence of HAIs, antimicrobial use, and infection prevention and control resources in European LTCFs. From May to September 2010, a first PPS in European LTCFs (HALT project, 2010) collected data from 722 LTCFs across 25 European countries (19). The prevalence of residents with at least one HCAI in participating LTCFs was 2.4%.

From April to May 2013, a second PPS in European LTCFs (HALT-2 project, 2013) collected data from 1181 LTCFs in 17 European countries (20). To date, the 2013 HALT-2 PPS, which will be soon replaced by the upcoming European-wide results of HALT-3, is the most recent European epidemiological study performed in this setting. The prevalence of residents with at least one HCAI was 3.4%. In particular, rates of respiratory tract infections, urinary tract infections (UTIs) and skin/wound infections were 38%, 29% and 16%, respectively (20).

Italian HALT-3 results have already been published. Data were collected from April to June 2017. 418 LTCFs were included and 24132 residents were enrolled. 3.9% was the prevalence of residents with at least one HCAI. In particular, rates of respiratory tract infections, UTIs and skin/wound infections were 36.6%, 26% and 15.7%, respectively. 253 pathogens were isolated, mainly from urine culture. 29.6% of strains displayed resistance to at least one tested drug. The most frequent isolates were *Escherichia coli* (37.3%; 27% resistant to third-generation cephalosporins and 3.2% resistant to carbapenems), *Proteus mirabilis* (24%; 23% resistant to third-generation cephalosporins and 6.6% resistant to carbapenems), *Klebsiella pneumoniae (*14.7%; 19% resistant to third-generation cephalosporins and 11% resistant to carbapenems), *Pseudomonas aeruginosa (*5.3%; 31% resistant to carbapenems), and *Acinetobacter baumannii* (2.7%; 28.5% resistant to carbapenems) (21).

Considering HALT-3 results in Veneto, 33 LTCFs were included and 3788 residents were enrolled. 3.3% was the prevalence of residents with at least one HCAI. In particular, rates of respiratory tract infections, UTIs and skin/wound infections were 38%, 23% and 16%, respectively. 26 pathogens were isolated, mainly from urine: 17 were Enterobacteriacee (8 *Escherichia coli*, 5 *Proteus mirabilis*, 3 *Klebsiella pneumoniae, 1 Providencia stuartii)*, 1 *Acinetobacter baumannii*, and 1 *Pseudomonas aeruginosa*. 6 Enterobacteriaceae were resistant to third-generation cephalosporins and 1 (*Klebsiella pneumoniae*) was not susceptible to carbapenems. Considering the non-fermenting Gram-negative rods, only *Acinetobacter baumannii* was resistant to carbapenems (21).

Although biased by many flaws, mainly linked to the point prevalence study design, HALT PPSs display relevant data to drive empirical antimicrobial treatment of the most frequent infections observed in LTCFs (20, 21).

**Antibiotic consumption**

Residents of LTCFs are at particular risk for HCAI (22), thus antibiotics are among the most commonly prescribed classes of medications for LTCF residents (23). Between 3% and 15% of LTCF residents are given antibiotics at any time according to point prevalence studies in Europe, USA and Australia (24-26). The incidence of antibiotic use varies considerably, with 50–80% of residents receiving at least an antibiotic course per year (23, 25, 27). There is substantial facility-level variation in antibiotic-prescribing incidence (at least five- to ten-fold) (25, 28, 29), which may partly explain the differences seen in the European-wide study of nursing homes between six defined daily doses per 1000 residents per day in Germany to 136 defined daily doses per 1000 residents per day in Northern Ireland (30). A recent systematic review showed that antibiotics are most frequently prescribed for urinary tract infections (32–66%), respiratory tract infections (15–36%) and skin and soft tissue infections (13–18%) (25).

According to 2013 HALT-2, 4.4% was the European crude prevalence of residents with at least one antimicrobial agent: on the day of the PPS, 3367 out of 77264 eligible LTCF residents received at least one antimicrobial agent. 94.5% received one antimicrobial and 5.2% received two agents. The crude prevalence of antimicrobial use varied between less than 2% in Croatia, Germany, and Hungary to more than 10% in the Czech Republic, Denmark and UK. The overall median prevalence in LTCFs for residents receiving at least one antimicrobial was 3.6%. On the survey day, 3561 antimicrobial agents were prescribed. These were mainly administered orally (87.3%), a parenteral route was used in 11.6% prescriptions. Antimicrobials were mainly prescribed in the LTCF itself (84.6%), 11.0% were prescribed in the hospital, and 4.1% elsewhere. They were primarily prescribed by general practitioners (54.0%) and medical doctors (32.2%) employed by the LTCF, otherwise by a specialist (12.0%) or another person such as a pharmacist or nurse (1.9%) (20).

Antimicrobials were most frequently prescribed for the treatment of an infection (72.8%), the remaining antimicrobials were prescribed for prophylactic use (27.2%). The percentage of antimicrobials prescribed for prophylaxis was highest in UK – Northern Ireland (53.3%), Norway (52.0%) and Denmark (50.7%). Antimicrobials were mostly prescribed for prophylaxis or treatment of a UTI (47.5%) or of a respiratory tract infection (30.1%). Skin or wound infections were the third most commonly reported indication (13.0%). In Italy respiratory tract infections were the most frequently reported indication (42.4%). The majority of the prophylactic prescriptions were for the prevention of UTIs: uroprophylaxis accounted for 22.0% of all antimicrobial use but this percentage varied greatly between countries. The most frequently used classes were beta-lactams/penicillins (29.3%), quinolones (16.0%), other beta-lactams (12.5%) and cotrimoxazole (11.9%) (20).

According to 2017 HALT-3, 4.2% was the Italian crude prevalence of residents with at least one antimicrobial agent. The overall median prevalence in LTCFs for residents receiving at least one antimicrobial was 3.3%. These were mainly administered orally (58.4%), a parenteral route was used in 41% prescriptions. Antimicrobials were most frequently prescribed for the treatment of an infection (87.7%), the remaining antimicrobials were prescribed for prophylactic use (12.3%). Considering infections, they were mostly prescribed for the treatment of a respiratory tract infection (39.6%) or of a UTI (26.3%). Skin or wound infections were the third most commonly reported indication (12.3%). The most frequently used classes were cephalosporins (29.4%), penicillins (23.9%), quinolones (21.4%), and cotrimoxazole (6%) (21).

Considering HALT-3 results in Veneto, 4.2% was the Italian crude prevalence of residents with at least one antimicrobial agent. Antibiotics were mainly prescribed in the LTCF itself (90%), 10% were prescribed in hospital or elsewhere. Antimicrobials were mainly administered parenterally (47%), an oral route was used in 46% prescriptions. Antimicrobials were most frequently prescribed for the treatment of an infection (90%), the remaining antimicrobials were prescribed for prophylactic use (10%). Considering infections, they were mostly prescribed for the treatment of a respiratory tract infection (40%) or of a UTI (24%). Skin or wound infections were the third most commonly reported indication (17%). The most frequently used classes were third-generation cephalosporins (25%), penicillins (24%), and quinolones (17%) (21).

**Epidemiology of colonisation with MDR Gram-negative bacteria**

Surveys exploring colonisation rates with ESBL producing Enterobacteriaceae in European LTCFs are quite heterogeneous in terms of facility sizes, resident characteristics and specimen types, therefore direct comparison between different studies would be subjected to bias. Nevertheless, high variability of colonisation rate for ESBL producing Enterobacteriaceae, ranging from close to zero up to more than 50%, can be derived from these studies; variability is high not only between countries but also between different LTCFs within a single country (31-46).

Despite the recent emergence and worldwide spread of CRE has generated an immediate infection threat to residence in LTCFs, which has been identified as an independent risk factor for CRE blood stream infections (47), colonisation with CRE has been investigated only by two European studies in LTCFs, both reporting a low colonisation prevalence: 0% in a study from Ireland (32) and 0.3 % in a study from the Netherlands (48).

Italy displays one of the highest rates of MDR bacteria isolated from blood cultures among European countries (49). Nevertheless, only a few point prevalence studies investigating MDR colonisation have been performed in Italian LTCFs during the last 10 years, including a limited number of centres located in northern provinces of the country. These surveys reported ESBL prevalence ranging from 49% to 64% and CRE prevalence ranging from 1% to 6.3% (50-53).

ESBL-producing *Escherichia coli* isolates frequently belong to the pandemic clonal group ST131 (mainly the H30-ST131 sub-clone) (54); the association of this group with LTCFs has been widely documented (55). In the European LTCFs, the ST131 group often harbours ESBL genes belonging to various CTX-M types (mostly CTX-M-15) (32, 35-37). In the Italian LTCFs, the most prevalent (79%–97%) ESBL-producing *Escherichia coli* harbours CTX-M-type enzymes as well, mostly CTX-M-15, belonging to the ST131 clonal group (51, 52, 56, 57). A study investigating rectal colonisation in 12 Italian LTCFs detected the H30-ST131 sub-clone in the majority of the ESBL-producing *Escherichia coli* (71%) (53). On the other hand, ESBLs in *Klebsiella pneumoniae* are mainly encoded by blaCTX-M or blaSHV-12 genes, whereas ESBLs in *Proteus mirabilis* and *Morganella morganii* are generally encoded by blaTEM-92 (51, 52, 56, 58).

Sporadic or epidemic CRE colonisations/infections have been reported in the European LTCF residents, due to oxacillinase 48 (OXA-48)-producing *Klebsiella pneumoniae* in the Netherlands (48), *Klebsiella pneumoniae* carbapenemase 2 (KPC-2)-producing *Escherichia coli* and *Klebsiella pneumoniae* in Greece (59), *Klebsiella pneumoniae* carbapenemase 3 (KPC-3)*-*producing *Klebsiella pneumoniae* in Portugal (60), and New Delhi metallo-β-lactamase-1 (NDM-1)-producing *Klebsiella pneumoniae* in Poland (61). The most common carbapenemase types in the Italian LTCF isolates are KPC (various types) and the Verona integron-encoded metallo-β-lactamase-1 (VIM-1). KPC-producing *Klebsiella pneumoniae* are widely distributed in the Italian LTCFs, mostly belonging to the clonal group ST258 (62). A study involving 489 residents in 12 Italian LTCFs found that only 5 isolates produced carbapenemases (1% colonised residents): 3 *Klebsiella pneumoniae* isolates harboured blaKPC-3 and 2 *Escherichia coli* isolates carried blaVIM-1 (53). Further sporadic KPC-2-producing *Klebsiella pneumoniae* and VIM-1-producing *Escherichia coli* (ST131) isolates were found by other authors in the Italian LTCF residents (51, 63, 64).

**Risk factors for colonisation with MDR Gram-negative bacteria**

LTCF residents are uniquely vulnerable to MDR colonisation and infections (13, 65). Many risk factors have been found significantly associated with MDR colonisation in European LTCFs: old age, male sex, physical disability, bedridden status, low functional status, prolonged duration of stay in LTCF, invasive medical devices (urinary catheter, percutaneous enteral gastrostomy tube, tracheostomy tube), previous administration of antibiotics within the preceding year, colonisation history by the same microorganism, MDR bacteria carriage of other residents, multiple room occupancy, MDR carrier in the same room, residency in specific unit within LTCF, prior admission to acute care hospital, surgical procedures within 30 days, cancer, decubitus ulcer, various wounds, skin lesions, peptic ulcer, use of antiacids, chronic renal failure, history of urinary tract infections, urinary and faecal incontinence, chronic obstructive pulmonary disease (COPD), and diabetes (31, 33-36, 38-43, 46, 66-72).

Nursing home residents are prone to exposure to the microbial flora of other residents, especially if they require frequent contact with healthcare providers. LTCF residents frequently depend on staff care for daily living activities with many opportunities for horizontal transmission of MDR organisms between residents and workers (resident-to-staff and staff-to-resident transmission). It has been well documented that handwashing rates are low among nursing home personnel (73). Moreover, the strict application of hospital hygiene measures in LTCFs is difficult because of encouraged social interactions.

Previous hospitalisation represents a further risk factor for MDR colonisation, as well as surgical procedures, chronic diseases, and outpatient care, which increase the contact of residents with the healthcare system (13).

Several further risk factors have been described, including the lack of infection control policies, inadequate staffing and high staff turnover, increased number of residents per bedroom and limited hand-washing facilities (13). Urinary catheterization and decubitus ulcers are frequent (74) and have been associated with colonisation with MDR Gram-negative bacilli (75).

With specific regard to ESBL, there is some evidence that nursing homes may serve as a reservoir for introduction of ESBL-producing bacteria into acute-care hospitals (76, 77). Conversely, patients with hospital-acquired colonisation or infection may return to their nursing home with ESBL carriage (78). Within nursing homes, antibiotic use is a risk factor for colonisation with ESBL-producing organisms. Use of third-generation cephalosporins has been identified as a predisposing event in some but not all studies (77). In contrast to the situation in acute-care hospitals, use of orally administered antibiotics (ciprofloxacin and/or trimethoprim-sulfamethoxazole) may also be a risk for colonisation with an ESBL-producing strain (77). Interestingly, a Dutch study found that colonisation with methicillin-resistant *Staphylococcus aureus* more than doubled the likelihood of colonisation with ESBL-producing *E. coli* (41); this finding might be explained by the similar transmission pathways followed by these MDR organisms among LTCF residents.

**Infection control measures**

There is no consensus on the most effective infection control (IC) intervention or the best combination of interventions to reduce transmission of MDR Gram-negative bacteria in LTCFs. In particular, there is no consensus on species or types that are more likely to require control measures, or on the role of screening to identify carriers. Several authors have discussed the components of an infection control program in the LTCF (79-84). These components generally are drawn from regulatory requirements, current nursing home practices, and extrapolations from hospital programs. The limited resources of most LTCFs affect the type and extent of developed programs (84). Most authors feel that an infection control program should include some form of surveillance for infections, an epidemic control program, education of employees in infection control methods, policy and procedure formation and review, environmental review, monitoring of antibiotic use and resident care practices, and reporting of diseases to public health authorities.

Considering 2013 HALT-2 results in Europe, LTCFs were asked whether there was a person with training in IC available to the staff, an IC committee, and/or formal access to help and advice from an external IC team. 66.5% facilities had an IC trained person at their disposal. The majority of institutions had an IC trained nurse (71.3%), while 23.3% had both a nurse and a doctor, and 5.4% facilities had an IC trained doctor; the majority was a member of the LTCF staff (60%), while 21.7% worked externally. 42.6% LTCFs had an IC committee and 79.1% institutions referred to an external IC team (20).

The availability of five IC protocols was also explored in the institutional questionnaire. Almost all LTCFs (95.9%) had a written protocol for hand hygiene. There was also a high availability of protocols for the management of MDR organisms (76.9%), urinary catheters (84%) and enteral feeding (76.8%). Only half of the institutions had a protocol for the management of venous catheters/lines (50%). 1.8% facilities had none of the five written protocols in place and 35.6% reported all five protocols (20).

Commonly performed practices included the followings: offer of annual immunisation for flu to all residents (88.5%), decisions on isolation and additional precautions for residents colonised with resistant microorganisms (80.8%), and development of care protocols (79.6%). Appropriate training of general practitioners and medical staff in infection prevention and control was uncommon (13.3%) (20).

Regarding the availability of personal protection equipment, all facilities had gloves at their disposal, and the vast majority had access to masks (95.0%), gowns (long sleeves; 93.1%) and aprons (short sleeves; 81.5%). Goggles were available in 65.1% LTCFs (20).

Regarding hand hygiene, the majority of the LTCFs used an alcohol-based solution for hand disinfection (56.2%). Hand washing with water and an antiseptic soap or non-antiseptic soap was used by 25.3% and 18.5% LTCFs, respectively. While liquid soap (98.2%) and alcohol-based rub solution (90.7%) were highly available in the LTCFs, alcohol wipes (23.3%) and bar soap (4.6%) were less common. 79.5% LTCFs reported the number of hand-alcohol litres used in the previous year: the median usage was 4.2 litres per 1000 resident days, assuming 95% occupancy (mean, 8 litres). The median consumption rates reported from single countries ranged from 0.3 to 16.1 litres. Hand hygiene training for care professionals was organised in 73.4% LTCFs during the previous year. Nurses and nurse aides (98.9%) and cleaning staff (71.3%) were most frequently involved (27.5% medical staff) (20).

According to 2017 HALT-3 results in Italy, 50% facilities had an IC trained person at their disposal. Almost all LTCFs (97.8%) had a written protocol for hand hygiene. There was also a high availability of protocols for the management of urinary catheters (96.2%), venous catheters/lines (94.3%), enteral feeding (88.8%), and MDR organisms (75.8%). Commonly performed practices included the followings: offer of annual immunisation for flu to all residents (94.3%), decisions on isolation and additional precautions for residents colonised with resistant microorganisms (86.8%), and development of care protocols (87.3%). Appropriate training of general practitioners and medical staff in infection prevention and control was uncommon (23.9%) (21).

According to 2017 HALT-3 results in Veneto, 31% facilities had an IC trained person at their disposal. The majority of institutions had both an IC trained nurse and an IC trained doctor (60%), while 30% had a nurse, and 10% facilities had an IC trained doctor; the majority was a member of the LTCF staff (90%). There was also a high availability of protocols for the management of urinary catheters (91%), venous catheters/lines (91%), enteral feeding (78%), and MDR bacteria (63%). Commonly performed practices included decisions on isolation and additional precautions for residents colonised with MDR bacteria (97%). Despite hand hygiene training for care professionals was organized just in 38% LTCFs during the previous year, 94% LTCFs had a written protocol for hand hygiene. The majority of the LTCFs used an alcohol-based rub solution and a liquid non-antiseptic soap for hand washing (56% and 34%, respectively). In the previous year, IC training for healthcare professionals was organised involving nurses and nurse aides in 66% LTCFs and medical staff in 13% facilities only (21).

**Strategies for active surveillance screening of MDR Gram-negative bacteria**

Active surveillance should provide useful information to reduce cross transmission of MDR pathogens. The best strategies for MDR Gram-negative bacteria (GNB) in LTCFs are still being defined. Active screening culture allows the early identification of patients with colonisation due to MDR-GNB in order to apply contact precautions and reduce person-to-person spread. This is based on the well-established evidence that a significant reservoir of MDR-GNB colonised patients would go undetected by relying on results from clinical specimens submitted for routine diagnostic testing (85-87).

Rectal/stool swab culture has been demonstrated the single most sensitive specimen type for detecting ESBL- and carbapenemase-producing Gram negative colonising bacteria. A recent clinical epidemiological investigation quantified the sensitivity of perianal/rectal surveillance cultures in detecting MDR-GNB bacteria and identified factors associated with false-negative surveillance culture results (88). In this study, the sensitivity of perianal/rectal surveillance swabs for detecting MDR-GNB colonisation was 78%. The percentage was higher than that reported in other studies, which ranged from 42% to 69% when only colonisation of the rectal site with non-Acinetobacter MDR-GN species was considered (89, 90). Most of the studies investigating colonisation with MDR Gram-negative bacteria in LTCFs collect rectal swabs, which display a high sensitivity, ranging from 77% to 96% (50, 51).

Considering that genotypic PCR-based approaches for screening of MDR-GNB are still at an early stage, phenotypic culture-based methodologies for screening are the most reliable option and remain the most favorable in terms of capacity and costs. Techniques using conventional bacterial culture methods on agar plates to screen individuals for MDR-GNB are well-established. CRE screening was carried out on chromogenic ESBL agar plates in two out of three Italian colonisation studies (50, 51). The most important and recent development for the phenotypic identification of cultured strains of ESBL-producing and carbapenemase-producing Enterobacteriaceae are the ESBL NDP and Carba NP tests, respectively. These biochemical tests are based on in vitro hydrolysis of cefotaxime and imipenem, respectively, detected by a change in the pH value of the indicator (red to yellow). These rapid (less than 2 hours) and low-cost identification techniques have been reported nearly 100% sensitive and 100% specific, as molecular techniques are. They detect not only all known β-lactamases in Enterobacteriaceae but identify also any new emerging hydrolytic enzyme, in contrast to molecular techniques (91, 92).

**Challenges in the antimicrobial stewardship in LTCFs**

In elderly persons, diagnosis of infection is often difficult, which may easily lead to the inappropriate prescription and increased use of antimicrobials, which entails an increased risk for the development of multi-resistant bacteria (22, 23). Considering that (a) approximately 50% of antimicrobial use in LTCFs has been deemed unnecessary or inappropriate, (b) antimicrobial stewardship programmes tend to be less well-organised and less resourced than in acute-care facilities, and (c) specific guidelines on antibiotic management are often lacking, antimicrobial stewardship is advocated in this setting (13, 21, 23, 25, 28, 93-99).

Diagnosis of infections in LTCFs can be challenging due to the lack of on-site diagnostic testing equipment (23). Loeb *et al.* noted a high frequency (90%) of inappropriate diagnostic work-up in LTCFs (99). Elderly residents may have undetected co-morbidities and predominance of vague systemic symptoms over blunted febrile responses (22, 23, 25). Referring to UTIs, D’Agata *et al.* found that 75% of suspected UTIs were treated with antibiotics, despite 84% of these episodes did not fulfilled the minimum clinical criteria to support antimicrobial initiation (100). The usefulness of urinary specimens in diagnosing UTIs in these residents is also questionable because urinalyses and urine cultures result positive in the vast majority of episodes despite the absence of minimum signs or symptoms.

The European Surveillance of Antimicrobial Consumption (ESAC) surveys highlighted that there can be many different types of care providers active in delivering medical care in LTCFs (101, 102). Care to residents can be delivered by the resident’s personal general practitioner or by medical doctors directly employed by the LTCF with wide variations between countries. The existence of more than one type of prescriber in LTCFs, as seen in many countries, can raise questions about the harmonisation of antimicrobial prescriptions between prescribers, and may complicate overall responsibility for antimicrobial stewardship.

Previous research has shown that in LTCFs, nursing staff often drives antibiotic prescribing (24, 25, 29, 30, 103, 104). In an American study, physicians reported that they often prescribed treatment for UTIs on the basis of nursing staff information about symptoms and signs (104). A Canadian study also showed that only 44% of the antibiotic recipients had an associated claim for a physician bedside visit (29). Despite this reliance on nursing staff, nurses are frequently not trained to evaluate residents with a possible infection, and educational efforts are hampered by high staff turnover and sometimes lack of resources (105).

2013 HALT-2 survey reported that the majority of LTCFs did not have a restrictive list of antimicrobials for prescription (76.4%). The most commonly restricted antimicrobials were vancomycin (60.5%), carbapenems (59.7%), intravenously administered antibiotics (51.1%), third generation cephalosporins (48.1%), glycopeptides (46.4%), fluoroquinolones (42.9%), broad-spectrum antibiotics (38.6%), and mupirocin (36.9%). The most commonly reported antimicrobial stewardship elements were the followings: therapeutic formulary, comprising a list of antibiotics (33.6%), advice from a pharmacist for antimicrobials not included in the formulary (20.7%), and written guidelines for appropriate antimicrobial use in the facility (20%). The presence of data on annual antimicrobial consumption by antimicrobial class (16%) and local antimicrobial resistance profile summaries (11%) were rarely reported. 34.8% LTCFs had a written therapeutic guideline for UTIs, 28.9% had a guideline for RTIs, and 35.3% for wound and soft tissue infections. Surveillance programmes were uncommon in LTCFs: the most frequently reported programme was surveillance of resistant microorganisms (38.5%), followed by surveillance of HCAIs (29.7%), and antimicrobial consumption (16.1%) (20).

According to 2017 HALT-3 results in Italy, the majority of LTCFs did not have a restrictive list of antimicrobials for prescription (64.8%). The most commonly reported antimicrobial stewardship elements were the followings: therapeutic formulary, comprising a list of antibiotics (75.6%), advice from a pharmacist for antimicrobials not included in the formulary (41.9%), and written guidelines for appropriate antimicrobial use in the facility (20.3%). The presence of local antimicrobial resistance profile summaries (37%) and data on annual antimicrobial consumption by antimicrobial class (25%) were rarely reported (21).

**METHODS**

**Objectives**

1. To assess the prevalence of MDR-GNB rectal colonisation, focusing on ESBL-producing and CRE-producing GNB
2. To assess risk factors for MDR-GNB rectal colonisation within the LTCFs in Verona district
3. To assess the prevalence of HCAI among residents within the LTCFs in Verona district
4. To assess the prevalence of antimicrobial consumption among residents within the LTCFs in Verona district
5. To identify any previously implemented measures for the IC within the LTCFs involved

**Population**

LTCF types eligible to participate were the followings:

* general nursing homes: facilities licensed with an organized professional staff and inpatient beds, which provide medical or skilled nursing and supervision 24h a day to residents who are not in the acute phase of an illness, mainly elderly with severe illnesses or injuries;
* specialised LTCFs: facilities targeting one specific type of care (e.g. physical impairment, chronic diseases such as multiple sclerosis, dementia, psychiatric illnesses, rehabilitation care, palliative care, intensive care);
* mixed LTCFs: facilities providing different types of care (a mix of the above mentioned LTCF types).

The following facilities were excluded:

* long-term care hospitals;
* residential cares (accommodations without any kind of nursing care);
* hostel care (hotel without any kind of nursing care);
* sheltered housing;
* day centers;
* home-based centers;
* protected living.

Included LTCFs were selected for invitation based on proximity to short-stay hospitals in the city of Verona, where district control efforts are focused, and because they were all members of a single corporation, which included most of the LTCFs in Verona district.

The following residents were eligible:

* residents living full-time (24 hours a day) in the LTCF;
* residents present in the LTCF on the day of the PPS, including those who were temporarily outside the LTCF (e.g. for diagnostic investigations or medical procedures; with family/friends; etc.);
* residents admitted in the LTCF at least one day before the PPS;
* residents not discharged from the LTCF at the time of the PPS;
* residents who needed constant supervision, high-skilled nursing care and/or assistance for daily activities.

The following residents were excluded:

* residents not living full-time in the LTCF (e.g. residents from day care centers)
* residents living full-time in the LTCF but not present on the day of the PPS (e.g. absent for leave or admitted to a hospital)
* residents hospitalised on the day of the PPS (i.e. inpatient in a hospital with a stay of at least one night)
* residents who did not display a signed informed consent.

Residents receiving chronic ambulatory care on a regular basis in an acute care hospital (e.g. haemodialysis or chemotherapy) were not excluded from the PPS if they were not hospitalised on the day of the PPS (hospital stay of at least one night).

**Study design and sample size**

A multicentre point prevalence survey (PPS) was conducted in 7 LTCFs.

There was no need for a formal sample size justification because of the pilot nature of this PPS.

**Time frame**

Data pertaining a single LTCF were collected in a single day. Nevertheless, data collection was carried out in two or more consecutive days where a large number of residents was provided (more than 50). All the beds set in the same ward were screened in the same day. Sample collection was carried out in one week, between 28th November and 2nd December 2016.

**Data collection**

Data were collected using two questionnaires, an institutional questionnaire (Appendix 1) and a resident questionnaire (Appendix 2).

The **institutional questionnaire** defined structural and functional features, denominator data and got knowledge about antimicrobial policies and infection control resources in the LTCF. In order to outline the profile of the LTCF, general data were collected (i.e. available/occupied beds, hospitalised residents, public/private ownership, number of qualified nurses), together with specific data concerning medical care, medical coordination, infection control sources, and antimicrobial policies. These data were used for the descriptive analyses of the participating LTCFs.

An **individual questionnaire** form was fulfilled for each eligible resident. In order to outline the profile of each resident, general data (i.e. year of birth, sex, length of stay in the LTCF at the time of sampling, hospitalisation over the last three months, and surgery and antimicrobial therapy over the last month) and seven case mix factors (urinary catheter, vascular catheter, pressure sores, wounds, incontinence, low mental status, impaired mobility) were collected. Data regarding active HCAIs were collected, considering aetiology and antimicrobial resistance patterns whenever available. Case definitions of infections were used to identify active HCAIs in eligible residents (106). An infection was considered active when signs/symptoms of the infection were present on the PPS date or when signs/symptoms had been detected in the previous days and the resident was still receiving treatment for that infection on the PPS date. The presence of symptoms and signs in the two weeks (14 days) preceding the PPS was verified in order to determine whether the treated infection matched one of the case definitions. Data regarding the antimicrobial consumption for each antibiotic class on the PPS day were collected as well.

**Sample collection**

A rectal swab was carried out to all the eligible residents, whether or not presenting sign/symptoms of active healthcare-associated infection.

Rectal sampling was performed by inserting a pre-moistened swab 3 – 4 cm past the anal sphincter, rotating the swab 360° and, then, inserting the swab immediately in the tube containing the transport medium, after having unscrewed and removed the cap making sure not to spill the medium. A label reporting the resident identification number was applied on the tube, after having replaced the cap securing it tightly.

Pooled tubes were sent to the microbiology laboratory on the same day of the survey. Specimens were transported at room temperature (within 48 hours from the collection).

**Microbiology**

The central laboratory belonging to the Microbiology Section of the Verona University Hospital performed the research of ESBL-producing and CRE-producing GNB on rectal swabs. Strain identification and antimicrobial susceptibility testing were carried out in the microbiology laboratory. Sample processing started within 48 hours from the specimen collection.

Samples were streaked out on chromogenic media supplemented with a third-generation cephalosporin (cefotaxime) and an ertapenem disk. The chromogenic media provided a presumptive identification of Enterobacteriaceae and other non-fermenting GNB(*Acinetobacter baumannii* and *Pseudomonas aeruginosa*), cefotaxime selected third-generation cephalosporin-resistant GNB and the ertapenem disk selected carbapenem-resistant GNB.

In order to identify ESBL-producing GNB among third-generation cephalosporin-resistant bacteria, a phenotypic confirmatory test with clavulanic acid was performed. ESBL-producing GNB turned out to grow on chromogenic media with the addition of clavulanic acid.

Carba NP, a phenotypic biochemical test, detected carbapenemase-producing GNB (92): isolated colony strains were suspended in a lysis buffer and mixed with a solution made of imipenem monohydrate (carbapenem) and pH indicator (phenol red solution). *In vitro* hydrolysis of imipenem (by the bacterial lysate) was detected by changes in pH values, using the indicator (phenol turned from red to yellow).

Positive isolates were analysed by multiplex and single polymerase chain reactions (PCRs) to identify the specific ESBL or carbapenemase gene. The most common ESBL (*bla*CTX-M) and carbapenemase (*bla*KPC, *bla*VIM, *bla*NDM, *bla*OXA48) genes were searched. Clonality and strain-genetic correlation were analysed by Pulse Field Gel Electrophoresis (PFGE) in order to detect and evaluate the spread of these strains.

Species identification was obtained with the MALDI-TOF system. The same code list for microorganisms (Appendix 3) was consulted to identify the appropriate codes for detected MDR-GNB and their antimicrobial resistance profiles.

**Primary endpoints**

* Prevalence of rectal colonisation with ESBL-producing GNB
* Prevalence of rectal colonisation with CRE-producing GNB

**Secondary endpoints**

* Associations between rectal colonisation with ESBL-producing GNB and independent variables
* Associations between rectal colonisation with CRE-producing GNB and independent variables
* Prevalence of HCAI
* Prevalence of antimicrobial consumption for each antibiotic class
* Description of the previously implemented IC measures

**Independent variables**

* Year of birth
* Sex
* Length of stay in the LTCF at the time of sampling
* Hospitalisation over the previous three months
* Surgery over the previous month
* Urinary catheter
* Vascular catheter
* Pressure sores
* Wounds or skin lesions
* Incontinence (urinary and/or faecal)
* Low mental status
* Impaired mobility
* Penicillin/β-lactamase inhibitors over the previous month
* Third generation cephalosporins over the previous month
* Fluoroquinolones over the previous month
* Cotrimoxazole over the previous month

**Data analysis**

Continuous variables were expressed as means with standard deviations (SD). Percentages were calculated for categorical variables. Proportions and 95% confidence interval (CI95) were estimated accounting for cluster effect of the sample hierarchical structure (data collection site).

The associations between rectal colonisation with ESBL-producing and carbapenemase-producing isolates, as two different dependent variables, and the set of independent clinical-demographic variables were assessed with a multilevel multivariate logistic regression model, considering the data collection site as random component. In order to perform a step-wise forward selection of the predictors to be included in the final multivariate analysis, a preliminary multilevel bivariate logistic regression analysis was carried out for all the independent variables, retaining in the model only those which were significantly associated (p < 0.05). Odds ratios (OR) and CI95 were calculated to evaluate the strength of any association; all *p* values were two sided and findings with *p* values < 0.05 were considered statistically significant.

All statistical analyses were performed using STATA software, version 15 (College Station, TX: StataCorp LP).

**Ethical issues**

This project obtained the approval from the local ethics committee (954CESC).

Eligible participants were requested to display a signed informed consent before taking part in the study. In case of named legal guardian, the person who covered this position was requested to sign the informed consent.

Patient identifiers were not used on any data collection form or label on specimens or in any report resulting from the study. At the beginning of the study, a study identification code number was assigned to each included resident and this number was used on the forms and on the specimens. Any information obtained in connection with this study was kept strictly confidential. Resident lists included resident identifiers for internal use at the time of the PPS: they were kept in the LTCF in a safe and confidential manner and destroyed at the end of the PPS. Data collected within the framework of the PPS were not used for purposes other than those described in the objectives.

**RESULTS**

**Primary outcomes: prevalence of rectal colonisation with ESBL-producing GNB and prevalence of rectal colonisation with CRE-producing GNB**

A total of 453 residents were enrolled in 7 LTCF.

Residents colonised with ESBL (88.8% *Enterobacteriaceae* and 11.2% non-fermenting GNB) and carbapenemase-producing GNB (77.8% *Enterobacteriaceae* and 22.2% non-fermenting GNB) were 39.5% (CI95, 32.5%-47%) and 4% (CI95, 2.8%-5.6%), respectively. Table 1 shows the distribution of ESBLs and carbapenemases among different GNB species.

|  |  |  |  |
| --- | --- | --- | --- |
| **GNB** | **Species** | **ESBL**  **N = 179** | **Carbapenemase**  **N = 18** |
| **Enterobacteriaceae**  **N = 173** | *Citrobacter* spp. | 1 | - |
| *Enterobacter cloacae* | 5 | - |
| *Escherichia coli* | 88 | 1 |
| *Klebsiella pneumoniae* | 35 | 13 |
| *Morganella* spp. | 2 | - |
| *Proteus mirabilis* | 28 | - |
| **Non-fermenting**  **N = 24** | *Acinetobacter baumannii* | 9 | 4 |
| *Burkholderia cepacia* | 1 | - |
| *Pseudomonas aeruginosa* | 10 | - |

**Table 1 – Distribution of ESBLs and carbapenemases among different GNB species**

The genotypic characterisation of the ESBL-encoding genes was performed on 16 *Escherichia coli* isolates. They all harboured a CTX-M gene, blaCTX-M-15, and belonged to the pandemic clonal group ST131.

The genotypic characterisation of the carbapenemase-encoding genes was performed on all the carbapenemase-producing GNB. The 14 Enterobacteriaceae (13 *Klebsiella pneumoniae* isolates and one *Escherichia coli*) harboured a KPC gene, whilst the 4 *Acinetobacter baumannii* strains harboured an OXA-23 gene.

Prevalence of colonisation at site level ranged from 14.3% to 57.1% for ESBL and from no detected cases to 9.5% for carbapenemase-producing GNB, as shown in Table 2 and 3.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Colonisation with**  **ESBL-producing GNB** | |  |
|  | No | Yes | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 18 | 6 | 24 |
| % | 75 | 25 | 100 |
| % | 6.57 | 3.35 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 16 | 8 | 24 |
| % | 66.67 | 33.33 | 100 |
| % | 5.84 | 4.47 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 97 | 73 | 170 |
| % | 57.06 | 42.94 | 100 |
| % | 35.4 | 40.78 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 78 | 54 | 132 |
| % | 59.09 | 40.91 | 100 |
| % | 28.47 | 30.17 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 18 | 24 | 42 |
| % | 42.86 | 57.14 | 100 |
| % | 6.57 | 13.41 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 29 | 11 | 40 |
| % | 72.5 | 27.5 | 100 |
| % | 10.58 | 6.15 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 18 | 3 | 21 |
| % | 85.71 | 14.29 | 100 |
| % | 6.57 | 1.68 | 4.64 |
|  |  |  |  |  |
| Total | n | 274 | 179 | 453 |
| % | 60.49 | 39.51 | 100 |
| % | 100 | 100 | 100 |

**Table 2 –** **Colonisation with ESBL-producing GNB at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Colonisation with carbapenemase-producing GNB** | |  |
|  | No | Yes | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.52 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.52 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 164 | 6 | 170 |
| % | 96.47 | 3.53 | 100 |
| % | 37.7 | 33.33 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 127 | 5 | 132 |
| % | 96.21 | 3.79 | 100 |
| % | 29.2 | 27.78 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 39 | 3 | 42 |
| % | 92.86 | 7.14 | 100 |
| % | 8.97 | 16.67 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 38 | 2 | 40 |
| % | 95 | 5 | 100 |
| % | 8.74 | 11.11 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 19 | 2 | 21 |
| % | 90.48 | 9.52 | 100 |
| % | 4.37 | 11.11 | 4.64 |
|  |  |  |  |  |
| Total | n | 435 | 18 | 453 |
| % | 96.03 | 3.97 | 100 |
| % | 100 | 100 | 100 |

**Table 3 – Colonisation with carbapenemase-producing GNB at site level**

**Secondary outcomes: associations between rectal colonisation with ESBL-producing GNB and independent variables and between rectal colonisation with CRE-producing GNB and independent variables**

74.6% residents were females. The mean age was 83.7 years (SD, 10.4 years). The majority of residents had urinary and/or faecal incontinence (81%), had spent more than one year in LTCF (78.4%), and had a low mental (70.2%) and functional (65.8%) status. 9.3% residents were administered penicillins/ß-lactamase inhibitors over the previous month, 4.2% were administered third-generation cephalosporins, 8.6% fluoroquinolones, and 9.7% cotrimoxazole (27.1% residents had received an antibiotic over the previous month). 16.6% had a urinary catheter, 15.7% had skin lesions, 14.6% had pressure sores, 9.5% had been hospitalised over the previous 3 months, 3.8% had a vascular catheter, and 1.1% underwent surgery over the previous month.

Two-way tables 4 – 19 show the distribution of independent variables at site level.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Sex** | |  |
|  | **Male** | **Female** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 17 | 7 | 24 |
| % | 70.8 | 29.2 | 100.0 |
| % | 14.8 | 2.1 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 1 | 20 | 21 |
| % | 4.8 | 95.2 | 100.0 |
| % | 0.9 | 5.9 | 4.6 |
|  |  |  |  |  |
| LTCF 3 | n | 5 | 19 | 24 |
| % | 20.8 | 79.2 | 100.0 |
| % | 4.4 | 5.6 | 5.3 |
|  |  |  |  |  |
| LTCF 4 | n | 37 | 133 | 170 |
| % | 21.8 | 78.2 | 100.0 |
| % | 32.2 | 39.4 | 37.5 |
|  |  |  |  |  |
| LTCF 5 | n | 36 | 96 | 132 |
| % | 27.3 | 72.7 | 100.0 |
| % | 31.3 | 28.4 | 29.1 |
|  |  |  |  |  |
| LTCF 6 | n | 9 | 33 | 42 |
| % | 21.4 | 78.6 | 100.0 |
| % | 7.8 | 9.8 | 9.3 |
|  |  |  |  |  |
| LTCF 7 | n | 10 | 30 | 40 |
| % | 25.0 | 75.0 | 100 |
| % | 8.7 | 8.9 | 8.8 |
|  |  |  |  |  |
| Total | n | 115 | 338 | 453 |
| % | 25.4 | 74.6 | 100 |
| % | 100 | 100 | 100 |

**Table 4 – Distribution of sex at site level**

|  |  |  |  |
| --- | --- | --- | --- |
| **LTCF** | **Mean age** | **Standard deviation** | Total |
| LTCF 1 | 59 | 9.9 | 24 |
| LTCF 2 | 85.4 | 7.62 | 24 |
| LTCF 3 | 84.5 | 8.4 | 170 |
| LTCF 4 | 85.7 | 8.18 | 132 |
| LTCF 5 | 82.8 | 7.8 | 42 |
| LTCF 6 | 87.5 | 6.86 | 40 |
| LTCF 7 | 84.5 | 14.51 | 21 |
| Total | 83.7 | 10.39 | 453 |

**Table 5 – Mean age at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Length of LTCF stay** | |  |
|  | **< 1 year** | **> 1 year** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 0 | 24 | 24 |
| % | 0 | 100 | 100 |
| % | 0 | 6.76 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 9 | 15 | 24 |
| % | 37.5 | 62.5 | 100 |
| % | 9.18 | 4.23 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 30 | 140 | 170 |
| % | 17.65 | 82.35 | 100 |
| % | 30.61 | 39.44 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 36 | 96 | 132 |
| % | 27.27 | 72.73 | 100 |
| % | 36.73 | 27.04 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 9 | 33 | 42 |
| % | 21.43 | 78.57 | 100 |
| % | 9.18 | 9.3 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 8 | 32 | 40 |
| % | 20 | 80 | 100 |
| % | 8.16 | 9.01 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 6 | 15 | 21 |
| % | 28.57 | 71.43 | 100 |
| % | 6.12 | 4.23 | 4.64 |
|  |  |  |  |  |
| Total | n | 98 | 355 | 453 |
| % | 21.63 | 78.37 | 100 |
| % | 100 | 100 | 100 |

**Table 6 – Length of LTCF stay (< 1 year *versus* > 1 year) at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Hospitalisation**  **over the previous 3 months** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.85 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 16 | 8 | 24 |
| % | 66.67 | 33.33 | 100 |
| % | 3.9 | 18.6 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 159 | 11 | 170 |
| % | 93.53 | 6.47 | 100 |
| % | 38.78 | 25.58 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 122 | 10 | 132 |
| % | 92.42 | 7.58 | 100 |
| % | 29.76 | 23.26 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 37 | 5 | 42 |
| % | 88.1 | 11.9 | 100 |
| % | 9.02 | 11.63 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 34 | 6 | 40 |
| % | 85 | 15 | 100 |
| % | 8.29 | 13.95 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 18 | 3 | 21 |
| % | 85.71 | 14.29 | 100 |
| % | 4.39 | 6.98 | 4.64 |
|  |  |  |  |  |
| Total | n | 410 | 43 | 453 |
| % | 90.51 | 9.49 | 100 |
| % | 100 | 100 | 100 |

**Table 7 – Hospitalisation over the previous 3 months at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Surgery**  **over the previous month** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.36 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 23 | 1 | 24 |
| % | 95.83 | 4.17 | 100 |
| % | 5.13 | 20 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 168 | 2 | 170 |
| % | 98.82 | 1.18 | 100 |
| % | 37.5 | 40 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 132 | 0 | 132 |
| % | 100 | 0 | 100 |
| % | 29.46 | 0 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 41 | 1 | 42 |
| % | 97.62 | 2.38 | 100 |
| % | 9.15 | 20 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 39 | 1 | 40 |
| % | 97.5 | 2.5 | 100 |
| % | 8.71 | 20 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 21 | 0 | 21 |
| % | 100 | 0 | 100 |
| % | 4.69 | 0 | 4.64 |
|  |  |  |  |  |
| Total | n | 448 | 5 | 453 |
| % | 98.9 | 1.1 | 100 |
| % | 100 | 100 | 100 |

**Table 8 – Surgery over the previous month at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Urinary catheter** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 22 | 2 | 24 |
| % | 91.67 | 8.33 | 100 |
| % | 5.82 | 2.67 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 18 | 6 | 24 |
| % | 75 | 25 | 100 |
| % | 4.76 | 8 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 148 | 22 | 170 |
| % | 87.06 | 12.94 | 100 |
| % | 39.15 | 29.33 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 109 | 23 | 132 |
| % | 82.58 | 17.42 | 100 |
| % | 28.84 | 30.67 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 28 | 14 | 42 |
| % | 66.67 | 33.33 | 100 |
| % | 7.41 | 18.67 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 33 | 7 | 40 |
| % | 82.5 | 17.5 | 100 |
| % | 8.73 | 9.33 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 20 | 1 | 21 |
| % | 95.24 | 4.76 | 100 |
| % | 5.29 | 1.33 | 4.64 |
|  |  |  |  |  |
| Total | n | 378 | 75 | 453 |
| % | 83.44 | 16.56 | 100 |
| % | 100 | 100 | 100 |

**Table 9 – Urinary catheter at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Vascular catheter** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.5 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 19 | 5 | 24 |
| % | 79.17 | 20.83 | 100 |
| % | 4.36 | 29.41 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 163 | 7 | 170 |
| % | 95.88 | 4.12 | 100 |
| % | 37.39 | 41.18 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 128 | 4 | 132 |
| % | 96.97 | 3.03 | 100 |
| % | 29.36 | 23.53 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 42 | 0 | 42 |
| % | 100 | 0 | 100 |
| % | 9.63 | 0 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 40 | 0 | 40 |
| % | 100 | 0 | 100 |
| % | 9.17 | 0 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 20 | 1 | 21 |
| % | 95.24 | 4.76 | 100 |
| % | 4.59 | 5.88 | 4.64 |
|  |  |  |  |  |
| Total | n | 436 | 17 | 453 |
| % | 96.25 | 3.75 | 100 |
| % | 100 | 100 | 100 |

**Table 10 – Vascular catheter at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Pressure sores** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 6.2 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 17 | 7 | 24 |
| % | 70.83 | 29.17 | 100 |
| % | 4.39 | 10.61 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 148 | 22 | 170 |
| % | 87.06 | 12.94 | 100 |
| % | 38.24 | 33.33 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 101 | 31 | 132 |
| % | 76.52 | 23.48 | 100 |
| % | 26.1 | 46.97 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 38 | 4 | 42 |
| % | 90.48 | 9.52 | 100 |
| % | 9.82 | 6.06 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 39 | 1 | 40 |
| % | 97.5 | 2.5 | 100 |
| % | 10.08 | 1.52 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 20 | 1 | 21 |
| % | 95.24 | 4.76 | 100 |
| % | 5.17 | 1.52 | 4.64 |
|  |  |  |  |  |
| Total | n | 387 | 66 | 453 |
| % | 85.43 | 14.57 | 100 |
| % | 100 | 100 | 100 |

**Table 11 – Pressure sores at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Skin lesions** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 6.28 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 20 | 4 | 24 |
| % | 83.33 | 16.67 | 100 |
| % | 5.24 | 5.63 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 137 | 33 | 170 |
| % | 80.59 | 19.41 | 100 |
| % | 35.86 | 46.48 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 114 | 18 | 132 |
| % | 86.36 | 13.64 | 100 |
| % | 29.84 | 25.35 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 36 | 6 | 42 |
| % | 85.71 | 14.29 | 100 |
| % | 9.42 | 8.45 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 32 | 8 | 40 |
| % | 80 | 20 | 100 |
| % | 8.38 | 11.27 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 19 | 2 | 21 |
| % | 90.48 | 9.52 | 100 |
| % | 4.97 | 2.82 | 4.64 |
|  |  |  |  |  |
| Total | n | 382 | 71 | 453 |
| % | 84.33 | 15.67 | 100 |
| % | 100 | 100 | 100 |

**Table 12 – Skin lesions at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Incontinence** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 6 | 18 | 24 |
| % | 25 | 75 | 100 |
| % | 6.98 | 4.9 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 7 | 17 | 24 |
| % | 29.17 | 70.83 | 100 |
| % | 8.14 | 4.63 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 34 | 136 | 170 |
| % | 20 | 80 | 100 |
| % | 39.53 | 37.06 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 11 | 121 | 132 |
| % | 8.33 | 91.67 | 100 |
| % | 12.79 | 32.97 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 2 | 40 | 42 |
| % | 4.76 | 95.24 | 100 |
| % | 2.33 | 10.9 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 14 | 26 | 40 |
| % | 35 | 65 | 100 |
| % | 16.28 | 7.08 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 12 | 9 | 21 |
| % | 57.14 | 42.86 | 100 |
| % | 13.95 | 2.45 | 4.64 |
|  |  |  |  |  |
| Total | n | 86 | 367 | 453 |
| % | 18.98 | 81.02 | 100 |
| % | 100 | 100 | 100 |

**Table 13 – Urinary and/or faecal incontinence at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Low mental status** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 15 | 9 | 24 |
| % | 62.5 | 37.5 | 100 |
| % | 11.11 | 2.83 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 6 | 18 | 24 |
| % | 25 | 75 | 100 |
| % | 4.44 | 5.66 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 64 | 106 | 170 |
| % | 37.65 | 62.35 | 100 |
| % | 47.41 | 33.33 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 24 | 108 | 132 |
| % | 18.18 | 81.82 | 100 |
| % | 17.78 | 33.96 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 1 | 41 | 42 |
| % | 2.38 | 97.62 | 100 |
| % | 0.74 | 12.89 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 16 | 24 | 40 |
| % | 40 | 60 | 100 |
| % | 11.85 | 7.55 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 9 | 12 | 21 |
| % | 42.86 | 57.14 | 100 |
| % | 6.67 | 3.77 | 4.64 |
|  |  |  |  |  |
| Total | n | 135 | 318 | 453 |
| % | 29.8 | 70.2 | 100 |
| % | 100 | 100 | 100 |

**Table 14 – Low mental status at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Impaired mobility** | |  |
|  | **No** | **Yes** | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 10 | 14 | 24 |
| % | 41.67 | 58.33 | 100 |
| % | 6.45 | 4.93 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 7 | 17 | 24 |
| % | 29.17 | 79.83 | 100 |
| % | 4.52 | 5.28 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 42 | 128 | 170 |
| % | 24.7 | 75.3 | 100 |
| % | 27.1 | 42.61 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 54 | 76 | 132 |
| % | 40.91 | 59.1 | 100 |
| % | 34.84 | 26.76 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 21 | 21 | 42 |
| % | 50 | 50 | 100 |
| % | 13.55 | 7.39 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 9 | 31 | 40 |
| % | 22.5 | 77.5 | 100 |
| % | 5.81 | 10.21 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 12 | 9 | 21 |
| % | 57.14 | 42.86 | 100 |
| % | 7.74 | 2.82 | 4.64 |
|  |  |  |  |  |
| Total | n | 155 | 298 | 453 |
| % | 34.22 | 65.78 | 100 |
| % | 100 | 100 | 100 |

**Table 15 – Impaired mobility at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Penicillins/ß-lactamase inhibitors over the previous month** | |  |
|  | No | Yes | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 23 | 1 | 24 |
| % | 95.83 | 4.17 | 100 |
| % | 5.6 | 2.38 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 18 | 6 | 24 |
| % | 75 | 25 | 100 |
| % | 4.38 | 14.29 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 152 | 18 | 170 |
| % | 89.41 | 10.59 | 100 |
| % | 36.98 | 42.86 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 127 | 5 | 132 |
| % | 96.21 | 3.79 | 100 |
| % | 30.9 | 11.9 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 37 | 5 | 42 |
| % | 88.1 | 11.9 | 100 |
| % | 9 | 11.9 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 35 | 5 | 40 |
| % | 87.5 | 12.5 | 100 |
| % | 8.52 | 11.9 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 19 | 2 | 21 |
| % | 90.48 | 9.52 | 100 |
| % | 4.62 | 4.76 | 4.64 |
|  |  |  |  |  |
| Total | n | 411 | 42 | 453 |
| % | 90.73 | 9.27 | 100 |
| % | 100 | 100 | 100 |

**Table 16 –** **Penicillins/ß-lactamase inhibitors over the previous month at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Third generation cephalosporins over the previous month** | |  |
|  | No | Yes | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.53 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 23 | 1 | 24 |
| % | 95.83 | 4.17 | 100 |
| % | 5.3 | 5.26 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 168 | 2 | 170 |
| % | 98.82 | 1.18 | 100 |
| % | 38.71 | 10.53 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 118 | 14 | 132 |
| % | 89.39 | 10.61 | 100 |
| % | 27.19 | 73.68 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 41 | 1 | 42 |
| % | 97.62 | 2.38 | 100 |
| % | 9.45 | 5.26 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 39 | 1 | 40 |
| % | 97.5 | 2.5 | 100 |
| % | 8.99 | 5.26 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 21 | 0 | 21 |
| % | 100 | 0 | 100 |
| % | 4.84 | 0 | 4.64 |
|  |  |  |  |  |
| Total | n | 434 | 19 | 453 |
| % | 95.81 | 4.19 | 100 |
| % | 100 | 100 | 100 |

**Table 17 –** **Third generation cephalosporins over the previous month at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Fluoroquinolones**  **over the previous month** | |  |
|  | No | Yes | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 23 | 2 | 25 |
| % | 92 | 8 | 100 |
| % | 5.56 | 5.13 | 5.52 |
|  |  |  |  |  |
| LTCF 2 | n | 23 | 1 | 24 |
| % | 95.83 | 4.17 | 100 |
| % | 5.56 | 2.56 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 159 | 12 | 171 |
| % | 92.98 | 7.02 | 100 |
| % | 38.41 | 30.77 | 37.75 |
|  |  |  |  |  |
| LTCF 4 | n | 120 | 7 | 127 |
| % | 94.49 | 5.51 | 100 |
| % | 28.99 | 17.95 | 28.04 |
|  |  |  |  |  |
| LTCF 5 | n | 29 | 15 | 44 |
| % | 65.91 | 34.09 | 100 |
| % | 7 | 38.46 | 9.71 |
|  |  |  |  |  |
| LTCF 6 | n | 39 | 1 | 40 |
| % | 97.5 | 2.5 | 100 |
| % | 9.42 | 2.56 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 21 | 1 | 22 |
| % | 95.45 | 4.55 | 100 |
| % | 5.07 | 2.56 | 4.86 |
|  |  |  |  |  |
| Total | n | 414 | 39 | 453 |
| % | 91.39 | 8.61 | 100 |
| % | 100 | 100 | 100 |

**Table 18 –** **Fluoroquinolones over the previous month at site level**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Cotrimoxazole**  **over the previous month** | |  |
|  | No | Yes | Total |
| **LTCF** |  |  |  |  |
| LTCF 1 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.87 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 2 | n | 24 | 0 | 24 |
| % | 100 | 0 | 100 |
| % | 5.87 | 0 | 5.3 |
|  |  |  |  |  |
| LTCF 3 | n | 142 | 28 | 170 |
| % | 83.53 | 16.47 | 100 |
| % | 34.72 | 63.64 | 37.53 |
|  |  |  |  |  |
| LTCF 4 | n | 125 | 7 | 132 |
| % | 94.7 | 5.3 | 100 |
| % | 30.56 | 15.91 | 29.14 |
|  |  |  |  |  |
| LTCF 5 | n | 38 | 4 | 42 |
| % | 90.48 | 9.52 | 100 |
| % | 9.29 | 9.09 | 9.27 |
|  |  |  |  |  |
| LTCF 6 | n | 35 | 5 | 40 |
| % | 87.5 | 12.5 | 100 |
| % | 8.56 | 11.36 | 8.83 |
|  |  |  |  |  |
| LTCF 7 | n | 21 | 0 | 21 |
| % | 100 | 0 | 100 |
| % | 5.13 | 0 | 4.64 |
|  |  |  |  |  |
| Total | n | 409 | 44 | 453 |
| % | 90.29 | 9.71 | 100 |
| % | 100 | 100 | 100 |

**Table 19 – Cotrimoxazole over the previous month at site level**

Several significant associations pertaining the carriage of ESBL-producing and carbapenemase-producing GNB were identified at the bivariate analysis, as shown in Table 20 and Table 21.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **ESBL,**  **n (%)**  N = 179 | **No ESBL,**  **n (%)**  N = 274 | **Odds ratio** | **CI 95%** | | ***p* value** |
| **Lower value** | **Higher value** |
| Age (mean) | 83.5 | 83.8 | 1 | 0.97 | 1.01 | 0.470 |
| Female sex | 120 (67) | 218 (79.6) | 0.48 | 0.31 | 0.75 | 0.001\* |
| LTCF stay a | 145 (81) | 210 (76.6) | 1.31 | 0.82 | 2.11 | 0.261 |
| Hospital stay b | 23 (12.9) | 20 (7.3) | 2.06 | 1.06 | 3.97 | 0.032\* |
| Surgery c | 3 (1.7) | 2 (0.7) | 2.36 | 0.38 | 14.76 | 0.359 |
| Urine catheter | 43 (24) | 32 (11.7) | 2.34 | 1.4 | 3.92 | 0.001\* |
| Vein catheter | 7 (3.9) | 10 (3.7) | 1.12 | 0.41 | 3.08 | 0.819 |
| Pressure sore | 34 (19) | 32 (11.7) | 1.75 | 1.02 | 2.99 | 0.043\* |
| Wounds, skin lesions | 41 (22.9) | 30 (11) | 2.41 | 1.43 | 4.07 | 0.001\* |
| Incontinence | 159 (88.8) | 208 (75.9) | 2.45 | 1.38 | 4.35 | 0.002\* |
| Low mental status | 129 (72) | 189 (69) | 1.06 | 0.68 | 1.66 | 0.793 |
| Impaired mobility | 76 (42.5) | 108 (39.4) | 2.3 | 1.49 | 3.55 | 0.000\* |
| Penicillin +  ß-lactamase inhibitor d | 22 (12.3) | 20 (7.3) | 1.93 | 1.01 | 3.68 | 0.048\* |
| Third generation cephalosporin d | 14 (7.8) | 5 (1.8) | 4.81 | 1.66 | 13.9 | 0.004\* |
| Fluoroquinolone d | 24 (13.4) | 15 (5.5) | 2.22 | 1.1 | 4.47 | 0.026\* |
| Cotrimoxazole d | 20 (11.2) | 24 (8.8) | 1.61 | 0.89 | 2.94 | 0.119 |

**TABLE 20 – Colonisation with ESBL-producing GNB: multilevel bivariate logistic regression analysis**

CI, confidence interval. a Over the previous year; b over the previous three months; c over the previous month; d assumption of a drug belonging to this antibiotic category over the previous month. \* Factor included in the multivariate analysis.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **CP-GNB,**  **n (%)**  N = 18 | **No CP-GNB,**  **n (%)**  N = 435 | **Odds ratio** | **CI 95%** | | ***p* value** |
| **Lower value** | **Higher value** |
| Age (mean) | 83.2 | 83.7 | 1 | 0.95 | 1.04 | 0.832 |
| Female sex | 10 (55.6) | 328 (75.4) | 0.41 | 0.16 | 1.06 | 0.066 |
| LTCF stay a | 11 (61.1) | 344 (79.1) | 0.42 | 0.16 | 1.1 | 0.078 |
| Hospital stay b | 7 (38.9) | 36 (8.3) | 7.05 | 2.58 | 19.31 | 0.000\* |
| Surgery c | 2 (11.1) | 3 (0.7) | 18 | 2.81 | 115.32 | 0.002\* |
| Urine catheter | 5 (27.8) | 70 (16.1) | 2.01 | 0.69 | 5.8 | 0.199 |
| Vein catheter | 0 (0) | 17 (3.9) | - | - | - | - |
| Pressure sore | 4 (22.2) | 62 (14.3) | 1.72 | 0.55 | 5.39 | 0.353 |
| Wounds, skin lesions | 8 (44.4) | 63 (14.5) | 4.72 | 1.8 | 12.43 | 0.002\* |
| Incontinence | 13 (72.2) | 354 (81.4) | 0.59 | 0.21 | 1.72 | 0.337 |
| Low mental status | 15 (83.3) | 303 (69.7) | 2.18 | 0.62 | 7.65 | 0.225 |
| Impaired mobility | 5 (27.8) | 179 (41.2) | 1.37 | 0.49 | 3.91 | 0.558 |
| Penicillin +  ß-lactamase inhibitor d | 3 (16.7) | 39 (9) | 1.98 | 0.55 | 7.11 | 0.298 |
| Third generation cephalosporin d | 2 (11.1) | 17 (3.9) | 3.07 | 0.65 | 14.45 | 0.155 |
| Fluoroquinolone d | 1 (5.6) | 38 (8.7) | 0.61 | 0.08 | 4.75 | 0.641 |
| Cotrimoxazole d | 4 (22.2) | 40 (9.2) | 2.9 | 0.62 | 13.56 | 0.177 |

**TABLE 21 – Colonisation with carbapenemase-producing GNB: multilevel bivariate logistic regression analysis**

CP-GNB, carbapenemase-producing Gram-negative bacteria; CI, confidence interval. a Over the previous year; b over the previous three months; c over the previous month; d assumption of a drug belonging to this antibiotic category over the previous month. \* Factor included in the multivariate analysis.

Male gender (OR, 2.2; CI 95%, 1.4 – 3.7; *p* = 0.002), previous exposure to third-generation cephalosporins (OR, 3.9; CI 95%, 1.3 – 12; *p* = 0.016) and an impaired mobility (OR, 1.7; CI 95%, 1 – 2.9; *p* = 0.043) were independently associated with ESBL-producing GNB carriage, whilst previous hospitalisation (OR, 4.1; CI 95%, 1.3 – 13.1; *p* = 0.02) was the only risk factor independently associated with carbapenemase-producing GNB colonisation, as shown in Table 22 and 23, which displays the multivariate analysis for both ESBL-producing GNB and carbapenemase-producing GNB carriages, respectively.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Odds ratio** | **CI 95%** | | ***p* value** |
| **Lower value** | **Higher value** |
| Female sex | **0.44** | 0.27 | 0.73 | **0.002** |
| Hospital stay a | 1.27 | 0.6 | 2.69 | 0.530 |
| Urine catheter | 1.29 | 0.71 | 2.33 | 0.406 |
| Pressure sore | 1.72 | 0.55 | 5.39 | 0.353 |
| Wounds, skin lesions | 1.59 | 0.89 | 2.85 | 0.115 |
| Incontinence | 1.5 | 0.79 | 2.86 | 0.213 |
| Impaired mobility | **1.71** | 1.02 | 2.89 | **0.043** |
| Penicillin +  ß-lactamase inhibitor b | 1.59 | 0.8 | 3.19 | 0.189 |
| Third generation cephalosporin b | **3.93** | 1.29 | 12 | **0.016** |
| Fluoroquinolone b | 2.06 | 0.99 | 4.29 | 0.054 |

**TABLE 22 – Colonisation with ESBL-producing GNB: multilevel multivariate logistic regression analysis**

a Over the previous three months; b over the previous month.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Odds ratio** | **CI 95%** | | ***p* value** |
| **Lower value** | **Higher value** |
| Hospital stay a | **4.05** | 1.25 | 13.14 | **0.020** |
| Surgery b | 3.49 | 0.41 | 29.75 | 0.254 |
| Wounds, skin lesions | 2.79 | 0.94 | 8.23 | 0.064 |

**TABLE 23 – Colonisation with carbapenemase-producing GNB: multilevel multivariate logistic regression analysis**

a Over the previous three months; b over the previous month.

**Secondary outcome: prevalence of active infections**

7.7% (n = 35) was the prevalence of residents with HCAI on the PPS day:

* 28.6% (n = 10) acute bacterial skin and skin-structure infections
* 20% (n = 7) upper respiratory tract infections
* 20% (n = 7) lower respiratory tract infections
* 20% (n = 7) urinary tract infections
* 5.7% (n = 2) gastroenteritis (*C. difficile* infection was never detected)
* 2.9% (n = 1) bloodstream infection
* 2.9% (n = 1) conjunctivitis

4 urinary tract infections were confirmed by the positivity of urine culture results, 3 *Escherichia coli* and 1 *Proteus mirabilis*. None of them displayed resistance to third-generation cephalosporins or carbapenems. The bloodstream infection, whose source remained unknown, was caused by a carbapenem-susceptible *Pseudomonas aeruginosa*. No other positive culture results pertaining active HCAI were available.

**Secondary outcome: prevalence of active antibiotic consumption**

21 residents (4.6%) received at least one antibiotic on the day of the PPS. One subject only was administered combined therapy (two drugs). Administration followed an oral route (54.5%) more than a parenteral one (45.5%). Antimicrobials were mainly prescribed in the LTCF itself (81.8%), whereas 18.2% were prescribed in an acute-care hospital. They were primarily prescribed by general practitioners (77.3%), otherwise by a specialist (22.7%).

The frequencies of active consumption per antibiotic category were the followings:

* 27.3% (n = 6) penicillins/ß-lactamase inhibitors
* 18.2% (n = 4) fluoroquinolones
* 13.6% (n = 3) rifamycins
* 9.1% (n = 2) third generation cephalosporins
* 9.1% (n = 2) carbapenems
* 9.1% (n = 2) glycopeptides
* 4.5% (n = 1) cotrimoxazole
* 4.5% (n = 1) aminoglycoside
* 4.5% (n = 1) macrolide

2 antibiotics were administered for prophylactic purposes, aiming at the prevention of urinary tract infections after urinary catheter replacement. The remaining antimicrobials were administered for the treatment of the following infections:

* 35% (n = 7) urinary tract infections
* 35% (n = 7) lower respiratory tract infections
* 25 % (n = 5) acute bacterial skin and skin-structure infections
* 5% (n = 1) bloodstream infections

**Secondary outcome: description of the previously implemented IC measures**

Considering that all the 7 included LTCFs belonged to the same corporation, infection control measures were evenly distributed.

LTCFs did not have an internal IC committee in place and were not supported by an external IC team on a regular basis. Nevertheless, an internal nurse with training in IC was reported available to the LTCF staff.

Medical care for residents was provided by general practitioners visiting the LTCFs, one of them was in charge of coordinating medical activities. The reported tasks performed by the coordinating physician were the coordination of the resident vaccination policy (annual immunisation for flu was offered to all the residents), the development of care strategies, and the organisation of meetings to harmonise medical care practices/policies.

The available IC measures are listed below:

* written protocol for the hand hygiene;
* written protocol for the management of urinary catheters;
* written protocol for the management of venous catheters/lines;
* written protocol for the management of enteral feeding;
* list of antimicrobials whose prescription was restricted, including carbapenems and glycopeptides.

A hand hygiene training session was organised in the previous year, targeting nurses, nurse aides, physiotherapists, and cleaning staff (not doctors). Hand washing with water and an antiseptic soap was the most frequently used hand hygiene method (alcohol rub solution was not available).

The following IC measures were NOT available anywhere:

* regular reporting of outbreaks;
* regular reporting of HCAIs;
* regular reporting of residents colonised with MDR bacteria;
* regular reporting of local antibiotic resistance profiles;
* written protocol for the management of colonisation/infection with MDR;
* local guidelines for the therapeutic management of bacterial infections.

**DISCUSSION**

In this multicentre point-prevalence survey, a remarkable high rate of colonisation with MDR-GNB was observed among LTCF residents in Verona district. Almost 40% included residents were colonised with ESBL-producing GNB bacteria and 4% with carbapenemase-producing GNB.

In comparison with previous investigations, the ESBL colonisation rate here reported is strikingly higher than the one found in other countries (with the only exception of a study conducted in Ireland), although our findings are in line with the limited data available for Italy (31-33, 51, 53). Actually, this high rate was mostly due to *Escherichia coli*, suggesting that LTCFs might be a reservoir of this microorganism for the healthcare system. The molecular typing of MDR-GNB allowed a better understanding of their epidemiology. Indeed, the carriage of ESBL-producing GNB was found to be associated with the spread of the international ST131 sub-clone, harbouring CTX-M-15 type and showing additional resistance to ciprofloxacin. The distribution of these strains among different LTCFs and Verona University Hospital highlighted a close relationship between circulating clones, suggesting that both intra-facility transmission and local dissemination should have occurred. These results are in line with previous studies conducted in Italian and European acute-care hospitals, indicating that the CTX-M types have disseminated in both *Escherichia coli* and *Klebsiella pneumoniae* species, partially replacing the SHV- and TEM-type ESBLs (107, 108).

On the contrary, the rate of LTCF residents colonised with carbapenemase-producing GNB was low. This finding is surprising considering that *Klebsiella pneumoniae* carrying KPC carbapenemase has become endemic in acute-care hospitals in Italy (109). In particular, a high rate of carbapenem-resistant *Klebsiella pneumoniae* has been recently reported (36.2%) among invasive isolates, with the most resistant ones (97%) actually harbouring KPC carbapenemase (109). According to data retrieved from literature, the prevalence of carbapenemase-producing GNB carriage varied widely in LTCFs, with the highest rates in residents with prolonged critical illnesses (1, 110). A possible explanation for the results of this study might be the limited use of carbapenems among residents in LTCFs (9.1% of those receiving antibiotics), resulting in low antibiotic selective pressure.

Despite the prevalence of colonisation with antibiotic-resistant bacteria varies depending on the geographic location, the level of care provided, and the patient population, these results are strikingly in line with the point-prevalence study conducted in four Italian cities in 2015 (53).

The role of various potential risk factors for MDR-GNB rectal colonisation was assessed. Risk analysis indicated that an impaired mobility was independently associated with ESBL-producing GNB. According to previous investigations, residents with impaired functional status require more assistance in activities of daily living and more frequent contacts with health-care providers, therefore becoming prone to exposure to the microbial flora of other residents and increasing the likelihood of MDR-GNB cross-transmission (111, 112). Our findings are in line with these observations, demonstrating that residents colonised with ESBL-producing GNB were 1.71-fold more likely to be functionally impaired than those who were not colonised.

The administration of third-generation cephalosporins over the previous month was independently associated with the ESBL carriage, as well. As a matter of fact, case-control studies in LTCFs have clearly identified the parenteral administration of third-generation cephalosporins as a predisposing event for subsequent colonisation or infection with ESBL-producing GNB, due to the selective pressure exerted by this antibiotic class on the intestinal flora (31, 33, 35, 43, 46). Our results confirm this relationship, as residents colonised with ESBL were 3.93-fold more likely to have been exposed to third-generation cephalosporins than those who were not colonised, and highlight the urgent need to curb the prescription of third-generation cephalosporins, which involved more than 4% of enrolled residents over the month preceding the PPS.

Interestingly, the association between male sex and ESBL carriage resulted statistically significant at the multivariate analysis, although no plausible reasons have been found to explain this link.

As previously stated, the rate of LTCF residents colonised with carbapenemase-producing GNB was low in this PPS and was independently associated with the hospitalisation over the previous three months. The Verona acute-care hospital, where the carbapenem consumption was widespread (unpublished data) and could exert a selective pressure, showed a stunningly high rate of patients colonised with carbapenemase-producing *Klebsiella pneumoniae* (unpublished data) at the PPS time, possibly accounting for these results, as patients with hospital-acquired colonisation may be taken or retaken in charge by the local LTCFs. The large variation between some LTCFs in the prevalence of ESBL-producing and carbapenemase-producing GNB is an indication that some of the participating LTCFs, one in particular, are step-down facilities with a very different resident case-mix than an average nursing home.

Of note, age, length of stay in the LTCF at the time of sampling, surgery over the previous month, urinary and/or vascular catheter, pressure sores, wounds or skin lesions, urinary and/or faecal incontinence, and low mental status were not associated with MDR-GNB carriage at the multivariate analysis, even though many of them showed a statistically significant association at the bivariate analysis (regarding ESBL-producing GNB colonisation, hospital stay over the previous three months, urine catheter, pressure sores, wounds or skin lesions, urinary and/or faecal incontinence, and administration of fluoroquinolones and penicillins/ß-lactamase inhibitors over the previous month; regarding carbapenemase-producing GNB colonisation, surgery over the previous month and wounds or skin lesions).

This survey also collected valuable information on the prevalence of HCAIs and active antibiotic consumption on the PPS day. The crude prevalence of active infections was 7.7%. Respiratory tract infections were the most commonly reported HCAIs (40%), followed by acute bacterial skin and skin-structure infections (28.6%) and urinary tract infections (20%). These results partially deviate from that of the Italian and regional HALT PPS in 2017, which identified a crude prevalence rate of 3.9% and 3.3%, respectively, and respiratory tract infections as the most frequent HCAIs, followed by urinary tract infection and acute bacterial skin and skin-structure infections (21). Although the PPS study design itself prevents from an unbiased comparison, the difference in crude prevalence could be explained by the seasonality of infections, as this survey was conducted in late November, whilst the HALT-3 was performed in the spring time.

The crude prevalence of residents receiving at least one antimicrobial agent was 4.6%. Penicillins/ß-lactamase inhibitors (27.3%) and quinolones (18.2%) were the most commonly prescribed antibiotic classes. These results partially deviate from that of the Italian and regional HALT PPS in 2017, which identified a crude prevalence rate of 4.2% and third generation cephalosporins as the most frequently prescribed antibiotic class (29.4% and 25%, respectively) (21). Overall, rates concerning the oral route and prophylactic courses were quite similar (54.5% *vs.* 58.4% and 46%, respectively; 9.1% *vs.* 12.3% and 10%, respectively) (21).

The survey data allow the identification of targets for future infection control and antimicrobial stewardship interventions, such as prophylaxis for UTIs, whose inappropriateness at urine catheter replacement was informally assessed during the PPS. Infection prevention and control resources in LTCFs should be strengthened, although implementation will be challenging as residents live, long-term or permanently, in a confined environment in close proximity with other residents and the staff, input from physicians are low, the access to laboratory or radiology is limited, and workload levels are extremely high, due to the high care load and unfavourable nurse to patient ratios. According to the institutional questionnaire, there is room for improvement in the hand hygiene practices, implementing and promoting the proper use of alcohol rub solution and observing the degree of compliance with hand hygiene after training sessions for all the healthcare providers.

The strengths of this survey include the use of a standardised protocol across all participating LTCFs and the inclusion of a wide variety of LTCF residents. The reports for participating LTCF provided staff with awareness of their local situation in comparison with national and European data, empowering them to take targeted actions against antimicrobial resistance. Repeating the survey at a regional level with regular time intervals can encourage the development of a surveillance network for LTCFs.

This study has some limitations. First, the point prevalence study design, as a survey conducted on one single day, provided results prone to variations; nevertheless, this methodology was chosen because of its feasibility when applied in settings with limited resources for antimicrobial resistance surveillance, as the LTCFs actually are. Furthermore, the screening of healthcare workers and staff was not performed; therefore, their role in the MDR-GNB transmission can be only hypothesised but cannot be assessed. Lastly, generalisation of these results is difficult because they specifically refer to a limited number of LTCFs located in Verona district; thus, data extrapolation to inform infection control policies and antimicrobial stewardship strategies in LTCFs located elsewhere is not appropriate.

**CONCLUSIONS**

This study documents a high prevalence of colonisation with MDR-GNB, especially ESBL-producing organisms, among LTCF residents in Verona district, thus emphasizing the role of these facilities as reservoir of MDR-GNB for acute-care hospitals. LTCFs and acute-care hospitals should be considered as part of a one-health system, in which each part plays a crucial role for the effective prevention of MDR-GNB transmission.

Besides the exposure to third-generation cephalosporins, functional impairment, and the subsequent exposure to enhanced contacts with healthcare staff, was associated with the carriage of ESBL-producing GNB, highlighting the need for improving specific infection control measures targeting MDR-GNB horizontal transmission, such as hand hygiene, use of gloves, and education of healthcare workers. In the LTCFs participating in this study, protocols on hand hygiene and the management of indwelling catheters, as well as hand hygiene training sessions, were in place but still insufficient in containing the spread of the MDR-GNB, thus emphasizing the need for optimising the effectiveness of infection control measures and monitoring compliance with best practices.

The evidence from this study hopefully contributes to raise awareness of MDR-GNB epidemiology and to the development of regional and national guidelines for infection control and antimicrobial stewardship in LTCFs.

**ACKNOWLEDGEMENTS**

I am gratefulto the residents, the health-care and the administrative personnel of the *Pia Opera Ciccarelli* foundation (*Centro residenziale* *Berto Barbarani*, Verona; *Casa Ferrari*, San Giovanni Lupatoto; *Residenza Casa Serena*, Verona; *Centro Residenziale Monsignor Ciccarelli*, San Giovanni Lupatoto; *Residenza Policella*, Castel d’Azzano; *Residenza* *Villa Italia*, San Giovanni Lupatoto; *Villa San Giacomo*, Bosco Chiesanuova).

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**APPENDIX 1**

**QUESTIONARIO DI STRUTTURA**

**RILEVATORE\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

NOTA: è fondamentale che questo questionario venga completato per ogni LTCF coinvolta, poiché raccoglie informazioni essenziali relativamente alle caratteristiche strutturali/funzionali della LTCF, relativamente al denominatore nonché alle indicazioni interne di terapia antibiotica e di prevenzione/controllo delle infezioni.

Si raccomanda che il compilatore svolga abitualmente la sua attività all’interno della struttura valutata; se non è in grado di rispondere ad alcuni quesiti, è necessario che sottoponga il questionario ad altri in grado di farlo. Questo è **particolarmente importante per le domande relative agli antibiotici**.

1. **INFORMAZIONI GENERALI**

DATA DELLA PPS: --/--/----

CODICE IDENTIFICATIVO DELLA STRUTTURA: ————————

NATURA GIURIDICA DELLA STRUTTURA 🞎 pubblica

🞎 privata for profit

🞎 privata non for profit

DEFINIZIONE DI STRUTTURA (barrare la risposta corretta, solo una possibile)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tipo di struttura | General nursing home | LTCF psichiatrica | LTCF  per disabili mentali | LTCF per disabili fisici | Centro di riabilitazione | Struttura di assistenza palliativa | Sanatorio | LTCF  miste |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Permanenza media  dei residenti | Temporanea breve  (< 3 mesi) | Temporanea media  (3-12 mesi) | Temporanea lunga  (>12 mesi) | Permanenza definitiva | Altro |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tipo di assistenza garantita | Assistenza  neuro-cognitiva | Assistenza fisica | Assistenza psichiatrica | Riabilitazione fisico-motoria | Assistenza alla convalescenza | Cure intensive | Alcune delle precedenti | Tutte |

PERSONALE INFERMIERISTICO QUALIFICATO DISPONIBILE H24

Sì 🞎 NO 🞎

NELLA STRUTTURA:

- numero totale di INFERMIERI ABILITATI FTE **\_ \_ \_ \_**

- numero totale di OSS FTE **\_ \_ \_ \_**

- numero totale di stanze di degenza **\_ \_ \_ \_**

**-** numero totale di stanze di degenza singole **\_ \_ \_ \_**

* numero di stanze singole con servizi igienici privati \_ \_ \_ \_

1. **DATI DEL DENOMINATORE**

IL GIORNO DELL’INDAGINE SPECIFICARE, IL **NUMERO TOTALE** DI:

* POSTI LETTO NELLA STRUTTURA (sia occupati che non) \_\_\_\_\_\_\_
* POSTI LETTO OCCUPATI \_\_\_\_\_\_\_

OSPITI DEGENTI H24 NELLA LTCF IL GIORNO DELL’INDAGINE: \_\_\_\_\_\_\_

(prescindendo dalla firma del consenso informato)

1. **ASSISTENZA MEDICA ED ORGANIZZAZIONE**
2. All’interno della LTCF, l’assistenza medica (compresi i prescrittori di antibiotici) è fornita:

🞎 solo dal curante (MMG) o dal/dagli studio/i medico/i associato/i

🞎 solo da personale medico attivo esclusivamente all’interno della LTCF

🞎 entrambi i tipi di figura medica

1. Le attività mediche all’interno della LTCF sono coordinate/organizzate da un medico dedicato (medico coordinatore)?

🞎 Sì, è presente un coordinatore medico interno alla LTCF

🞎 Sì, è presente un coordinatore medico esterno alla LTCF

🞎 Sì, sono presenti sia un coordinatore medico interno che esterno

🞎 NO, non è presente né una figura interna né una esterna

1. Può qualunque figura, tra quelle riportate di seguito, consultare la documentazione sanitaria di tutti gli ospiti residenti nella LTCF?

* coordinatore medico in LTCF 🞎 Sì 🞎 NO 🞎 NON PRESENTE
* lo staff infermieristico 🞎 Sì 🞎 NO

1. **ATTIVITA’ DI CONTROLLO DELLE INFEZIONI**
2. Ci sono nella LTCF persone che dispongono di formazione nell’ambito della prevenzione/controllo delle infezioni? 🞎 Sì 🞎 NO
3. Se presente, si tratta di

🞎 un infermiere 🞎 un medico 🞎 sia un medico che un infermiere

Questa/e persona/e:

🞎 lavora all’interno della LTCF (interno)

🞎 non lavora all’interno della LTCF (esterno)

🞎 sono presenti sia interni che esterni alla LTCF

1. Nella LTCF c’è / ci sono (**è possibile più di una risposta**):

🞎 Formazione del personale infermieristico in misure di prevenzione e controllo delle infezioni

🞎 Formazione specifica in prevenzione e controllo delle infezioni ai medici di medicina generale e personale medico

* Sistemi di alert e registrazione di residenti con infezione/colonizzazione da germi multiresistenti e/o *C. difficile*
  + *Staphylococcus aureus* resistente alla meticillina/oxacillina (MRSA)

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Enterobacteriaceae* resistenti alle cefalosporine di III generazione

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Enterobacteriaceae* resistenti ai carbapenemici

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Enterococcus* spp.vancomicino-resistente

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Extremely drug resistant* (XDR) *Pseudomonas aeruginosa*, sensibile a non più di 2 classi antibiotiche (la resistenza di un singolo agente incluso è sufficiente a determinare la resistenza all’intera classe), tra le seguenti: aminoglicosidi, penicilline anti-*Pseudomonas* (piperacillina/tazobactam), cefalosporine anti-*Pseudomonas* (ceftazidime, cefepime), carbapenemi anti-*Pseudomonas* (meropenem, imipenem), aztreonam, fluorochinoloni anti-*Pseudomonas* (levofloxacina, ciprofloxacina), colistina

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Acinetobacter baumannii* resistente ai carbapenemici

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Clostridium difficile*

🞎 Sì 🞎 NO 🞎 NON NOTO

* Misure di isolamento ed ulteriori precauzioni per gli ospiti colonizzati da germi multiresistenti agli antibiotici e/o *C. difficile*
  + MRSA

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Enterobacteriaceae* resistenti alle cefalosporine di III generazione

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Enterobacteriaceae* resistenti ai carbapenemici

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Enterococcus* spp.vancomicino-resistente

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Pseudomonas aeruginosa* XDR

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *Acinetobacter baumannii* resistente ai carbapenemici

🞎 Sì 🞎 NO 🞎 NON NOTO

* + *C. difficile*

🞎 Sì 🞎 NO 🞎 NON NOTO

🞎 Nomina di una figura responsabile nel notificare e gestire epidemie

🞎 Feedback sui risultati della sorveglianza al personale medico/infermieristico della struttura

* Sistemi di controllo della corretta disinfezione/sterilizzazione dei dispositivi medici/sanitari
* Pappagalli 🞎 Sì 🞎 NO 🞎 NON NOTO
* Padelle/comode 🞎 Sì 🞎 NO 🞎 NON NOTO
* Strumenti per le medicazioni 🞎 Sì 🞎 NO 🞎 NON NOTO
* Carrelli 🞎 Sì 🞎 NO 🞎 NON NOTO

🞎 Offerta di una vaccinazione annuale contro l’influenza a tutti i residenti

🞎 Organizzazione, controllo e feedback regolari dei processi di sorveglianza sulle procedure e sulle prassi in tema di infezioni

🞎 Nessuna delle precedenti

1. Nella struttura è presente una commissione interna di controllo delle infezioni? 🞎 Sì 🞎 NO

**Se sì,** quanti incontri della commissione di controllo infezioni sono stati organizzati nell’anno precedente?

*Numero totale di incontri dello scorso anno (2017)* \_\_\_\_\_\_\_\_\_\_

1. La struttura può richiedere assistenza e competenze in maniera formale ad un gruppo esterno di controllo (IC) (ad es. gruppo ICI di un ospedale locale/ICI dell’ULSS di competenza)? 🞎 Sì 🞎 NO

**Se sì**, è stato fatto?

*Numero totale di incontri dello scorso anno (2017)* \_\_\_\_\_\_\_\_\_\_

1. Nella struttura, è disponibile un protocollo scritto per la gestione di (non considerare i protocolli di terapia antibiotica):

* MRSA 🞎 Sì 🞎 NO
* *Enterobacteriaceae* resistenti a cefalosporine 3° 🞎 Sì 🞎 NO
* *Enterobacteriaceae* resistenti ai carbapenemici 🞎 Sì 🞎 NO
* *Enterococcus* spp.vancomicino-resistente 🞎 Sì 🞎 NO
* *Pseudomonas aeruginosa* XDR 🞎 Sì 🞎 NO
* *Acinetobacter baumannii* resistente ai carbapenemici 🞎 Sì 🞎 NO
* *C. difficile* 🞎 Sì 🞎 NO
* igiene delle mani 🞎 Sì 🞎 NO
* cateteri urinari 🞎 Sì 🞎 NO
* cateteri venosi centrali e periferici 🞎 Sì 🞎 NO
* piaghe da decubito o ulcere trofiche 🞎 Sì 🞎 NO
* nutrizione enterale 🞎 Sì 🞎 NO

1. È presente un programma di sorveglianza periodico delle HCAI (report del numero di infezioni urinarie, tratto respiratorio, …) 🞎 Sì 🞎 NO
2. Nella struttura, quali dei seguenti prodotti sono disponibili per l’igiene delle mani? (**possibile più di una risposta**)

* soluzione idro-alcolica (hand-rub) 🞎 Sì 🞎 NO
* salviette imbevute (alcool) 🞎 Sì 🞎 NO
* sapone liquido medicato 🞎 Sì 🞎 NO
* sapone liquido non medicato 🞎 Sì 🞎 NO
* sapone solido 🞎 Sì 🞎 NO

1. Quale metodo di igiene delle mani è più frequentemente usato nella struttura quando le mani non sono visibilmente sporche? (**una sola risposta**)

🞎 disinfezione delle mani mediante frizione con soluzione alcolica

🞎 lavaggio delle mani con acqua e sapone non antisettico

🞎 lavaggio delle mani con acqua e sapone antisettico

1. Quanti litri di soluzione alcolica per l’igiene delle mani sono stati utilizzati lo scorso anno?

*Consumo annuo complessivo in litri (2015)*  \_\_\_\_\_\_\_\_\_

1. Lo scorso anno è stato organizzata una sessione di formazione sull’igiene delle mani per gli operatori sanitari della struttura? 🞎 Sì 🞎 NO

1. Lo scorso anno (2017) è stato effettuato uno studio sul n° di opportunità di igiene delle mani nella vostra struttura? 🞎 Sì 🞎 NO

**Se sì**, quante sono risultate le opportunità di igiene delle mani attese?

Numero occasioni osservate \_\_\_\_\_\_\_\_\_\_ dello scorso anno (2015).

1. **PRASSI E PROTOCOLLI SULL’UTILIZZO DI ANTIBIOTICI**
2. La struttura utilizza una lista di antibiotici “soggetti a restrizione”? (la cui prescrizione richiede l’aurizzazione di una persona designata)

🞎 Sì 🞎 NO

1. Se questa lista è disponibile, quali antibiotici comprende (**è possibile più di una risposta**)?

🞎 carbapenemi (imipenem/meropenem/ertapenem)

🞎 cefalosporine di 3°/4°/5° generazione per via endovenosa o per os

(cefotaxime, ceftriaxone, ceftazidime, cefixime, cefditoren, ceftibuten, cefepime, ceftobiprole, ceftarolina)

🞎 fluorochinoloni (ciprofloxacina, levofloxacina, moxifloxacina, prulifloxacina, norfloxacina)

🞎 vancomicina per via endovenosa

🞎 vancomicina per os

🞎 teicoplanina

🞎 daptomicina

🞎 dalbavancina

🞎 linezolid

🞎 tigeciclina

🞎 colistina

🞎 aminoglicosidi (gentamicina, amikacina)

🞎 altro (specificare la classe antibiotica e/o il principio attivo) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

1. Quali dei seguenti strumenti è disponibile all’interno della struttura (**è possibile più di una risposta**)?

🞎 comitato per la definizione dei protocolli antibiotici

🞎 corso di formazione annuale regolare sulla prescrizione appropriata degli antibiotici

🞎 linee guida scritte per l’uso appropriato (buon uso) degli antibiotici nella struttura

🞎 disponibilità di dati sul consumo di antibiotici annuo per classe antibiotica

🞎 strumenti per ricordare al personale sanitario l’importanza dei campioni microbiologici nel guidare la scelta antibiotica migliore

🞎 report locali (es: regionali/provinciali) relativi al profilo di resistenza antibiotica dei germi più frequentemente isolati consultabili nella LTCF o negli ambulatori del medico generale

🞎 sistemi per l’autorizzazione da parte di personale designato alla prescrizione restrittiva di antibiotici non inclusi nel formulario terapeutico locale

🞎 consulenza di un farmacista relativamente ad antibiotici non compresi nel formulario

🞎 prontuario terapeutico, comprendente una lista di tutti gli antibiotici

🞎 reportistica per i medici (MMG) locali relativamente al consumo di antibiotici all’interno della struttura

🞎 nessuno dei precedenti

1. Se nella struttura sono disponibili linee guida terapeutiche scritte, queste sono relative a:

* infezioni del tratto respiratorio 🞎 Sì 🞎 NO
* infezioni del tratto urinario 🞎 Sì 🞎 NO
* infezioni di ferite e cute e tessuti molli 🞎 Sì 🞎 NO
* infezioni del tratto gastro-enterico 🞎 Sì 🞎 NO
* infezione da *C. difficile* 🞎 Sì 🞎 NO

1. In caso di sospetta infezione del tratto urinario, l’uso del dipstick è:

🞎 di routine

🞎 solo a volte

🞎 mai

1. All’interno della struttura è in atto un programma di sorveglianza e di feedback del consumo degli antibiotici? 🞎 Sì 🞎 NO
2. All’interno della struttura è attivo un programma per la sorveglianza di germi antibiotico-resistenti? (report di sintesi annuale per *MRSA, Clostridum difficile, Enterobacteriaceae* resistenti alle cefalosporine di III generazione, *Enterobacteriaceae* resistenti ai carbapenemici, *Enterococcus* spp.vancomicino-resistente, *Pseudomonas aeruginosa* o *Acinetobacter baumannii* resistenti ai carbapenemici, *C. difficile)* 🞎 Sì 🞎 NO
3. Come vengono forniti gli antibiotici alla vostra struttura?

* Da più di una farmacia 🞎 Sì 🞎 NO
* Vengono forniti da una sola farmacia 🞎 Sì 🞎 NO
* Questa struttura non acquista antibiotici direttamente; gli antibiotici sono acquistati dai residenti (es. forniti dalla famiglia) 🞎 Sì 🞎 NO

1. Con quanti laboratori microbiologici lavorate? (è possibile **una sola risposta**)

🞎 Con più di un laboratorio microbiologico di natura giuridica pubblica

🞎 Con più di un laboratorio microbiologico di natura giuridica privata

🞎 Con più di un laboratorio microbiologico di natura giuridica composita

🞎 Con un solo laboratorio microbiologico di natura giuridica pubblica

🞎 Con un solo laboratorio microbiologico di natura giuridica privata

🞎 Questa struttura non invia campioni microbiologici ad alcun laboratorio; ogni medico di medicina generale può lavorare con un laboratorio microbiologico a sua scelta

**F. SVOLGIMENTO DELLA RILEVAZIONE NELLA STRUTTURA**

1. Chi ha raccolto i dati (**è possibile una sola risposta**)? (sia il questionario di struttura che quello degli ospiti)

🞎 medico

🞎 infermiere

🞎 altro

1. Nel caso in cui non sia stato coinvolto un medico nella raccolta dei dati, questo li ha validati successivamente?

🞎 Sì 🞎 NO

**APPENDIX 2**

**QUESTIONARIO OSPITE**

**Questa pagina è da compilare per tutti i degenti reclutati**

GENERE 🞎 F 🞎 M

DATA DI NASCITA \_ \_ \_ \_ (YYYY)

DURATA DELLA DEGENZA IN STRUTTURA 🞎 < 1 anno

🞎 > 1 anno

RICOVERO IN OSPEDALE NEI 🞎 Sì 🞎 NO

3 MESI PRECEDENTI

INTERVENTO CHIRURGICO NEI 🞎 Sì 🞎 NO

30 GIORNI PRECEDENTI

PRESENZA DI:

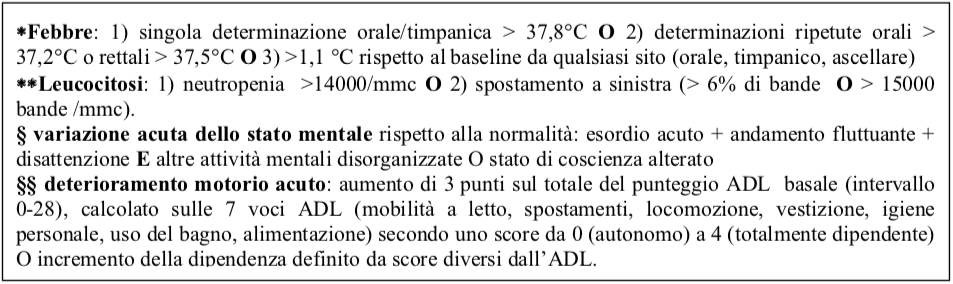
* CATETERE URINARIO 🞎 Sì 🞎 NO
* CATETERE VASCOLARE 🞎 Sì 🞎 NO
* INCONTINENZA (urinaria e/o fecale) 🞎 Sì 🞎 NO
* FERITE
  + PIAGHE DA DECUBITO 🞎 Sì 🞎 NO
  + ALTRE FERITE 🞎 Sì 🞎 NO
* DISORIENTAMENTO 🞎 Sì 🞎 NO

(nello spazio e/o nel tempo)

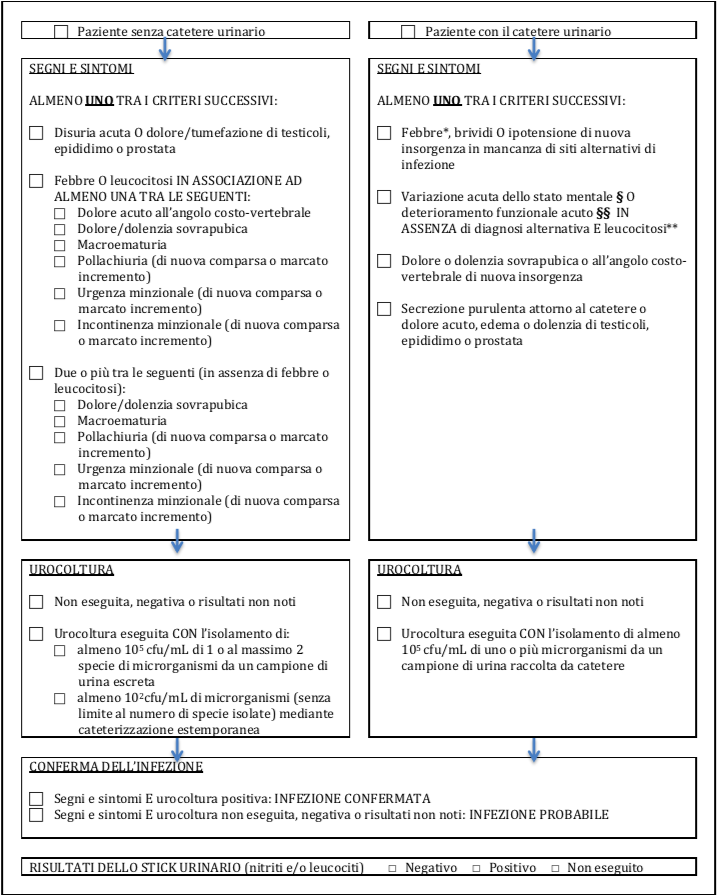
MOTRICITA’ 🞎 deambulante 🞎carrozzina 🞎 allettato

**PARTE A: SEGNI E SINTOMI DI INFEZIONE ATTIVA**

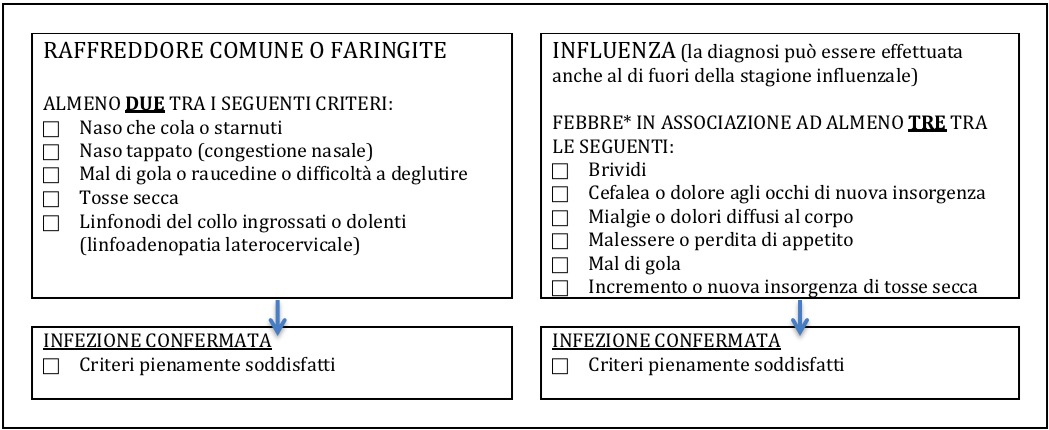
Devono essere riportate tutte le infezioni associate all’assistenza **in atto** il giorno dell’indagine di sorveglianza. Un’infezione è in atto quando i segni/sintomi che la caratterizzano sono presenti il giorno dell’indagine **O** erano presenti in precedenza ed il giorno dell’indagine il paziente sta ancora assumendo il trattamento antibiotico prescritto per quell’infezione. Si dovrebbe verificare la presenza di segni/sintomi di infezione nei 14 giorni precedenti l’indagine per verificare se l’infezione trattata corrisponde ad una delle tipologie di HAI definite.



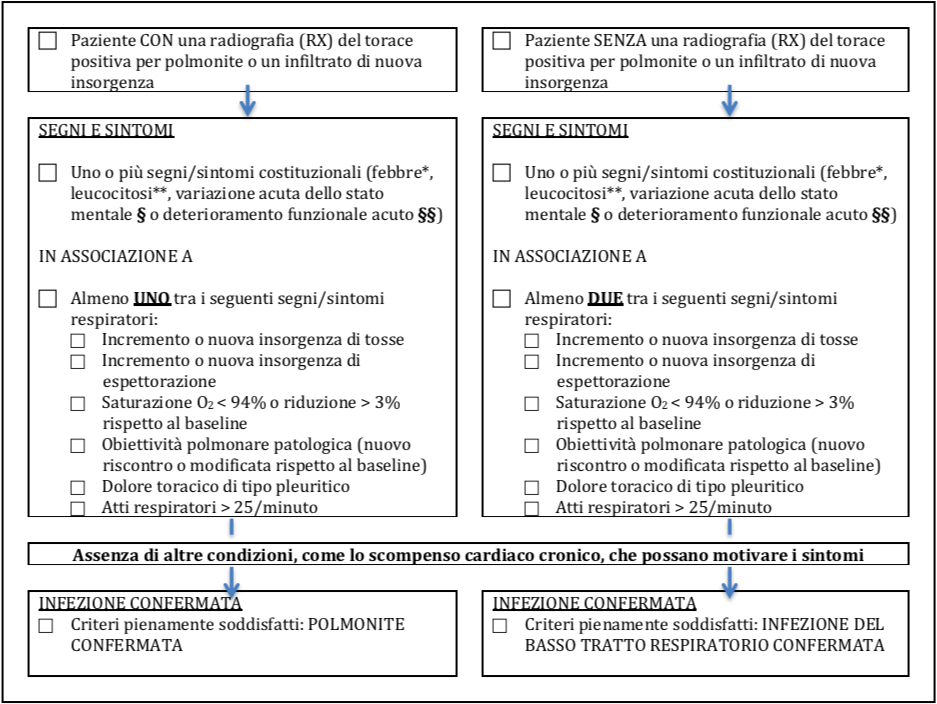
**INFEZIONI DEL TRATTO URINARIO**

****

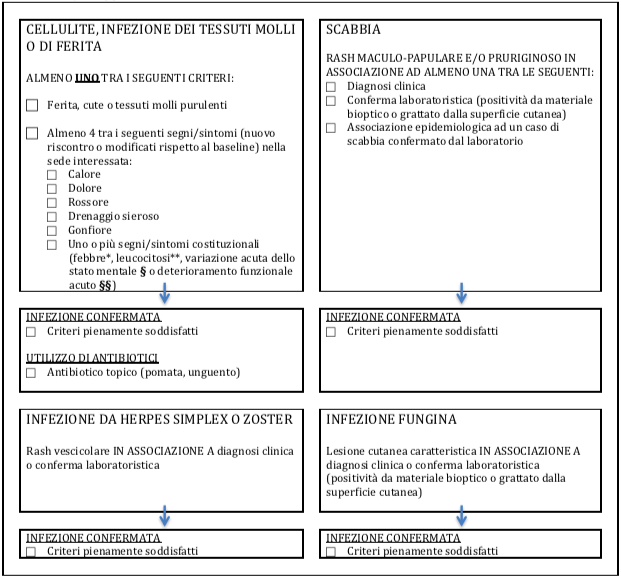
**INFEZIONI DEL TRATTO RESPIRATORIO SUPERIORE**



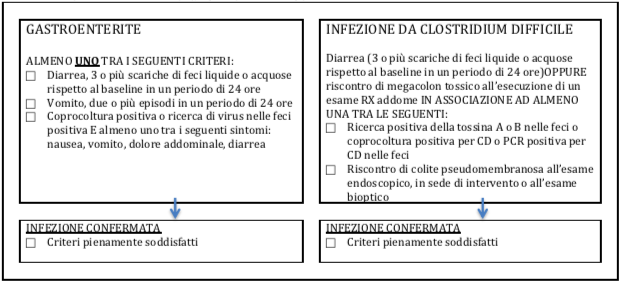
**INFEZIONI DEL TRATTO RESPIRATORIO INFERIORE**



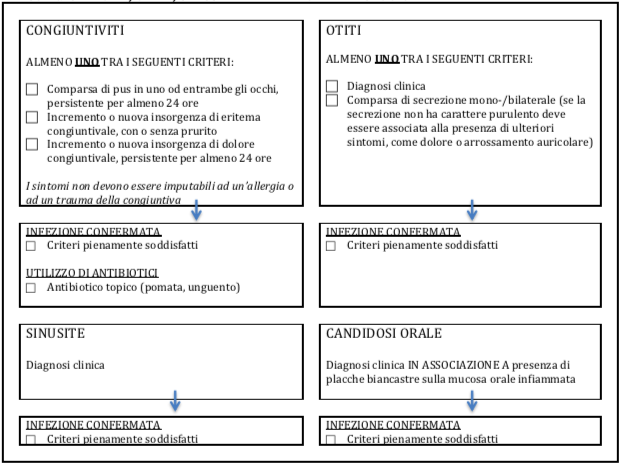
**INFEZIONI CUTANEE**



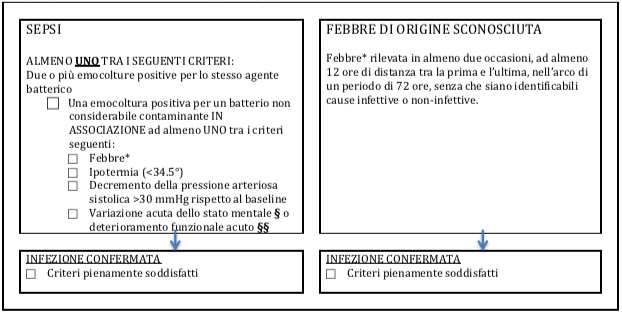
**INFEZIONI DEL TRATTO GASTROENTERICO**

****

**CONGIUNTIVITI, OTITI, SINUSITI ED INFEZIONI DEL CAVO ORALE**

****

**SEPSI E FEBBRE DI ORIGINE SCONOSCIUTA**

****

**PARTE B: UTILIZZO DEGLI ANTIBIOTICI NEGLI ULTIMI 30 GIORNI**

Devono essere **inclusi** nello studio, quindi indicati nella “Parte B - utilizzo degli antibiotici negli ultimi 30 giorni” della scheda Residente, i seguenti antibiotici, qualora la via di somministrazione sia orale, parenterale (endovenosa), intramuscolare, sottocutanea, inalatoria o rettale:

* antibiotici per uso sistemico, antimicotici per infezioni sistemiche e antimicotici per infezioni cutanee
* antibiotici/antinfettivi intestinali
* antiprotozoari
* anti-micobatterici utilizzati per il trattamento delle infezioni da micobatteri (inclusa la tubercolosi) o per il trattamento di salvataggio nelle infezioni da batteri multi-resistenti

I seguenti agenti antibiotici devono essere **esclusi**:

* agenti antivirali per uso sistemico
* agenti antibiotici per uso topico
* agenti antisettici

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Antibiotico 1** | **Antibiotico 2** | **Antibiotico 3** | **Antibiotico 4** |
| **NOME ANTIBIOTICO** |  |  |  |  |
| **PERIODO**  **(dal… al…)** | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ |
| **SOMMINISTRATO**  **PER VIA** | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro |
| **DATA NOTA**  **DI FINE TERAPIA?** | 🞎 SI 🞎 NO | 🞎 SI 🞎 NO | 🞎 SI 🞎 NO | 🞎 SI 🞎 NO |
| **TIPO DI TRATTAMENTO** | 🞎 profilassi  🞎 terapia | 🞎 profilassi  🞎 terapia | 🞎 profilassi  🞎 terapia | 🞎 profilassi  🞎 terapia |
| **INDICAZIONE** | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro |
| **LUOGO DI PRESCRIZIONE** | 🞎 in LTCF  🞎 in ospedale  🞎 altrove | 🞎 in LTCF  🞎 in ospedale  🞎 altrove | 🞎 in LTCF  🞎 in ospedale  🞎 altrove | 🞎 in LTCF  🞎 in ospedale  🞎 altrove |

§ Infezione da *C. difficile*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Antibiotico 5** | **Antibiotico 6** | **Antibiotico 7** | **Antibiotico 8** |
| **NOME ANTIBIOTICO** |  |  |  |  |
| **PERIODO**  **(dal… al…)** | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ | \_ \_ / \_ \_ / \_ \_ \_ \_  \_ \_ / \_ \_ / \_ \_ \_ \_ |
| **SOMMINISTRATO**  **PER VIA** | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro | 🞎 orale  🞎 parenterale  (IM, IV, SC)  🞎 altro |
| **DATA NOTA**  **DI FINE TERAPIA?** | 🞎 SI 🞎 NO | 🞎 SI 🞎 NO | 🞎 SI 🞎 NO | 🞎 SI 🞎 NO |
| **TIPO DI TRATTAMENTO** | 🞎 profilassi  🞎 terapia | 🞎 profilassi  🞎 terapia | 🞎 profilassi  🞎 terapia | 🞎 profilassi  🞎 terapia |
| **INDICAZIONE** | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro | 🞎 tratto urinario  🞎 tratto genitale  🞎 cute/tessuti molli  🞎 tratto respirat.  🞎 gastroenterico  🞎 occhio  🞎 ORL  🞎 sito chirurgico  🞎 tubercolosi  🞎 sepsi  🞎 febbre di ndd  🞎 osso  🞎 CDI§  🞎 non chiaro |
| **LUOGO DI PRESCRIZIONE** | 🞎 in LTCF  🞎 in ospedale  🞎 altrove | 🞎 in LTCF  🞎 in ospedale  🞎 altrove | 🞎 in LTCF  🞎 in ospedale  🞎 altrove | 🞎 in LTCF  🞎 in ospedale  🞎 altrove |

§ Infezione da *C. difficile*

**APPENDIX 3**

**LISTA DEI CODICI RELATIVI AI MICRORGANISMI**

1. Se è stato eseguito un esame microbiologico, indicare il microrganismo isolato (**fino a 3**) o selezionare una delle opzioni seguenti:

**\_NOEXA** ESAME NON ESEGUITO: non è stato eseguito alcun esame microbiologico

**\_NA** RISULTATO NON DISPONIBILE: un esame microbiologico è stato eseguito ma il risultato non è ancora disponibile o non è reperibile

**\_NONID** MICRORGANISMO NON IDENTIFICATO: il microrganismo individuato non può essere correttamente classificato

**\_STERI** ESAME NEGATIVO: un esame microbiologico è stato eseguito ma è risultato negativo (ad esempio, coltura negativa)

1. Per ciascuno dei microrganismi riportati in esteso in neretto, indicare la suscettibilità utilizzando la **tabella sottostante**.

**S** SENSIBILE o SUSCETTIBILE

**R** RESISTENTE o NON-SUSCETTIBILE

N.B.: in caso di sensibilità intermedia (I), il batterio dev’essere classificato come resistente (**R**); in caso la suscettibilità risulti sconosciuta, indicare con il punto interrogativo (**?**)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **0** | **1** | **2** | **?** |
| **Staphylococcus aureus** | Oxacillino-S  **MSSA** | Oxacillino-R  **MRSA** |  | Ignota |
| **Enterococcus species** | Glicopeptidi-**S** | Glicopeptidi-R  **VRE** |  | Ignota |
| **Enterobacteriaceae**  Escherichia coli  Klebsiella species  Enterobacter species  Proteus species  Citrobacter species  Serratia species  Morganella species | Cefalo 3a gen-**S**  E  carbapenemici-**S** | Cefalo 3a gen-**R**  E  carbapenemici-**S** | Carbapenemici-**R** | Ignota |
| **Pseudomonas aeruginosa** | Carbapenemico-**S** | Carbapenemico-**R** |  | Ignota |
| **Acinetobacter baumanni** | Carbapenemico-**S** | Carbapenemico-**R** |  | Ignota |

Glicopeptidi = vancomicina, teicoplanina

Carbapenemici = imipenem, meropenem, doripenem

Cefalo 3a gen. (cefalosporine di terza generazione) = cefotaxime o ceftriaxone

**ACHSPP** ACHROMOBACTER SPECIES

**ACIBAU ACINETOBACTER BAUMANNII**

**ACICAL** ACINETOBACTER CALCOACETICUS

**ACIHAE** ACINETOBACTER HAEMOLYTICUS

**ACILWO** ACINETOBACTER LWOFFI

**ACINSP** ACINETOBACTER SPECIES, non specificato

**ACIOTH** ACINETOBACTER SPECIES, altro

**ACTSPP** ACTINOMYCES SPECIES

**AEMSPP** AEROMONAS SPECIES

**AGRSPP** AGROBACTERIUM SPECIES

**ALCSPP** ALCALIGENES SPECIES

**ANANSP** ANAEROBI, non specificato

**ANAOTH** ANAEROBI, altro

**ASPFUM** ASPERGILLUS FUMIGATUS

**ASPNIG** ASPERGILLUS NIGER

**ASPNSP** ASPERGILLUS SPECIES, non specificato

**ASPOTH** ASPERGILLUS SPECIES, altro

**GPBNSP** BACILLI, GRAM POSITIVI, non specificato

**GPBOTH** BACILLI, GRAM POSITIVI, altro

**BACSPP** BACILLUS SPECIES

**BCTOTH** BATTERI, altro

**BCTNSP** BATTERI, non specificato

**BATFRA** BACTEROIDES FRAGILIS

**BATNSP** BACTEROIDES SPECIES, non specificato

**BATOTH** BACTEROIDES SPECIES, altro

**BURCEP** BURKHOLDERIA CEPACIA

**CAMSPP** CAMPYLOBACTER SPECIES

**CANALB** CANDIDA ALBICANS

**CANGLA** CANDIDA GLABRATA

**CANKRU** CANDIDA KRUSEI

**CANPAR** CANDIDA PARAPSILOSIS

**CANNSP** CANDIDA SPECIES, non specificato

**CANOTH** CANDIDA SPECIES, altro

**CANTRO** CANDIDA TROPICALIS

**CHLSPP** CHLAMYDIA SPECIES

**CITFRE CITROBACTER FREUNDII**

**CITDIV CITROBACTER KOSERI**

**CITNSP CITROBACTER SPECIES, non specificato**

**CITOTH CITROBACTER SPECIES, altro**

**CLODIF** CLOSTRIDIUM DIFFICILE

**CLOOTH** CLOSTRIDIUM, altro

**GNCNSP** COCCHI, GRAM NEGATIVI, non specificato

**GNCOTH** COCCHI, GRAM NEGATIVI, altro

**GPCNSP** COCCHI, GRAM POSITIVI, non specificato

**GPCOTH** COCCHI, GRAM POSITIVI, altro

**CORSPP** CORYNEBACTERIUM SPECIES

**ENBAER ENTEROBACTER AEROGENES**

**ENBAGG ENTEROBACTER AGGLOMERANS**

**ENBCLO ENTEROBACTER CLOACAE**

**ENBGER ENTEROBACTER GERGOVIAE**

**ENBSAK ENTEROBACTER SAKAZAKII**

**ENBNSP ENTEROBACTER SPECIES, non specificato**

**ENBOTH ENTEROBACTER SPECIES, altro**

**ETBNSP** ENTEROBACTERIACEAE, non specificato

**ETBOTH** ENTEROBACTERIACEAE, altro

**ENCFAE ENTEROCOCCUS FAECALIS**

**ENCFAI ENTEROCOCCUS FAECIUM**

**ENCNSP ENTEROCOCCUS SPECIES, non specificato**

**ENCOTH ENTEROCOCCUS SPECIES, altro**

**ESCCOL ESCHERICHIA COLI**

**FLASPP** FLAVOBACTERIUM SPECIES

**FUNNSP** FUNGHI, non specificato

**FUNOTH** FUNGHI, altro

**GARSPP** GARDNERELLA SPECIES

**HAEINF** HAEMOPHILUS INFLUENZAE

**HAEPAI** HAEMOPHILUS PARAINFLUENZAE

**HAENSP** HAEMOPHILUS SPECIES, non specificato

**HAEOTH** HAEMOPHILUS SPECIES, altro

**HAFSPP** HAFNIA SPECIES

**HELPYL** HELICOBACTER PYLORI

**KLEOXY KLEBSIELLA OXYTOCA**

**KLEPNE KLEBSIELLA PNEUMONIAE**

**KLENSP KLEBSIELLA SPECIES, non specificato**

**KLEOTH KLEBSIELLA SPECIES, altro**

**LACSPP** LACTOBACILLUS SPECIES

**LEGSPP** LEGIONELLA SPECIES

**LISMON** LISTERIA MONOCYTOGENES

**MORCAT** MORAXELLA CATHARRALIS

**MORNSP** MORAXELLA SPECIES, non specificato

**MOROTH** MORAXELLA SPECIES, altro

**MOGSPP MORGANELLA SPECIES**

**MYCATY** MYCOBACTERIUM, atipico

**MYCTUB** MYCOBACTERIUM TUBERCULOSIS COMPLEX

**MYPSPP** MYCOPLASMA SPECIES

**NEIMEN** NEISSERIA MENINGITIDIS

**NEINSP** NEISSERIA SPECIES, non specificato

**NEIOTH** NEISSERIA SPECIES, altro

**NOCSPP** NOCARDIA SPECIES

**PAROTH** PARASSITI, altro

**PASSPP** PASTEURELLA SPECIES

**PRESPP** PREVOTELLA SPECIES

**PROSPP** PROPIONIBACTERIUM SPECIES

**PRTMIR PROTEUS MIRABILIS**

**PRTNSP PROTEUS SPECIES, non specificato**

**PRTOTH PROTEUS SPECIES, altro**

**PRTVUL PROTEUS VULGARIS**

**PRVSPP** PROVIDENCIA SPECIES

**PSENSP** FAMIGLIA PSEUDOMONADACEAE, non specificato

**PSEOTH** FAMIGLIA PSEUDOMONADACEAE, altro

**PSEAER PSEUDOMONAS AERUGINOSA**

**SALENT** SALMONELLA ENTERITIDIS

**SALNSP** SALMONELLA SPECIES, non specificato

**SALOTH** SALMONELLA SPECIES, altro

**SALTYM** SALMONELLA TYPHIMURIUM

**SALTYP** SALMONELLA TYPHI o PARATYPHI

**SERLIQ SERRATIA LIQUEFACIENS**

**SERMAR SERRATIA MARCESCENS**

**SERNSP SERRATIA SPECIES, non specificato**

**SEROTH SERRATIA SPECIES, altro**

**SHISPP** SHIGELLA SPECIES

**STAAUR STAPHYLOCOCCUS AUREUS**

**STAEPI** STAPHYLOCOCCUS EPIDERMIDIS

**STAHAE** STAPHYLOCOCCUS HAEMOLYTICUS

**STACNS** STAFILOCOCCI, COAGULASI-NEGATIVI, non specificato

**STAOTH** STAFILOCOCCI, COAGULASI-NEGATIVI (CNS), altro

**STANSP** STAPHYLOCOCCUS SPECIES, non specificato

**STEMAL** STENOTROPHOMONAS MALTOPHILIA

**STRHCG** STREPTOCOCCAE, EMOLITICO (gruppo C, G), altro

**STRAGA** STREPTOCOCCUS AGALACTIAE (gruppo B)

**STRPNE** STREPTOCOCCUS PNEUMONIAE

**STRPYO** STREPTOCOCCUS PYOGENES (gruppo A)

**STRNSP** STREPTOCOCCUS SPECIES, non specificato

**STROTH** STREPTOCOCCUS SPECIES, altro

**VIRADV** ADENOVIRUS

**VIRCMV** CITOMEGALOVIRUS (CMV)

**VIRENT** ENTEROVIRUS (POLIO, COXSACKIE, ECHO)

**VIRHAV** VIRUS dell’EPATITE A

**VIRHBV** VIRUS dell’EPATITE B

**VIRHCV** VIRUS dell’EPATITE C

**VIRHIV** VIRUS dell’IMMUNODEFICIENZA UMANA (HIV)

**VIRHSV** HERPES SIMPLEX VIRUS

**VIRINF** INFLUENZA VIRUS

**VIRNOR** NOROVIRUS

**VIRPIV** PARAINFLUENZAVIRUS

**VIRRHI** RHINOVIRUS

**VIRROT** ROTAVIRUS

**VIRRSV** VIRUS RESPIRATORIO SINCIZIALE (RSV)

**VIRSAR** SARS-CORONAVIRUS

**VIRVZV** VARICELLA-ZOSTER VIRUS

**VIRNSP** VIRUS, non specificato

**VIROTH** VIRUS, altro

**YEAOTH** LIEVITI, altro

**YERSPP** YERSINIA SPECIES