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**Healthcare-associated infections and antimicrobial use in long-term care facilities (HALT3): an overview of the Italian situation**

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# Healthcare-Associated Infection and Antimicrobial Use in Long-Term Care Facilities (HALT3): an Overview of the Italian Situation

## Introduction

Currently, rapid ageing of the population is causing an increase in the demand for intermediate healthcare addressed both to patients recently discharged from hospitals and to those who struggle to manage and cope with their chronic healthcare needs [1]. At the same time, as a natural consequence, the number of long-term care facilities (LTCFs) that provide these services is increasing, together with the interest and awareness regarding issues of healthcare-associated infections (HAIs) and the use of antimicrobial agents in these structures [2]. In fact, infections inside LTCFs are a common cause of residents' morbidity and mortality, and they represent an important socio-economic burden [3]. Moreover, the elderly, who usually compose the large majority of the LTCF population, are more vulnerable to infections, due to their reduced immunological competence, which is driven by their age. Beside this, the elderly also report higher risks of underlying chronic illnesses that, while generally not fatal in most adults, may result in severe pathologies [4]–[7].

Other challenges that LTCFs usually must face when referring to infections are the frequent occurrence of outbreaks, transfers of residents within different structures, the spread of HAIs between acute care facilities and LTCFs and cross-infections. The latter are favoured to spread among different facilities for the following reasons: difficulties in diagnosing the infections because of atypical clinical presentation and cognitive impairment in the elderly, limited access to laboratories or radiology, low levels of physician input or unfavourable nurse/patient ratios [8], [9]. Together, these aspects may lead to an inappropriate prescription of antimicrobials, enhancing the possible development of high colonization rates of multi-resistant bacteria [10], [11] and microorganisms [5] such as methicillin-resistant *Staphylococcus aureus* [3], [8], [12], [13].

Furthermore, as shown by other studies, more than half of the antibiotic courses prescribed and started in LTCFs are unnecessary, or when necessary, the prescribed antimicrobials often are excessively broad spectrum or administered for longer than required for the correct treatment of the underlying infection. Thus, the overuse and misuse of antibiotics in LTCFs are the major causes of adverse drug events and future infections, such as those caused by *Clostridium difficile* and antibiotic-resistant bacteria [14].

On the other hand, the improvement and correct implementation of basic good practices, such as

promoting a thoughtful and rational use of antimicrobial agents by prescribing doctors or increasing hand hygiene and infection control precautions, may lead to a substantial improvement in the main outcomes for HAIs in this setting [2], [15].

At the same time, the implementation of antimicrobial stewardship programmes may improve the appropriateness of antibiotics prescriptions and reduce the rates of infections by *C. Difficile* and by certain types of multidrug-resistance organisms [16]

To increase awareness of the abovementioned topics and to provide an estimate of the burden of HAIs in LTCFs, in 2009, the European Centre for Disease Prevention and Control (ECDC) started and funded the “Healthcare-Associated Infections in European Long-Term Care Facilities” (HALT) project. The main purpose of this project is to develop and implement a sustainable methodology that can help estimate the prevalence of infections and antimicrobial resistance and use across European LTCFs, and at the same time, assess the status of infection control programmes in the EU region.

On these premises, the ECDC commissioned three point prevalence surveys (PPS) focused on the surveillance of HAI and antimicrobial use in long-term care facilities (HALT) across Europe [17], [18]. The first HALT PPS was conducted in 2010 [8], and the results included a total of 61932 eligible residents surveyed in 722 different LTCFs across 28 countries [19]; this was followed by a second survey conducted in 2013 (HALT2), in which 19 countries participated [20].

Italy joined both these previous studies and, in 2017, conducted the third point prevalence survey of the ECDC’s HALT project (HALT3), the results of which are the substance of this paper.

The aim of this paper is to report the results of the Italian HALT3 survey results, analysing the prevalence of infections and antimicrobial use, verifying the presence and implementation of specific protocols and guidelines for the management of critical issues, as well as describing the characteristics of the LTCFs structures and their residing populations.

## **Materials and methods**

### *Study design*

The present study was designed as a point prevalence survey. Data regarding all active healthcare associated infections (HAIs) were collected, together with information about currently prescribed systemic antibiotics reported on patients’ clinical records on the day of the survey.

### *Point Prevalence Study (PPS) time schedule*

The survey was carried out in each facility within the time window from April to June 2017 (1/04/2017 to 30/06/2017), in accordance with the three periods indicated from the ECDC; data were collected preferably for one day, although, in large settings that included a high number of residents, data collection was spread over two or more consecutive days.

#### *Eligibility criteria for the LTCFs*

Participation in the study was agreed to on a voluntary basis by residents of the LTCFs.

Eligibility criteria for the institutions included:

- guaranteed 24/7 assistance
- opportunity for specialized nursing care
- presence of clinically stable residents
- presence of residents who do not require constant specialized medical assistance

Moreover, the structures involved in the survey were classified as “Nursing Homes”, “Residential Homes”, “Specialized LTCF”, and “Mixed LTCF” (classes definitions are reported in Table 1).

**Table 1:** ECDC classification of eligible LTCF in HALT3 study

<b>General Nursing homes</b>	In these facilities, residents need medical or skilled nursing and supervision 24 h a day. These facilities mainly provide care to seniors with severe illnesses or injuries.
<b>Residential homes</b>	In these facilities, residents are unable to live independently. They require supervision and assistance for the activities of daily living (ADL). These facilities usually include personal care, housekeeping and three meals a day.
<b>Specialized LTCFs</b>	These facilities are specialized in one specific type of care e.g., physical impairment, chronic diseases such as multiple sclerosis, dementia, psychiatric illnesses, rehabilitation care, palliative care, intensive care, etc.
<b>Mixed LTCFs</b>	These facilities provide different types of care in the same facility (a mix of the abovementioned LTCF types).

To enrol as many institutions as possible, the survey was widely advertised through the inter-regional network for HAIs surveillance (built for the national projects on healthcare infections surveillance funded by the Centro Nazionale per la Prevenzione e Controllo delle Malattie-CCM).

#### *Eligible residents of the LTCFs*

All residents living 24/7 in the institution were included in the survey, with the exception of those who refused to participate or were absent on the day of the survey because of a hospitalization in another facility. Residents receiving chronic ambulatory care on a regular basis in the acute care hospital (e.g., haemodialysis, chemotherapy, etc.) and residents absent for exams were included in the PPS study as long as they were not hospitalized on the day of the PPS.

Residents with invasive devices, such as mechanical ventilation, were excluded from the survey.

### *Ethical considerations*

According to local legislation, some ethics committees requested written consent from each resident with a diagnosed HAI or from those receiving an antimicrobial agent on the day of the PPS, or, if it was not possible to obtain consent from the resident himself (e.g., in the case of cognitive impairment), from a “proxy”, such as a caregiver or a medical professional.

Confidentiality of LTCF data and resident data was assured by national survey coordinators (NSCs), who assigned an LTCF survey number to each participating LTCF. The participating LTCFs were not identifiable by other LTCFs/persons. A unique resident survey number was allocated to each resident for whom a questionnaire was completed. The study obtained ethical approval from the ethical committee “Azienda Ospedaliero Universitaria San Luigi Gonzaga”, Orbassano (To), protocol number 50/2017.

### *Data collection*

Data were collected by local surveyors (designated physicians, infection control doctors/nurses and head nurses of the LTCF) or local surveyors supported by an external surveyor (infection control nurses of the local health authority).

Both local and externally trained surveyors visited the facility on the day of the survey and inspected each resident with the help of a nurse in charge, nurses’ aides and healthcare workers of the LTCF, looking for recent symptoms suggestive of infection, examining charts, case notes and drug charts. Possible infected patients were furtherly reviewed and, if possible, discussed with the attending physician.

All the facilities were asked to:

- 1) Fill out a form about institutional characteristics, called “Institutional Questionnaire”, providing specific information, such as the type of facility, its organization and/or coordination of medical care, the infection control and antibiotic policies and resources and other aggregated data regarding residents’ characteristics present on survey day (presence of urinary or vascular catheter, incontinence, wounds, disorientation in time and/or space, use of wheelchair or bedridden);
- 2) Compile a second form called “Ward List” for each ward including characteristics of all eligible residents in each LTCF ward;
- 3) Fill out a form (“Resident Questionnaire”) for each resident receiving at least one systemic antimicrobial agent on the day of the PPS and/or presenting signs and symptoms of at least one active infection on the day of the PPS, registering resident characteristics, eventual antimicrobial intake (antimicrobial class, administration route, treatment purpose, organ target) and/or HAI (source of infection, eventual isolated microorganism, antibiotic resistance testing).

Only new or acutely worse symptoms and infections that were not already displayed by the resident or in incubation at the time of admission or readmission (after hospitalization or community visit) to the nursing home were collected. The item “diagnosed by the attending physician” was added, together with additional clues of the presence of infection.

#### *Data analysis*

Collected data were analysed with Microsoft Excel software and statistical package SPSS 25.

## **Results**

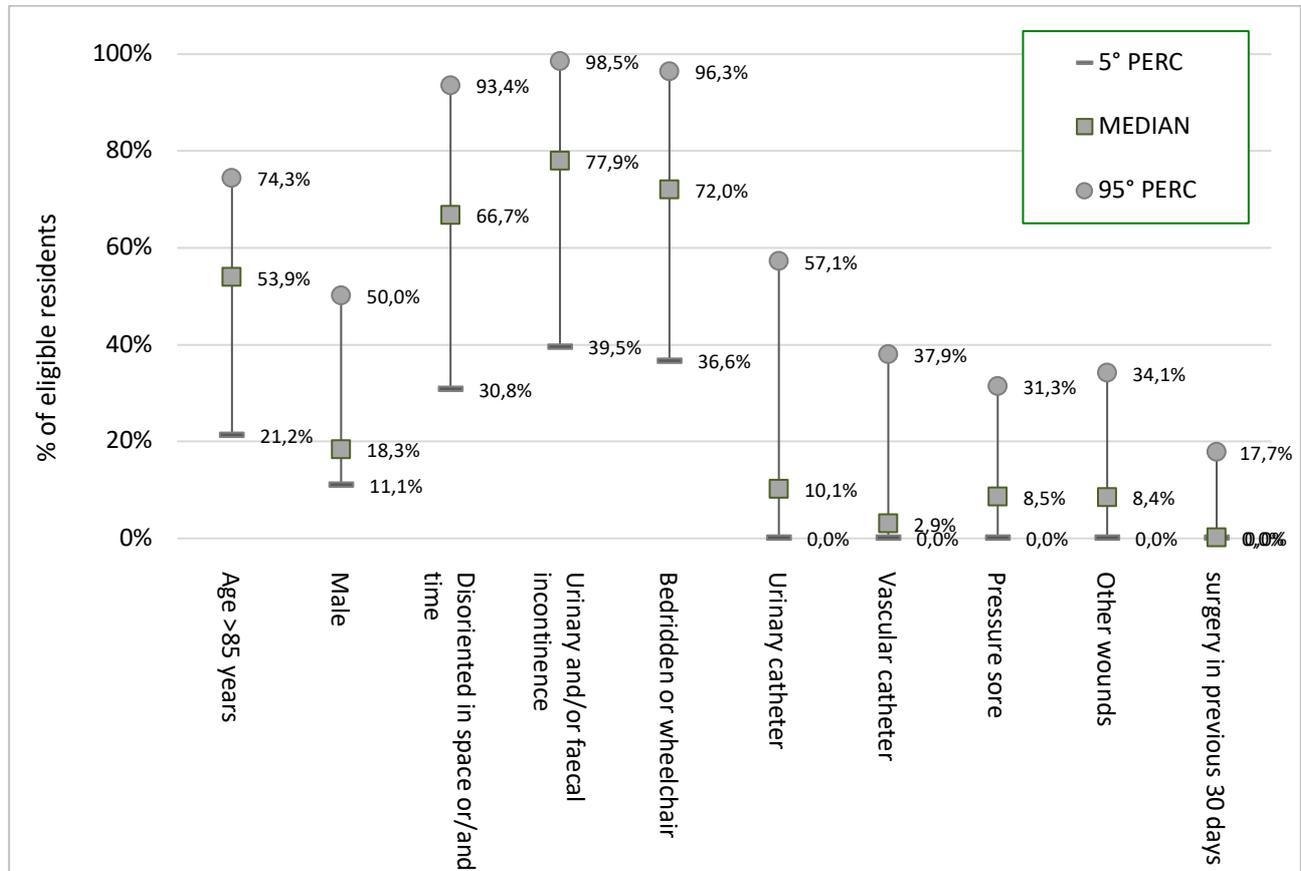
Globally, a number of 418 Italian facilities of 14 different regions (Piemonte, Emilia-Romagna, Valle d'Aosta, Liguria, Veneto, Friuli Venezia Giulia, Lombardia, Trentino Alto Adige, Toscana, Sardegna, Marche, Molise, Puglia, Sicilia) took part in the HALT3 study; 127 of these were nursing homes, 171 residential homes, 101 mixed LTCFs, and 15 were specialized LTCFs (4 facilities did not specify their model of care provision).

Among the considered LTCFs, the average bed availability was 62 beds (minimum 4 – maximum 574), with 93% mean occupancy.

Often, among these structures, medical care, which includes antimicrobial prescriptions, was provided by the personal general practitioner (GP) (61.7%); in 17% of the cases, medical care was provided by a member of the medical staff employed in the structure; and in the remaining 21% of facilities, it was provided by both.

Care load indicators and risk factors of the 24,132 eligible residents (97.99% of the overall residents in the LTCFs involved) are shown in Figure 1. The eligible sample was predominantly composed of residents over 85 years old (median 53.8%), who were female, disoriented in time and/or space, bedridden or using a wheelchair and incontinent. Differently, the rates concerning other risk factors, such as the use urinary or vascular catheters and the presence of pressure sores and/or other wounds were consistently lower. Some differences were found among the facilities, such as higher values for the presence of certain risk factors, especially urinary catheters, which reached 57.1% as the 95° percentile (Figure 1).

**Figure 1.** Care load indicators and risk factors: grey bars, squares and dots correspond respectively to 5° percentile, median and 95° percentile. Values are calculated on eligible patients and are means of single facility's prevalence.

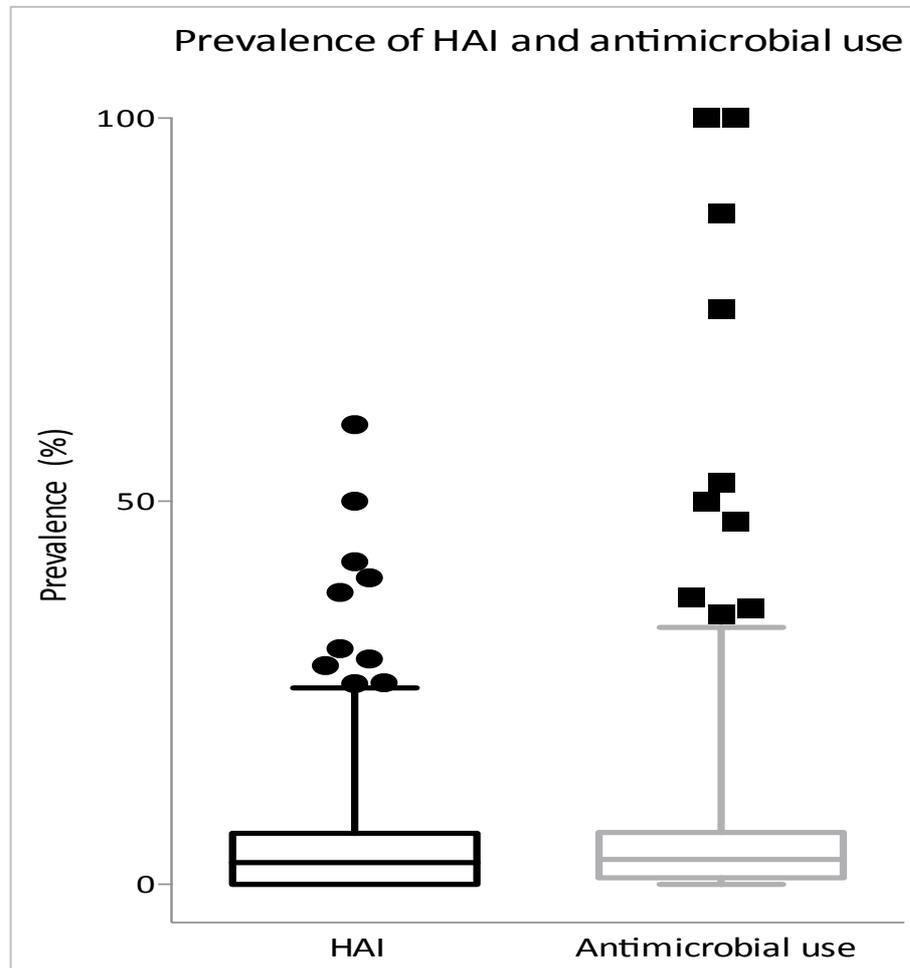


### *Prevalence of healthcare-associated infections*

On the day of the study, 957 HAIs were reported, with a prevalence rate of 3.9% (median value 2.9%); among these infections, 911 residents had one single infection, while 23 had two simultaneous infections. Moreover, describing the origin of HAIs distribution across the different structures, 80.9% were associated with the current LTCF, while 11.9% were imported from a hospital.

The most frequently noticed HAIs were respiratory infections (1.4/100 residents), especially those affecting the lower respiratory tract (73.7%); quite as common were the urinary infections (1/100 resident), with 46.2% of these confirmed by a positive urine culture. Lastly, skin, gastrointestinal and eyes, ears and mouth infections represented, respectively, 15.7%, 6.8% and 6.3% of the total number of reported HAIs. Less frequent sites of infection were fever of unknown origin, bloodstream infections and surgical site infections; the prevalence rates for these infection sites were, respectively, 3%, 0.9% and 0.1%. Data not shown in the text.

**Figure 2.** Distribution of HAIs and antimicrobial use prevalence rates among Italian LTCFs. Boxes represent the central 50% of LTCFs and the middle lines are the median values. Bars and dots/squares contain the remaining 25% above and below boxes. Dots/squares represent LTCFs with prevalence rates higher than 97.5° percentile.



### *Infection control measures*

The HALT3 study pointed out that in almost 50% of the studied facilities there was at least one professional specifically trained in infection control/prevention available on the staff. These professionals were physicians in 11% of cases, nurses in 42.3% of instances and both in 46.6% of medical staffs. Moreover, 79% of structures claimed they could ask for help and expertise from an external infection control (IC) team on a formal basis (e.g., IC from a local hospital), while 114 facilities (27.3% of the total) reported the presence of an internal or external infection surveillance committee.

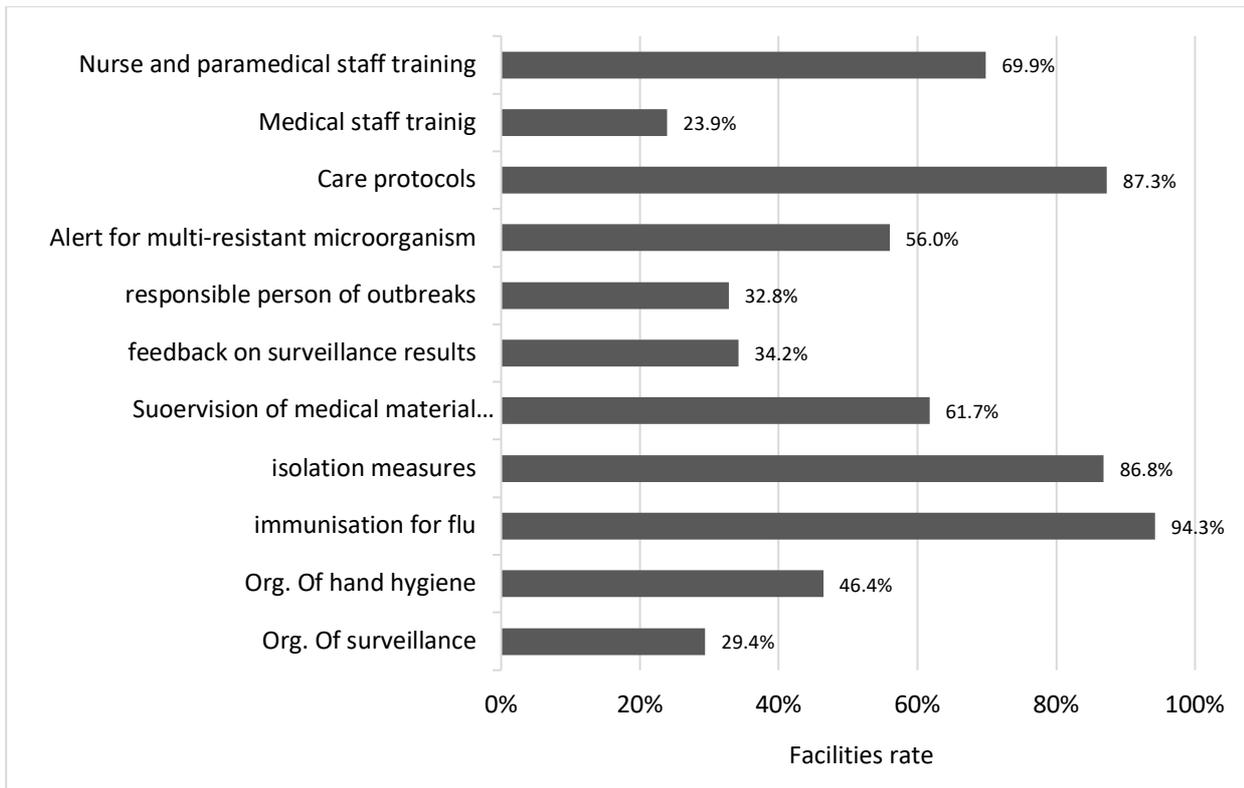
Furthermore, besides the presence of trained professionals, the surveyed LTCFs also reported the implementation of the following infection control practices and prevention measures (Figure 3):

- infection prevention and control training
- written health-care protocols
- prevention, management and surveillance of HAIs and MDRO

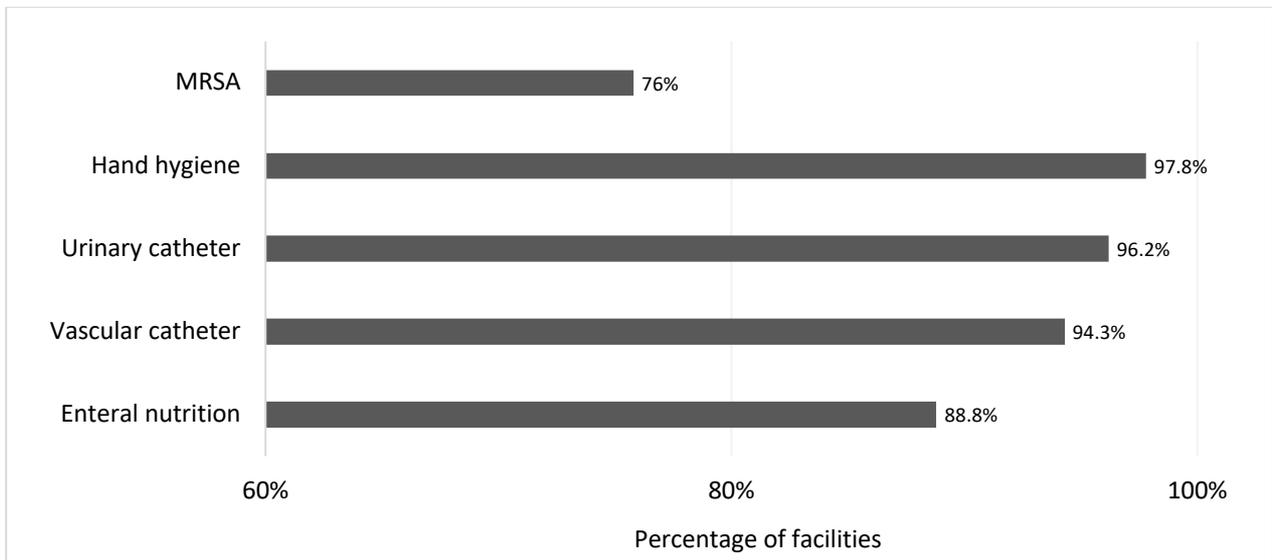
Despite this variety and diffusion of good prevention and infection control practices, only 24.2% of the LTCFs organized a specific HAI surveillance programme.

A wide use of different protocols and guidelines was also outlined from this survey; indeed, 97.4% of the participant LTCFs declared the existence of official written protocols for hand hygiene, 96.2% for urinary catheters and 94.3% for vascular catheters. Nevertheless, the number of LTCFs adopting specific protocols concerning enteral supplies, MRSA and other multi-drug resistant microorganisms (MDRO) was considerably lower (88.8% and 76%, respectively) (Figure 4).

**Figure 3.** Infection control practices: prevalence rates were calculated on the total number of facilities.



**Figure 4.** Written protocols: each prevalence rate corresponds to the number of facilities in which written protocols were implemented. Prevalence rates are calculated on the total number of LTCFs.



### Antimicrobial use

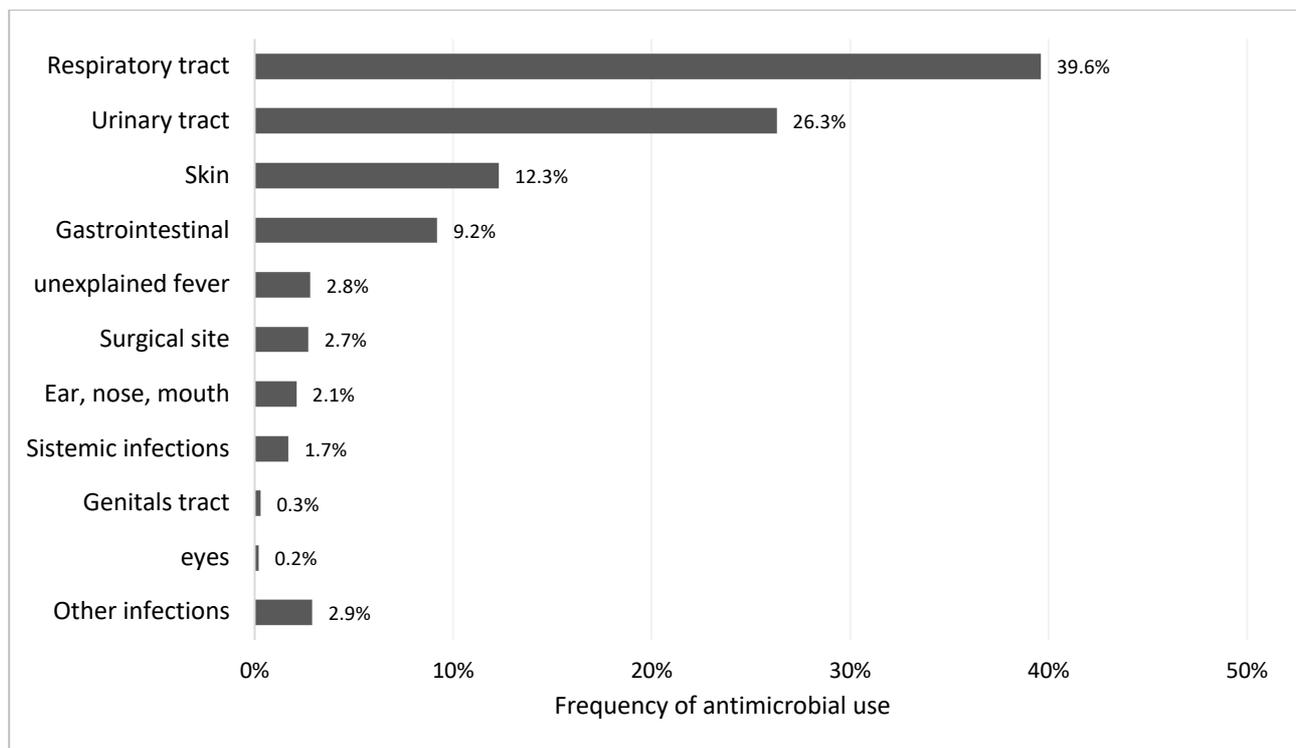
During the survey, 1022 residents were in therapy with at least one antimicrobial agent, with a total of 1102 prescribed antibiotics; the resulting prevalence was 4.2% of all residents, with a median value of 3.3% (Figure 2).

Most of the reported treatments were prescribed for respiratory tract infections (39.6%), followed by urinary tract (26.3%), skin infections (12.3%) and gastrointestinal ones (9.2%) (Figure 5), in line with the chart of infection origin sites displayed in Figure 1.

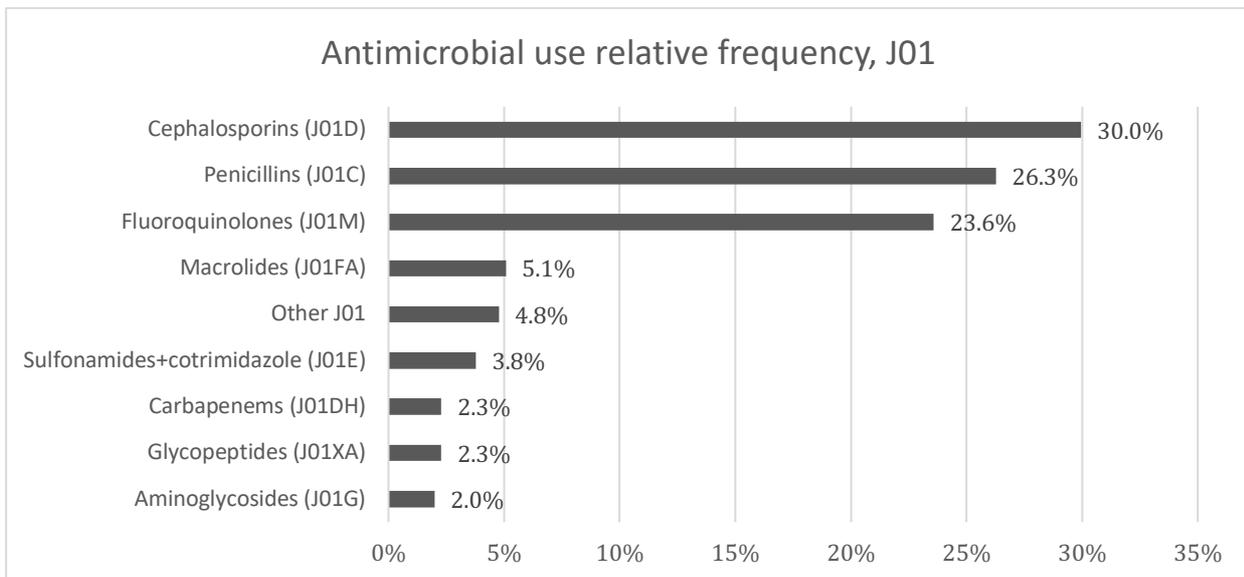
Antimicrobial agents for systemic use (ATC J01) represented 91.2% of all reported antimicrobials: *cephalosporins* (ATC classes J01DB-DC-DE) (30% of all antibacterial agents for systemic use), *penicillins* (ATC class J01C) (26.3%), *fluoroquinolones* (ATC class J01 M) (23.6%), *macrolides* (ATC class J01FA) (5.1%), *sulphonamides* (ATC class J01E) (3.8%), *carbapenems* (ATC class JO1DH) (2.3%), *glycopeptides* (ATC class JO1XA) (2.3%), *aminoglycosides* (ATC class JO1J) (2.0%), and *other (J01)* (4.8%) (Figure 6).

Other antimicrobial groups were prescribed in few cases: *intestinal anti-infectives* (ATC A07, 5.7%), *antiprotozoals* (ATC P01, 1.2%), *tuberculostatics* (ATC J04, 0.3%), *antimycotics for systemic use* (ATC J02, 1.6%).

**Figure 5.** Anatomical site of treatment: prevalence rate calculated on the total number of prescribed antimicrobial agents.



**Figure 6.** Antimicrobial classes: antimicrobial agents were classified according to ATC code. Their use rate is estimate on the total number of prescribed antibiotics.



#### Microorganisms and antimicrobial resistance

Overall, of the 957 infections observed, only 253 microbiological samples were collected (26.4%); 224 of these patients gave a positive outcome (88.5% of taken samples). Through the analyses conducted on the cultures, 253 microorganisms of 36 different types were isolated. In Table 2 the most frequently isolated microorganisms are listed.

**Table 2.** Microorganisms (N=253): rate calculated on total positive isolates exams

Microorganism name	%	N
<i>Escherichia coli</i>	25.7	65
<i>Clostridium difficile</i>	13.4	34
<i>Proteus mirabilis</i>	13.0	33
<i>Pseudomonas aeruginosae</i>	7.9	20
<i>Klebsiella pneumoniae</i>	7.5	19
<i>Staphylococcus aureus</i>	5.9	15
<i>Enterococcus faecalis</i>	3.2	8

Nevertheless, 26.9% of the total isolated microorganisms, among those indicated in the ECDC protocol, were resistant at least to one antimicrobial class. In particular, the isolated pathogens that displayed higher rates of antimicrobial resistance were *Staphylococcus aureus* (66.7%), *Proteus spp.* (45.9%), *Escherichia coli* (41.5%), *Klebsiella spp.* (33.3%), *Acinetobacter baumannii* (28.6%), *Pseudomonas aeruginosa* (20%) and *Morganella species* (16.7%). One *Staphylococcus aureus* out of

15 was a vancomycin-resistant *Staphylococcus aureus* (VRSA), and many microorganisms were resistant to carbapenems: 4.6% of *Escherichia coli*, 19% of *Klebsiella spp.*, 10.8% of *Proteus spp.*, and 28.6% of *Acinetobacter baumannii*.

Subsequently, researchers tested whether a hospital admission during the 3 months preceding the admission to the current LTCF may have been related to the presence of resistant microorganisms. The results show that, among residents with a microbiological sample, admission to a hospital in the previous three months was associated with a lower prevalence of resistant isolated pathogens (21.5% p=0.009).

Regarding the association between the presence of resistant microorganisms and type of structures, no significant differences were measured between residential homes and general nursing homes (p=0.69); on the contrary, a significant difference was founded between them and specialized and mixed LTCFs (p=0.023) (Table 3).

**Table 3.** Association between microorganism resistance and type of healthcare structure.

		Antibiotic Resistance		
		Yes (N=64)	No (N=153)	p*
<b>Hospital admission in previous 3 months</b>	Yes	21.5%	78.5%	<b>0.009</b>
	No	37.6%	62.4%	
<b>LTCF types</b>	Residential homes, general nursing homes	24.3%	75.7%	<b>0.023</b>
	Mixed, specialized and other LTCFs	39%	61%	

\*Chi-square test, significance level  $P \leq 0.05$ .

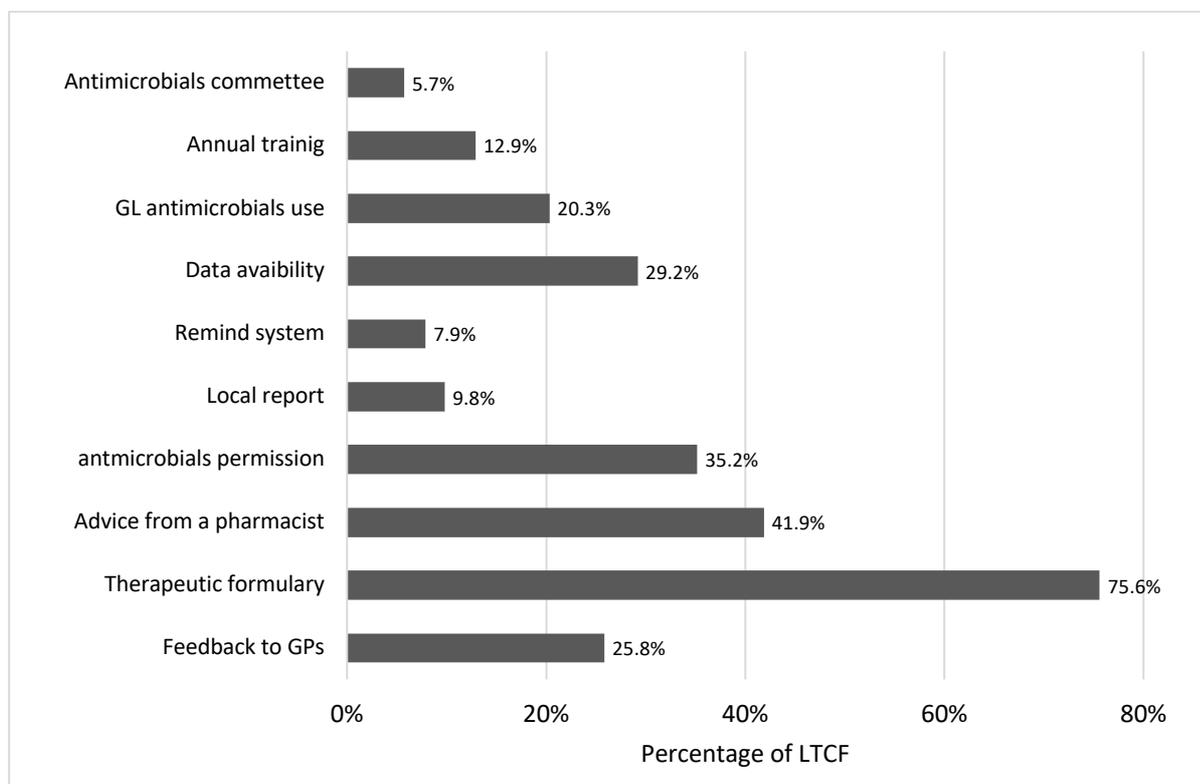
#### *Measures for use of antimicrobials*

More than half of the total enrolled LTCFs (55.7%) applied specific restrictions on the prescriptions of some antibiotics that were reported in official restriction lists. The most cited antibiotics in these lists are (frequency rates refer to the total number of LTCFs) carbapenems, 83.3%; vancomycin, 71%; glycopeptides, 59.2%; intravenous antimicrobials, 54.5%; cephalosporins, 37.8%; broad range antimicrobials, 26.2%; fluoroquinolones, 21%; and mupirocin, 13.7%.

Moreover, all LTCFs declared that they had adopted one or more of the following antimicrobial policies (Figure 7):

- a therapeutic formulary, comprising a list of antibiotics (in 75.6% of LTCFs)
- advice from a pharmacist for prescriptions of antimicrobials not included in the formulary (41.9%)
- presence of a supervisor for prescription of restricted antimicrobials' allowance (35.2%)
- full availability of data on annual antimicrobial consumption, by antimicrobial class (29.2%)
- feedback to the GP on antimicrobial consumption in the facility (25.8%)
- written guidelines for appropriate use of antimicrobials (good practice) in the facility (20.3%)
- annual training on appropriate antimicrobial prescribing (12.9%)
- local (i.e., for that region/locality) antimicrobials resistance profile summaries available in the LTCF or in the surgeries of GP who prescribe that medicine (9.8%)
- a system to remind healthcare workers of the importance of microbiological samples to the best antimicrobial choice (7.9%)
- an antibiotic committee (5.7%)

**Figure 7.** Antimicrobials use control practices: percentages are calculated on total number of LTCF



Regarding the presence of therapeutic guidelines, 28.9% of LTCFs used guidelines for the treatment

of urinary infections, 25% used them for wounds and soft tissues infections, and 23% for respiratory infections.

Moreover, most facilities (72.5%) declared they did not use urine dipsticks for the detection of urinary infections, in contrast with a small percentage (22.5%) that used it sometimes. Out of 418 LTCFs, 16 claimed to routinely use the urine dipsticks.

As results show, the use of urine dipsticks was significantly higher in the facilities in which medical care was provided by personal general practitioners (GPs) ( $p < 0.01$ ), while urine cultures were more often used in the structures that only employed an internal medical staff ( $p < 0.01$ ), Table 4.

**Table 4.** Association between diagnostic exams and medical care assistance.

		Use of dipstick			Use of microbiological testing		
		Yes (N=318)	No (N=884)	p*	Yes (N=294)	No (N=638)	p*
<b>Medical care provider</b>	GP	35.6%	64.4%	<b>&lt;0.01</b>	23.7%	76.3%	<b>&lt;0.01</b>
	Facility medical staff	13.9%	86.1%		51.0%	49.0%	
	Both	20.1%	79.9%		25.4%	74.6%	

\*Chi-square test, significance level  $P \leq 0.05$ .

To summarise, the obtained results regarding antimicrobial policies inside LTCFs show that, when the PPS was performed, approximately 25% of the surveyed Italian LTCFs had an organised surveillance and feedback programmes on antimicrobial consumption, and at the same time, 37% of these facilities claimed to organize surveillance systems of multi-drug resistant microorganisms.

## Discussion

The present study is the final result of the third Italian national point prevalence survey aimed at measuring the occurrence of healthcare-associated infections in long-term care facilities, after similar projects were conducted in 2010 (HALT PPS) and in 2013 (HALT2). The number of participating facilities was higher than in the previous studies (418 vs 92 in 2010 and 235 in 2013), as was the number of involved regions (14 vs 11) [19], [20]. Although our sample was considerably wider than that required in order to achieve national representativeness, participation of the structures in the study was still uneven when considering the territorial distribution of the various facilities included in the paper. Since, in Italy, a comprehensive register of LTCFs (public and private) is still not available, establishing a systematic random sample drawn from a national register was not possible. Therefore, our recruitment method was based on voluntary participation, which led to the consequential presence of substantial differences among the studied features of the LTCFs across different regions.

Most of the facilities were classified as “nursing home” and “residential home”, and just as in 2013, more than half of the total number of residents was over 85 years old; thus, their conditions usually required high loads of care (more than 65% of the patients were disoriented and/or immobilized and/or incontinent). As already mentioned, these data do not differ from those obtained during the conduction of the previous studies in Italy, but they are higher compared to those of the European region reported in 2013 [20]. This difference could be explained by a recent report of the National Institute of Statistics (ISTAT): In Italy, people over 75 years old are generally more affected by chronic diseases (one or more) than are the elderly elsewhere in Europe. Although the life expectancy is one of the highest in Europe, the Italian elderly tend to present worse health conditions during their last years of life [21]. Furthermore, this aspect might explain the higher prevalence rates of urinary catheters (10% vs 6.3%) and pressure sores (8.5% vs 4.2%) than those of the European LTCFs’ population.

The main objective of the study was to assess the prevalence of residents with HAIs (3.9%, a value that is worse than the one measured by HALT2 (3.3% in Italy, 3.4% in Europe)).

Another difference from the previous European study results regards the most frequent infection site, here represented by the respiratory tract, while in HALT2, this appeared to be the urinary tract. This result does appear to be in line with previous Italian studies [8], [20]. Another relevant aspect shown by the data is that more than 70% of respiratory infections in this survey are classified as “other lower respiratory tract infection” since they were not confirmed by an X-ray exam. In this

context, in fact, it can be challenging to perform radiological exams that require the patient's transfer from an LTCF to a hospital, and this might lead to a more difficult interpretation and differentiation among this kind of infections. Moreover, gastrointestinal infections represented 6.8% of the total HAIs number, and about half of them proved to be caused by *C. difficile* [22], [23]. The prevalence of antimicrobial use measured in this study is similar to that observed in the HALT2 study (4.2% vs 3.9% in Italy and 4.4% in Europe). The most prescribed antimicrobials were cephalosporins and penicillins. The use of cephalosporins is higher than what it used to be in Europe in 2013 (30% vs 11.8%), as is the use of carbapenems (2.3% vs 0.75%) and quinolones (23.6% vs 16%). Moreover, the study also highlighted a more frequent use of intestinal anti-infectives (5,7% vs 0,3%) [20]. The discussion on topics related to antimicrobial resistance should carefully consider these results and these data, in order to better shape the implementation of new antimicrobial use policies inside long-term care facilities.

Another aspect to be considered is that microbiological testing still involved only a minimum portion of the infected residents (26.4% of the registered infections), as the majority of the facilities reported they did not use urine dipsticks for the detection of urinary infections, while only a small percentage use them sometimes. Apparently, the use of urine dipsticks was higher in the facilities in which medical care was provided by personal general practitioners (GP), while urine culture was more common in those that employed an internal medical staff. Considering the Italian context, this aspect can be explained by different attitudes towards infections diagnoses: GPs can be more prone to use dipsticks because they usually check infections with them in their daily medical practice, while the medical staff of a facility can more easily require the necessary exams be sent to a laboratory. The microbiological exams conducted on the infections showed that 26.9% of microorganisms were resistant to at least one antimicrobial agent, and this can be partially due to a selection bias: In fact, one crucial aspect that emerged from the HALT study is that, apparently, microbiological cultures and exams were performed only in those cases presenting infected residents who were not responding to empirical treatments [24]. For the HAI rates mentioned above, the prevalence of antibiotic resistance is still higher in Italy's LTCFs than in Europe's [20], [25] for several microorganisms: *Staphylococcus aureus*, *Proteus mirabilis*, and *Escherichia coli*. Moreover, one *Staphylococcus aureus* out of 15 was VRSA, and 19% of *Klebsiella* spp was resistant to carbapenems (versus 10.9% in Europe in 2013). Regardless, this result is in line with other studies performed in Italy [26], [27].

Moreover, unexpectedly, the admission to a hospital in the previous three months was not

associated with a higher prevalence of resistance (Table 4). These data confirmed that microorganism resistance is still a relevant problem in Italy; indeed, it not only affects hospital settings, but it is also assuming more importance inside the LTCFs [26]. In contrast, a significant difference was measured between the facilities hosting residents with less complex care needs (residential and general nursing homes) and specialized LTCFs ( $p=0.023$ ).

In this overall context, antimicrobial stewardship and resistance control for microorganisms have become a milestone for the control and management of HAIs. The number of implemented measures of antimicrobial stewardship inside the LTCFs (such as permissions for prescribing restricted antimicrobials, requiring and receiving advice from pharmacists and strictly following the indications reported on therapeutic formularies) were considerably higher compared to previous studies conducted in Europe. Moreover, 75.8% of facilities had an MDRO protocol (49% in the HALT2 in Italy), almost reaching European levels (76.9% in 2013) [20].

There are some limitations to this study. For instance, being a point prevalence study, the results regarding factors associated with resistance and facility features can only be interpreted through descriptive analyses. Another limitation is the difference in participation in the study among regions, which can affect national representativeness. It is, therefore, necessary to encourage the involvement of more regions in future surveys.

In conclusion, the study was useful to quantify the prevalence of infections, antibiotic use and antimicrobial resistance in long-term care facilities and the diffusion of infection surveillance and control programmes. Italy has successfully improved infection control practices and antimicrobial policies, which appear to be, at the moment, the more practical measures to reduce HAIs and all the outcomes linked to antibiotic resistance issues. The positive results that will follow the strict and correct application of the already mentioned “good practices” might lead to safer healthcare assistance for LTCF residents, which is one of the goals of surveillance, and to a reduced number of HAIs (both in hospitals and in LTCFs), as well as to a more than desirable reduction of antibiotic resistance, which surely represents one of the most crucial topics of today’s public health agenda[15], [28].

It would also be interesting for future studies to collect the characteristics of the residents who did not show signs of infection, in order to analyse possible risks and protective factors associated with healthcare associated infections and/or antibiotic prescriptions.

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