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

M.F. Furmenti, P. Rossello, S. Bianco, E. Olivero*, R. Thomas, I.N. Emelurumonye, C.M. Zotti; HALT3 Italian Collaborating Group[1]

Department of Public Health and Paediatrics, University of Turin, Turin, Italy

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SUMMARY

Background: Awareness of healthcare-associated infections (HAIs) and antimicrobial use in long-term care facilities (LTCFs) is increasing. In 2017, the third national point prevalence survey (PPS) was conducted in Italy as part of the third 'Healthcare-Associated Infections in European Long-Term Care Facilities' (HALT3) study.

Aim: To report the results of HALT3 and analyse the resident population of LTCFs, implementation of good practices, prevalence of infections and antimicrobial use.

Methods: The survey was designed as a PPS, carried out from April to June 2017. All residents who lived full-time in the institution were included. All facilities were asked to complete an institutional questionnaire, a ward list for all residents, and a resident questionnaire for those residents presenting with signs/symptoms of active infection and/or receiving an antimicrobial agent.

Findings: In total, 418 facilities took part in the study; 24,132 residents were eligible, and most were aged >85 years, disoriented and incontinent. The prevalence of HAIs was 3.9%, and 50% of the institutions reported that they had a professional trained in infection control on their staff. Only 26.4% of infections were confirmed by a microbiological sample, and 26.9% of the isolated micro-organisms were resistant to at least one antimicrobial class. In total, 1022 residents received at least one antimicrobial agent, and cephalosporins were prescribed most commonly.

Conclusion: The number of infection control and antimicrobial stewardship measures implemented was found to be considerably higher in this study compared with previous studies. This could lead to a reduction in the prevalence of HAIs, antimicrobial use and antimicrobial resistance. Further studies are needed to monitor these aspects.

Introduction

A rapidly ageing population is causing increased demand for intermediate health care in patients recently discharged from hospitals and patients who struggle to manage with their chronic healthcare needs [1]. At the same time, the number of

* Corresponding author. Address: Department of Public Health Sciences and Paediatrics, Via Santena 5bis, 10126, Torino, Italy. Tel.: +39 0116705817; fax: +39 0116705889.
E-mail address: elena.olivero@unito.it (E. Olivero).

[1] Members of the HALT3 Italian Collaborating Group are listed in the Acknowledgements.

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long-term care facilities (LTCFs) that provide these services is increasing, together with awareness of healthcare-associated infections (HAIs) and use of antimicrobial agents [2]. In fact, infections at LTCFs are a common cause of residents' morbidity and mortality, and represent an important socio-economic burden [3]. Moreover, the elderly, who usually comprise the large majority of the LTCF population, are more vulnerable to infections, due to their reduced immunological competence, due to multiple morbidities and chronic illness [4–7].

Other factors can favour the spread of HAIs in these facilities, including difficulties in diagnosing infections because of atypical clinical presentation and cognitive impairment in the elderly, limited access to laboratories or radiology, low levels of physician input and unfavourable nurse/patient ratios [8,9]. Together, these aspects may lead to inappropriate prescription of antimicrobials, enhancing the possible development of high colonization rates of multi-resistant bacteria [10,11] and micro-organisms [5–13]. Furthermore, as shown by other studies, more than half of the antibiotic courses prescribed and started in LTCFs are unnecessary; overuse and misuse of antibiotics in LTCFs represent major causes of adverse drug events and future infections [14].

On the other hand, the improvement and correct implementation of basic good practices, such as antimicrobial stewardship programmes or hand hygiene and infection control precautions, may lead to substantial improvement in the main outcomes for HAIs, the appropriateness of antibiotic prescriptions and a reduction in the infections caused by *Clostridium difficile* and other multi-drug-resistant organisms (MDROs) [2,15,16].

To increase awareness of the abovementioned topics and estimate the burden of HAIs in LTCFs, the European Centre for Disease Prevention and Control (ECDC) started and funded the 'Healthcare-Associated Infections in European Long-Term Care Facilities' (HALT) project in 2009. The main purpose of this project was to develop and implement a sustainable methodology to help estimate the prevalence of infections, antimicrobial resistance and antimicrobial use across European LTCFs, and assess the status of infection control programmes in the European Union (EU). On these premises, ECDC commissioned three point prevalence surveys (PPS) [17,18]. The first HALT PPS was conducted in 2010 [8] across 28 countries [19]; this was followed by a second survey in 2013 (HALT2) across 19 countries [20]. Italy joined these previous studies and conducted the third PPS within the ECDC's HALT project (HALT3) in 2017.

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

Methods

Study design

This study was designed as a PPS. The survey was carried out in each facility within the time window from 1st April 2017 to 30th June 2017, in accordance with the three periods indicated by ECDC; ideally, data were collected on a single day, although, in large settings that included a high number of residents, data collection was spread over two or more consecutive days. According to the ECDC protocol, the recommended minimum number of LTCFs to be recruited in Italy was 67 and the recommended sample size was 5724 residents [21]. Study participation was voluntary.

Study population

Eligibility criteria for the institutions included:

- guaranteed assistance for 24 h/day;
- opportunity for specialized nursing care;
- presence of clinically stable residents; and
- presence of residents who do not require constant specialized medical assistance.

Moreover, the facilities involved in the survey were classified as general nursing homes, residential homes, specialized LTCFs and mixed LTCFs. Residents of general nursing homes need medical or skilled nursing and supervision 24 h/day, while residents of residential homes are unable to live independently and require supervision and assistance for activities of daily living. Specialized LTCFs are specialized in one specific type of care (chronic diseases, rehabilitation care etc.), and mixed LTCFs provide different types of care in the same facility.

In order to enrol as many institutions as possible, the survey was widely advertised through the inter-regional network for HAI surveillance [built for the national projects on healthcare infection surveillance funded by the Centro Nazionale per la Prevenzione e Controllo delle Malattie (CCM)].

All full-time residents at the institution were included in the survey, with the exception of those who refused to participate or who were absent on the day of the survey because of hospitalization in another facility. Residents receiving chronic ambulatory care on a regular basis in an acute care hospital (e.g. haemodialysis, chemotherapy, etc.) and residents absent for examination were included in the PPS as long as they were not hospitalized on the day of the PPS. Residents receiving mechanical ventilation were excluded from the survey.

This study obtained ethical approval from the ethics committee 'Azienda Ospedaliero Universitaria San Luigi Gonzaga', Orbassano (Protocol No. 50/2017). 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 him/herself (e.g. in the case of cognitive impairment), from a 'proxy', such as a caregiver or a medical professional.

Data collection

Data were collected by local surveyors (designated physicians or nurses). All facilities were asked to complete an institutional questionnaire, a ward list and a resident questionnaire. The institutional questionnaire collected denominator data, structural and functional characteristics (e.g. public/private ownership, presence of qualified nurses, medical coordination), and information about antimicrobial policies and infection control resources at the LTCF. The ward list collected information from each eligible resident, and was developed to aid the collection of denominator data for the institutional questionnaire. Finally, the resident questionnaire

had to be completed for each resident presenting signs or symptoms of an active infection and/or receiving an antimicrobial agent [21].

Data analysis

Collected data were analysed using Excel (Microsoft Corp., Redmond, WA, USA) and SPSS Version 25 (IBM Corp., Armonk, NY, USA). The results were expressed as absolute numbers, mean, median and percentages. Chi-squared test was used to ascertain statistical associations, and $P<0.05$ was taken to indicate statistical significance.

Results

Characteristics of the sample

Globally, 418 Italian facilities from 14 different regions (Piemonte, Emilia-Romagna, Valle d'Aosta, Liguria, Veneto, Friuli Venezia Giulia, Lombardia, Trentino Alto Adige, Toscana, Sardegna, Marche, Molise, Puglia and Sicilia) participated in HALT3: 127 general nursing homes, 171 residential homes, 101 mixed LTCFs and 15 specialized LTCFs. Four facilities did not specify their model of care provision.

Care load indicators and risk factors for the 24,132 eligible residents (97.99% of all residents in the LTCFs involved) are shown in Figure 1. The eligible sample was predominantly composed of residents aged >85 years (median 53.8%), female, disoriented in time and/or space, bedridden or using a wheelchair, and incontinent. The rates for other risk factors, such as the use of urinary or vascular catheters and the presence of pressure sores and/or other wounds, were consistently lower (Figure 1).

Prevalence of infections, antimicrobial resistance and antimicrobial use

On the day of the study, 957 HAIs were reported, with a prevalence rate of 3.9% (median 2.9%, Figure 2). Among these infections, 911 residents had a single infection, while 23 residents had two simultaneous infections. The prevalence of infections in LTCFs is influenced by the type of facility (3.3% in residential homes, 3.5% in general nursing homes and 5.6% in mixed LTCFs).

The most frequently reported HAIs were respiratory infections (1.4/100 residents), particularly those affecting the lower respiratory tract (73.7%), and urinary infections (1/100 residents), with 46.2% of these confirmed by a positive urine culture. Skin, gastrointestinal and eye/ear/mouth infections represented 15.7%, 7.7% and 5.2% of the total number of reported HAIs, respectively. Less common types of infection were fever of unknown origin, surgical site infections and bloodstream infections (2.8%, 2.3% and 1.6% of all reported HAIs, respectively).

Overall, of the 957 infections observed, only 253 had microbiological samples collected (26.4%), with 224 of these cultures showing a positive result (88.5% of samples taken). Through analyses conducted on the cultures, 253 micro-organisms of 36 different types were isolated; the most frequently isolated micro-organisms were *Escherichia coli* (25.7%), *Clostridium difficile* (13.4%), *Proteus mirabilis* (13%), *Pseudomonas aeruginosa* (7.9%), *Klebsiella pneumoniae* (7.5%), *Staphylococcus aureus* (5.9%) and *Enterococcus faecalis* (3.2%). In total, 26.9% of the isolated micro-organisms from those indicated in the ECDC protocol were resistant to at least one antimicrobial class. One of the 15 *S. aureus* was resistant to vancomycin (VRSA), and several micro-organisms were resistant

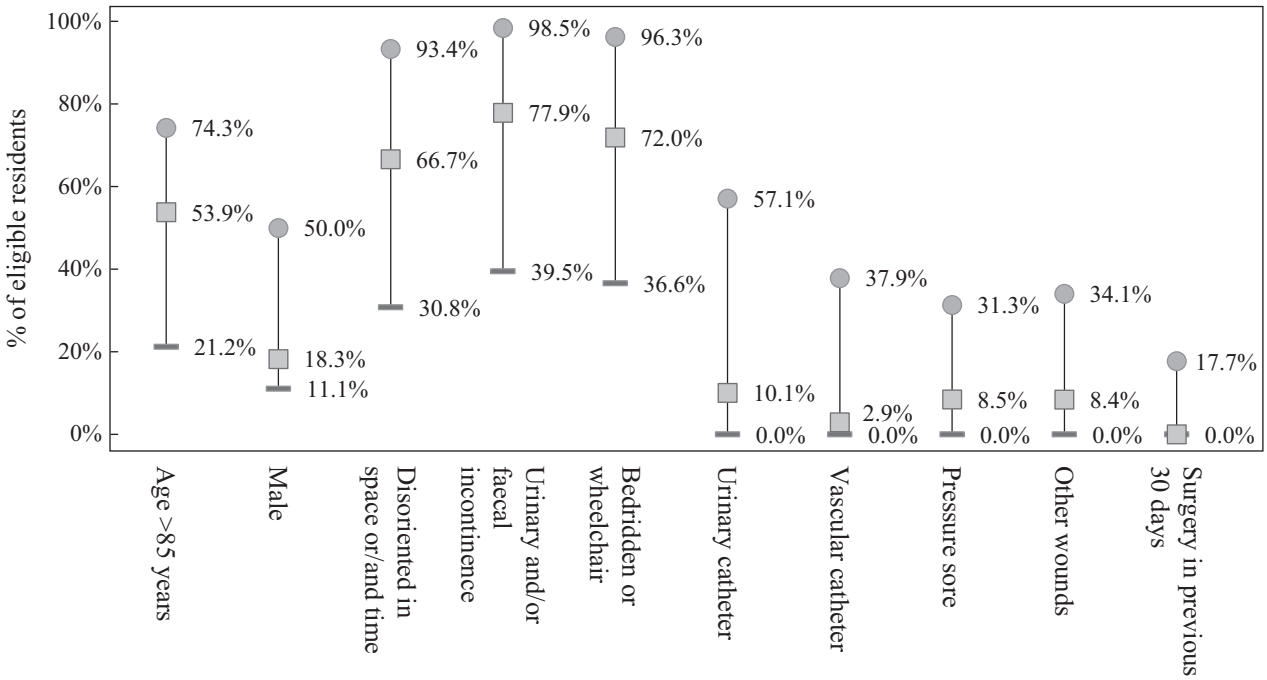

Figure 1. Care load indicators and risk factors: grey bars, squares and circles correspond to fifth percentile, median and 95th percentile, respectively. Values are calculated on eligible patients and are the mean values for prevalence at single facilities.

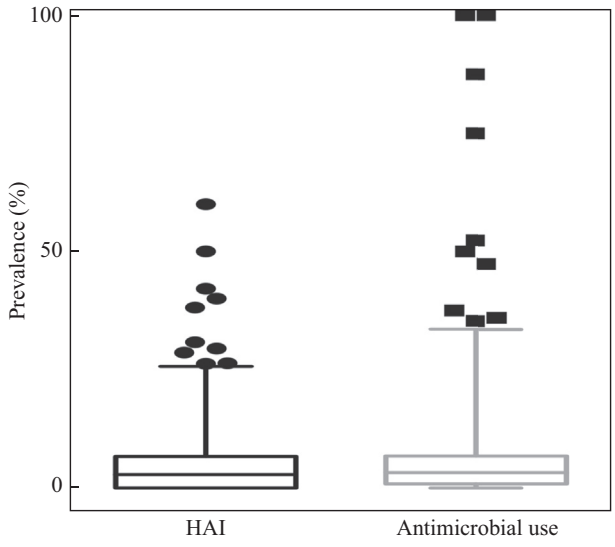

Figure 2. Distribution of the prevalence of healthcare-associated infections (HAIs) and antimicrobial use among Italian long-term care facilities (LTCFs). Boxes represent the central 50% of LTCFs and the middle lines are the median values. Bars and circles/squares represent the remaining 25% above and below boxes. Circles/squares represent LTCFs with prevalence rates >97.5th percentile.

to carbapenems: 4.6% of *E. coli*, 19% of *Klebsiella* spp., 10.8% of *Proteus* spp. and 28.6% of *Acinetobacter baumannii*.

During the survey, 1022 residents were receiving therapy with at least one antimicrobial agent, with a total of 1102 residents prescribed antibiotics; the resulting prevalence was 4.2% of all residents (3.5% in residential homes, 3.9% in general nursing homes and 5.7% in mixed LTCFs), 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 infections (26.3%), skin infections (12.3%) and gastrointestinal infections (9.2%). Antibiotics were less frequently prescribed for unexplained fever (2.8%), surgical site infections (2.7%), ear/nose/mouth infections (2.1%), systemic infections (1.7%), genital tract infections (0.3%), eye infections (0.2%) and other infections (2.9%).

Antimicrobial agents for systemic use [Anatomical Therapeutic Chemical (ATC) class 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 J01M) (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 ATC class JO1 (4.8%). Other antimicrobial groups were prescribed in a few cases: intestinal anti-infectives (ATC class A07, 5.7%), antiprotozoals (ATC class P01, 1.2%), tuberculostatics (ATC class J04, 0.3%) and antimycotics for systemic use (ATC class J02, 1.6%).

Antimicrobial policies and infection control resources in LTCFs

HALT3 demonstrated that in almost 50% of the studied facilities, there was at least one healthcare professional specifically trained in infection prevention and control. Furthermore, besides the presence of trained professionals, the surveyed LTCFs also reported the presence of numerous infection control practices and prevention measures, such as isolation measures (86.8%), alerts for multi-resistant organisms (56%), organization of hand hygiene (46.4%) and organization of a specific HAI surveillance programme (29.4%).

Widespread use of different protocols and guidelines was identified in this survey; 97.4% of the participating LTCFs declared the existence of official written protocols for hand hygiene, 96.2% for urinary catheters and 94.3% for vascular catheters. The number of LTCFs adopting specific protocols for enteral supplies and MRSA and other MDROs was considerably lower (88.8% and 76%, respectively).

More than half of the total enrolled LTCFs (55.7%) applied specific restrictions on the prescription of certain antibiotics that were reported in official restriction lists, while only 20.3% of LTCFs used written guidelines for appropriate use of antimicrobials (good practice) in the facility.

Moreover, most facilities (72.5%) reported that they did not use urine dipsticks for the detection of urinary tract infections, and a small percentage (22.5%) reported that they used them sometimes. Out of 418 LTCFs, 16 claimed to use urine dipsticks routinely. The use of urine dipsticks was significantly higher in facilities in which medical care was provided by general practitioners (GPs) ($P<0.01$), and urine cultures were used more often used in facilities that employed internal medical staff ($P<0.01$).

LTCF characteristics and antimicrobial resistance

Researchers tested whether hospital admission during the three-month period preceding admission to the current LTCF may have been associated with the presence of resistant micro-organisms. The results show that, among residents with a microbiological sample, hospital admission in the preceding three months was associated with a lower prevalence of resistant pathogens (21.5%, $P=0.009$). Regarding the association between presence of resistant micro-organisms and type of facility, no significant differences were detected between residential homes and general nursing homes ($P=0.69$), but a significant difference was found between them and specialized and mixed LTCFs ($P=0.023$) (Table I).

Discussion

This study is the final result of the third Italian national PPS to measure the occurrence of HAIs in LTCFs. 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]. Since a comprehensive register of LTCFs (public and private) is still not available in Italy, the recruitment method was based on voluntary participation, which led to substantial differences in the number of LTCFs enrolled across different regions.

Most facilities were classified as nursing homes and residential homes, and, just as in 2013, more than half of the total number of residents were aged >85 years; as such, their conditions usually required high levels of care (>65% of patients were disoriented and/or incontinent). These data are higher compared with those for the European region reported in 2013 [20]; this difference could be explained by a recent report from

Table I
Association between micro-organism resistance and type of healthcare structure in residents with at least one positive culture (N=217)

		Antibiotic resistance		
		% Yes (N=64)	% No (N=153)	P[a]
Hospital admission in previous 3 months	Yes (N=107)	21.5% (N=23)	78.5% (N=84)	0.009
	No (N=109)	37.6% (N=41)	62.4% (N=68)	
LTCF type	Residential homes, general nursing homes (N=140)	24.3% (N=34)	75.7% (N=106)	0.023
	Mixed, specialized and other LTCFs (N=77)	39% (N=30)	61% (N=47)	

LTCF, long-term care facility.
[a] Chi-squared test, significance level $P \leq 0.05$.

the National Institute of Statistics: in Italy, people aged >75 years generally have more chronic diseases (one or more) than elderly people elsewhere in Europe. Although life expectancy in Italy is among the highest in Europe, Italian elderly tend to develop worse health conditions during their last years of life [22]. This aspect might explain the higher prevalence rates of urinary catheters (10% vs 6.3%) and pressure sores (8.5% vs 4.2%) in Italian elderly.

The main objective of this study was to assess the prevalence of HAIs among residents of LTCFs. The finding of 3.9% is higher than that measured by HALT2 (3.3% in Italy, 3.4% in Europe), but is in line with that measured in the EU/European Economic Area (EEA) sample (3.7%, country range 0.9–8.5%) [20,23]. Another difference from HALT2 regards the most common infection site (respiratory tract in HALT3, but urinary tract in HALT2). This result does appear to be in line with previous Italian studies [8,20].

The prevalence of antimicrobial use measured in this study is similar to that observed in HALT2 (4.2% vs 3.9% in Italy and 4.4% in Europe) [20] and slightly lower than that in the EU/EEA sample (4.9, country range 0.7–10.5%) [24]. The most commonly prescribed antimicrobials were cephalosporins and penicillins. This study found that the use of cephalosporins is higher than it was 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 more frequent use of intestinal anti-infectives (5.7% vs 0.3%) [20].

Another aspect to be considered is that microbiological testing was only undertaken for a small proportion of the infected residents (26.4% of registered infections), and the majority of facilities reported that they did not use urine dipsticks, and a small percentage only used them sometimes. The use of urine dipsticks was higher in facilities in which medical care was provided by GPs, while urine culture was more common in facilities that employed internal medical staff. Considering the Italian context, this aspect can be explained by different attitudes towards infection diagnoses: GPs use dipsticks more frequently in their daily medical practice, while internal medical staff can send samples to a laboratory for culture more easily.

The microbiological tests conducted on the samples showed that 26.9% of micro-organisms were resistant to at least one antimicrobial agent, and this may be partially due to selection bias. One crucial aspect that emerged from the HALT study is that microbiological cultures and examinations were only performed for infected residents who were not responding to empirical treatments [8]. Microbiological methods for pathogen susceptibility were not investigated in the study, and this could be a limitation, especially for rare multi-drug-resistant phenotypes such as VRSA, carbapenem-resistant *E. coli* or *Proteus* spp. For the HAI rates mentioned above, the prevalence of antibiotic resistance is still higher in LTCFs in Italy compared with those in Europe [20,25] for several micro-organisms, including *S. aureus*, *P. mirabilis* and *E. coli*. Moreover, one *S. aureus* out of 15 was VRSA, and 19% of *Klebsiella* spp. were resistant to carbapenems (vs 10.9% in Europe in 2013). These results are in line with other studies performed in Italy [26,27].

Hospital admission in the three months preceding the survey was unexpectedly associated with lower prevalence of resistance (Table I). This could be due to confounding factors: for instance, residents who had been admitted to hospital in the preceding three months may have spent a shorter period in a healthcare facility than residents who did not report a previous hospital stay. Further research may be required to analyse this aspect. Nevertheless, these data confirm that resistance is still a relevant problem in Italy; indeed, it not only affects hospital settings, but also assumes more importance inside LTCFs [26]. In contrast, a significant difference was measured between facilities hosting residents with less complex care needs (residential and general nursing homes) and specialized LTCFs (P=0.023).

Overall, antimicrobial stewardship and the control of resistant organisms have become milestones for the control and management of HAIs. The number of implemented measures of antimicrobial stewardship inside LTCFs (e.g. permission for prescribing restricted antimicrobials, requiring and receiving advice from pharmacists, and strict adherence to the indications reported on therapeutic formularies) was considerably higher compared with previous studies conducted in Europe. Moreover, 75.8% of facilities had an MDRO protocol (49% in HALT2 in Italy), almost reaching European levels (76.9% in 2013) [20].

This study had some limitations. For instance, being a PPS, the results regarding factors associated with resistance and facility features can only be interpreted through descriptive analyses. Another limitation is the difference in participation rates between regions, which may affect national representativeness. It is, therefore, necessary to encourage the involvement of more regions in future surveys.

In conclusion, this study was useful to quantify the prevalence of infections, antibiotic use and antimicrobial resistance in LTCFs and the distribution of infection surveillance and control programmes. In Italy, the focus on infection control practices and antimicrobial policies has been growing, albeit

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

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Conflict of interest statement
None declared.

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