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Impact of COVID-19 on healthcare-associated infections and antimicrobial use in Italy, 2022

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Background: It is unknown whether COVID-19 patients are at higher risk due to demographic and clinical characteristics associated with higher COVID-19 infection risk and severity of infection, or due to the disease and its management.
Aim: To assess the impact of COVID-19 on healthcare-associated infection (HAI) transmission and antimicrobial use (AMU) prevalence during the later stages of the pandemic.
Methods: A point-prevalence survey (PPS) was conducted among 325 acute care hospitals of 19 out of 21 Regions of Italy, during November 2022. Non-COVID-19 patients were matched to COVID-19 patients according to age, sex, and severity of underlying conditions. HAI and AMU prevalence were calculated as the percentage of patients with at least one HAI or prescribed at least one antimicrobial over all included patients, respectively.
Findings: In total, 60,403 patients were included, 1897 (3.14%) of which were classified as COVID-19 patients. Crude HAI prevalence was significantly higher among COVID-19 patients compared to non-COVID-19 patients (9.54% vs 8.01%; prevalence rate ratio (PRR): 1.19; 95% confidence interval (CI): 1.04–1.38; $P < 0.05$), and remained higher in the matched sample; however, statistical significance was not maintained (odds ratio (OR): 1.25; 95% CI: 0.99–1.59; $P = 0.067$). AMU prevalence was significantly higher among COVID-19 patients prior to matching (46.39% vs 41.52%; PRR: 1.21; 95% CI: 1.11–1.32; $P < 0.001$), and significantly lower after matching (OR: 0.77; 95% CI: 0.66–0.89; $P < 0.001$).
Conclusion: COVID-19 patients could be at higher HAI risk due to underlying clinical conditions and the intensity of healthcare needs. Further efforts should be dedicated to antimicrobial stewardship among COVID-19 patients.

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Introduction

Healthcare-associated infections (HAIs) are an important patient safety issue. According to previous estimates, the burden attributable to the six most common HAIs in Europe in terms of disability-adjusted life-years (DALYs) exceeded that of all other communicable diseases under surveillance by the European Center for Disease Prevention and Control (ECDC), including influenza and tuberculosis, in the EU/EEA in 2011–2012 [1]. Italy ranks among the highest European countries in regards to HAI prevalence, antimicrobial resistance (AMR) rates, and respective attributable deaths and DALYs [2–4].

Early publications debated what impact the COVID-19 pandemic would have on HAI transmission and AMR, due to enhanced infection prevention and control (IPC) efforts and awareness of infectious diseases on the one hand, and to the pressure on health systems due to the surge of critical patients admitted to acute care hospitals, as well as to the diversion of IPC resources to COVID-19 management on the other [5–7]. In fact, growing evidence suggests that HAI rates increased during the COVID-19 pandemic [8–10]. A recent US retrospective analysis found that HAI rates among non-COVID-19 patients during the pandemic were similar to HAI rates among inpatients prior to the pandemic, suggesting that COVID-19 patients could be more susceptible to HAIs [11]. However, whether COVID-19 patients are at higher risk due to demographic and clinical characteristics associated with higher COVID-19 infection risk and severity of infection, or due to the disease and its management, remains to be determined [12,13].

The ECDC promotes repeated point-prevalence surveys (PPS) of HAIs and antimicrobial use (AMU) among acute care hospitals of EU/EEA countries every five years. The third edition of the PPS was conducted in 2022–2023, with COVID-19 variables collected for the first time [14]. In this study, we analysed results from the Italian national survey, with the objective of assessing the impact of COVID-19 on HAI and AMU prevalence. Prevalence rates were compared among COVID-19 and non-COVID-19 patients, aiming to identify opportunities for improvement in terms of IPC and antimicrobial stewardship interventions in both patient groups.

Methods

Study design, protocol, and definitions

A PPS was conducted among acute-care hospitals during November 2022, within the second window identified by the ECDC for the European study (September to November 2022). A standardized protocol was developed by ECDC and used across European nations. The University of Turin's Department of Public Health and Paediatrics was the National coordinating centre for the study in Italy, which was promoted by the National Health Institute (Istituto Superiore di Sanità, ISS).

The ECDC protocol version 6.1 adopted HAI definitions from both European (Hospitals in Europe Link for Infection Control through Surveillance, HELICS) and US (National Healthcare Safety Network, NHSN) frameworks. In Italy, the methodology and definitions outlined by the ECDC protocol version 6.0 were applied, with the exception of the newly introduced HAI category, healthcare-acquired COVID-19 (HA COVID-19). According to the ECDC PPS3 Protocol, a patient is considered a probable or confirmed case of HA COVID-19 if symptom onset or, in the case of asymptomatic patients, the date of the first positive swab, occurred on day 8 or later from the current hospitalization (with day of hospitalization considered day 1). For the Italian survey, patients identified as positive for HA COVID-19 according to the definitions provided by the ECDC, or admitted for COVID-19, were classified as COVID-19 patients [14,15].

Sample size

The ECDC established a sample size of 55 acute-care hospitals for Italy, based on the number of hospitals and patients needed to estimate an HAI prevalence of 6% (±1%), with design effect depending on the average acute care hospital size in the country [14]. To achieve this recommended sample size, each Italian Region was assigned a minimum number of hospitals to enrol, which was established in proportion to the respective population, number of acute-care hospital bed-days and of discharges from acute care facilities. This approach was chosen to reflect the regionalized structure of the Italian National health system [16]. The number of hospitals assigned to each Region ranged from a minimum of one up to nine hospitals. Regions tasked with enrolling more than one hospital were invited to include facilities of different size in terms of number of beds. Beyond the minimum assigned number of hospitals, Regions were free to participate to a greater extent [15].

Data collection

The methodology for data collection is described in detail in the ECDC PPS protocol [14]. During November 2022, trained local hospital staff conducted data collection on a single day per ward, with the entire process within each hospital concluding within three weeks. All wards within participant hospitals were included, with the exception of accident and emergency departments. All patients admitted to included wards before 08:00 on the survey day and still present at the time of the PPS were included.

Data were collected at the hospital, ward, and patient levels. Concerning the latter, demographic and clinical data, including risk factors such as invasive devices and severity of underlying medical conditions assessed through the McCabe score, were gathered for each patient. Additional details were collected for patients receiving antimicrobials on the survey day, including agent, administration route, dosage, indication, anatomical site of infection, and whether the reason for AMU was documented in the patient chart/notes. For active HAIs, additional information included date of onset, origin of infection, microbiological test results and susceptibility to selected AMR markers when available.

A national web-based data collection software was employed, which was developed and tested through a pilot study [17]. Only authorized users were granted access to the data collection instrument, in compliance with the EU General Data Protection Regulation (GDPR). The National coordinating centre received anonymized data between December 2022 and March 2023.

Statistical analysis

Descriptive statistics were used to summarize hospital and patient characteristics. Quantitative variables were summarized using median and interquartile ranges (IQRs) due to non-normal distribution (Shapiro—Wilk tests). HAI and AMU prevalence were calculated as the percentage of patients with at least one HAI or prescribed at least one antimicrobial over all included patients, respectively. Prevalence rate ratio (PRR) was used to compare HAI and AMU rates between the two groups, with 95% confidence intervals (CIs) obtained with Taylor series.

The analysis included two steps. First, crude data were compared, including all patients enrolled in the study. Second, analyses were repeated after performing 'fuzzy' case—control matching. Matched controls were obtained among non-COVID-19 patients for each COVID-19 patient according to age, sex, and severity of underlying conditions according to the McCabe score. Propensity score matching is obtained by running a logistic regression to construct the matching criterion. Odds ratios (ORs) for HAI and AMU were calculated comparing non-COVID-19 to COVID-19 patients within the matched sample, with 95% CI obtained with Taylor series. Analyses were conducted using IBM Version 28.0 (IBM Corp., Armonk, NY, USA) and the FUZZY extension command (available from: https://github.com/IBMPredictiveAnalytics/FUZZY).

Results

Overall, 325 hospitals from 19 out of 21 Regions of Italy participated in the PPS, totalling 60,403 patients (covering >34% of all beds, including non-acute beds, in acute care facilities in the country) [18]. Participation per Region in terms of number of acute care facilities is shown in Figure 1.

Of 325 participating hospitals, 173 (53.23%) had <200 beds, 102 (31.38%) between 200 and 500 beds and 50 (15.38%) were large facilities with >500 beds. The majority of enrolled hospitals were public (279, 85.85%), with 42 (12.92%) private facilities participating in the study. Concerning level of care provided, 83 (25.54%) hospitals provided primary care, 139 (42.77%) provided secondary care, 74 (22.77%) provided tertiary care, and 28 (8.62%) provided specialized care.

Descriptive characteristics of included patients are summarized in Table I. The proportion of patients classified as COVID-19 over all patients was 3.14% (*N* = 1897). Of these, 1025 (54%) were positive for HA COVID-19 according to ECDC definitions, and of these, 509 patients (49.66% of patients positive for HA COVID-19) were asymptomatic.

COVID-19 patients were significantly older, more frequently assigned an ultimately fatal or rapidly fatal McCabe score, had longer hospital stays prior to the PPS, and more frequently had ≥1 invasive devices, notably intubation and urinary catheter (Table I). After matching, COVID-19 patients remained slightly older, were assigned a non-fatal McCabe score less frequently, and were more frequently exposed to invasive devices such as central vascular and urinary catheters.

Among non-COVID-19 patients, 5117 HAIs were recorded from 4686 patients, with a ratio of 1.09 HAIs per patient with an HAI. The five most frequent HAI types were: lower respiratory tract infections (LRTIs; *N* = 1158, 22.63% of HAIs), bloodstream infections (BSIs; *N* = 1090, 21.30%), urinary tract infections (UTIs; *N* = 1054, 20.60%), surgical site infections (SSIs; *N* = 654, 12.78%), and gastrointestinal infections (*N* = 422, 8.25%).

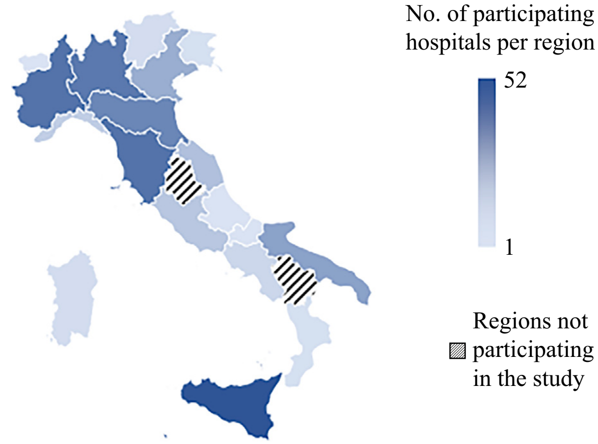

Figure 1. Number of hospitals per Region participating in the National point-prevalence survey of healthcare-associated infections and antimicrobial use in acute care hospitals, Italy, 2022.

Among COVID-19 patients, 192 HAIs were recorded from 181 patients, with a ratio of 1.06 HAIs per patient with an HAI. The five most frequent HAI types were LRTIs (*N* = 52, 27.08% of HAIs), UTIs (*N* = 50, 26.04%), BSIs (*N* = 35, 18.23%), systemic infections (*N* = 15, 7.81%), and gastrointestinal infections (*N* = 14, 7.29%).

HAI prevalence was significantly higher among COVID-19 patients prior to matching, and remained higher in the matched sample, but statistical significance was not maintained (Table II). The OR for HAI also did not maintain statistical significance comparing COVID-19 to non-COVID-19 patients in the propensity score matched sample (Table III).

Concerning AMU, overall 25,170 (41.67%) patients were undergoing at least one antibiotic treatment on the day of the PPS. In total, 32,808 antibiotic agents were prescribed, with a ratio of 1.3 and 1.31 agents per patient receiving antibiotics among non-COVID-19 and COVID-19 patients respectively. The five most frequently prescribed agents among non-COVID-19 patients were: ceftriaxone (*N* = 5108, 16.13%), piperacillin and β-lactam inhibitors (*N* = 5038, 15.92%), cefazolin (*N* = 2873, 9.07%), amoxicillin and β-lactam inhibitors (*N* = 1915, 6.05%), and meropenem (*N* = 1903, 6.01%). The five most frequently prescribed agents among COVID-19 patients were: ceftriaxone (*N* = 245, 21.23%), piperacillin and β-lactam inhibitors (*N* = 228, 19.76%), meropenem (*N* = 97, 8.41%), linezolid (*N* = 46, 3.99%), and vancomycin (*N* = 41, 3.55%).

AMU prevalence was significantly higher among COVID-19 patients prior to matching, and significantly lower after matching (Table IV). Prior to matching, treatment indications were more frequent among COVID-19 patients, notably for infections acquired in long-term care facilities (LTCF), whereas prophylaxis indications, notably surgical prophylaxis, were more frequent among non-COVID-19 patients. In the matched sample, COVID-19 patients were more frequently prescribed

Table I
Characteristics of included patients according to COVID-19 status

Characteristic	Unmatched ($N = 60,403$)			Matched ($N = 3770$)		
	Non-COVID-19 patients ($N = 58,506$)	COVID-19 patients ($N = 1897$)	PRR (95% CI)	Non-COVID-19 patients ($N = 2745$)	COVID-19 patients ($N = 1025$)	PRR (95% CI)
Age group (years)						
0–14	4512 (7.71%)	5 (0.26%)	0.03 (0.01–0.08)**	36 (1.31%)	2 (0.19%)	0.19 (0.05–0.74)*
15–64	19,399 (33.16%)	265 (13.97%)	0.34 (0.3–0.38)**	654 (23.83%)	171 (16.68%)	0.71 (0.62–0.83)**
>65	33,073 (56.53%)	1622 (85.50%)	4.37 (3.85–4.96)**	2055 (74.86%)	852 (83.12%)	1.46 (1.27–1.7)**
Unknown	1522 (2.60%)	5 (0.26%)	0.1 (0.04–0.24)**	0	0	–
Sex						
Female	28,435 (48.60%)	926 (48.81%)	1 (0.92–1.1)	1350 (49.18%)	504 (49.17%)	1 (0.9–1.11)
Male	29,947 (51.19%)	971 (51.19%)	1 (0.92–1.09)	1395 (50.82%)	521 (50.83%)	1 (0.9–1.11)
Unknown	124 (0.21%)	0	–	0	0	–
Days to PPS, median (IQR)	6 (2–12)	11 (6–20)**	–	6 (3–13)	16 (10–25)**	–
Days to HAI (HAI patients), median (IQR)	8 (2–19)	10 (5–18)**	–	6 (4–10)	5 (2–8)**	–
McCabe score						
Non-fatal	40,122 (68.58%)	1077 (56.77%)	0.61 (0.56–0.67)**	1645 (59.93%)	564 (55.02%)	0.86 (0.78–0.96)*
Ultimately fatal	10,783 (18.43%)	512 (26.99%)	1.61 (1.46–1.78)**	724 (26.38%)	297 (29.98%)	1.098 (0.98–1.23)
Rapidly fatal	3786 (6.47%)	193 (10.17%)	1.61 (1.39–1.86)**	293 (10.67%)	100 (9.76%)	0.93 (0.78–1.11)
Unknown	3815 (6.52%)	115 (6.06%)	0.93 (0.77–1.12)**	83 (3.02%)	64 (6.24%)	1.64 (1.36–1.99)**
Invasive devices						
Central vascular catheter	8926 (15.26%)	315 (16.61%)	1.1 (0.98–1.24)	448 (16.32%)	196 (19.12%)	1.15 (1.01–1.31)*
Urinary catheter	20,127 (34.40%)	896 (47.23%)	1.68 (1.54–1.83)**	1088 (39.64%)	479 (46.73%)	1.23 (1.11–1.37)**
Intubation	2132 (3.64%)	52 (2.74%)	0.75 (0.57–0.99)*	94 (3.42%)	39 (3.80%)	1.08 (0.83–1.42)
>1 device	5722 (9.78%)	237 (12.49%)	1.3 (1.14–1.49)**	320 (11.66%)	122 (11.90%)	1.02 (0.87–1.2)
Surgery since admission	18,516 (31.65%)	309 (16.29%)	0.43 (0.38–0.48)**	603 (21.97%)	266 (25.95%)	1.17 (1.04–1.32)*

CI, confidence interval; HAI, healthcare-associated infection; IQR, interquartile range; PPS, point-prevalence survey; PRR, prevalence rate ratio.
Matched controls were obtained among non-COVID-19 patients for each COVID-19 patient according to age, sex, and severity of underlying conditions according to the McCabe score.
*$P < 0.05$; **$P < 0.001$.

Table II
Prevalence and characteristics of healthcare-associated infections (HAIs) among included patients according to COVID-19 status

Characteristic	Unmatched ($N = 60,403$)			Matched ($N = 3770$)		
	Non-COVID-19 patients ($N = 58,506$)	COVID-19 patients ($N = 1897$)	PRR (95% CI)	Non-COVID-19 patients ($N = 2745$)	COVID-19 patients ($N = 1025$)	PRR (95% CI)
No. of patients with at least one HAI	4686	181	–	238	109	–
HAI prevalence, % (95% CI)	8.01 (7.79–8.23)	9.54 (8.26–10.95)	1.19 (1.04–1.38)*	8.67 (7.67–9.78)	10.63 (8.89–12.68)	1.22 (0.99–1.52)
HAI origin (% of HAIs)						
Same hospital	3752 (80.07%)	150 (82.87%)	1.04 (0.97–1.11)	210 (82.87%)	96 (88.07%)	1.42 (0.86–2.37)
Other hospital	397 (8.47%)	16 (8.84%)	1.05 (0.65–1.69)	23 (9.69%)	8 (7.34%)	0.85 (0.46–1.58)
LTCF	206 (4.40%)	8 (4.42%)	1 (0.5–2)	18 (7.56%)	2 (1.83%)	0.32 (0.09–1.21)*
Other/unknown	331 (7.06%)	7 (3.87%)	0.55 (0.26–1.14)	5 (2.10%)	3 (2.75%)	1.26 (0.51–3.13)

CI, confidence interval; LTCF, long-term care facility; PRR, prevalence rate ratio.
Matched controls were obtained among non-COVID-19 patients for each COVID-19 patient according to age, sex, and severity of underlying conditions according to the McCabe score.
*$P < 0.05$.

antibiotics for HAI treatment and for medical prophylaxis. Both prior to and following matching, COVID-19 patients had a significantly higher proportion of antibiotics with an unknown indication. The OR for AMU was significantly lower ($P < 0.001$) comparing COVID-19 with non-COVID-19 patients in the propensity score matched sample (Table III).

Table III
Prevalence of healthcare-associated infections (HAIs) and antimicrobial use (AMU) among included patients according to COVID-19 status

Characteristic	Unmatched ($N = 60,403$)			Matched ($N = 3770$)		
	Non-COVID-19 patients ($N = 58,506$)	COVID-19 Patients ($N = 1897$)	OR (95% CI)	Non-COVID-19 patients ($N = 2745$)	COVID-19 patients ($N = 1025$)	OR (95% CI)
HAI prevalence, % (95% CI)	8.01 (7.79–8.23)	9.54 (8.26–10.95)	1.21 (1.04–1.42)*	8.67 (7.67–9.78)	10.63 (8.89–12.68)	1.25 (0.99–1.59)
AMU prevalence, % (95% CI)	41.52 (41.12–41.92)	46.39 (44.13–48.66)	1.22 (1.11–1.34)**	47.72 (45.86–49.59)	41.17 (38.2–44.21)	0.77 (0.66–0.89)**

CI, confidence interval; OR, odds ratio.
Matched controls were obtained among non-COVID-19 patients for each COVID-19 patient according to age, sex, and severity of underlying conditions according to the McCabe score.
*$P < 0.05$; **$P < 0.001$.

Discussion

This study reports national-level data, which can be considered representative of Italian acute care hospitals due to surveillance requirements and to the high level of participation. Through this study, we assessed the impact of COVID-19 on HAI transmission in Italian hospitals in the later stages of the pandemic, and compared HAI and AMU prevalence among COVID-19 and non-COVID-19 patients.

Comparing results of this study concerning non-COVID-19 patients with those of the previous edition of the PPS, which was conducted in 2016, demographic and clinical characteristics were similar in terms of age, sex, McCabe score, and length of stay prior to the PPS [2]. HAI prevalence remained stable around 8% in both editions, even though a higher proportion of BSIs was found in 2022 (21.3% of HAIs vs 18.3% in 2016). AMU prevalence decreased from 44.5% in 2016 to 41.5% in 2022.

Health services in Italy were severely affected by the pandemic during its early stages [19]; however, our study was conducted in a period of relatively low SARS-CoV-2 circulation, during which hospitals were not experiencing extraordinary circumstances in terms of critical patient caseloads, altered workflows, or operational challenges; further, the majority of the population was previously immunized against SARS-CoV-2 either through previous infection or vaccination, and guidelines regarding the clinical management of COVID-19 patients were available [20,21]. Previous studies found an increase in HAI rates during pandemic waves, notably concerning BSIs, and due to specific AMR bacteria, such as meticillin-resistant *Staphylococcus aureus*, *Acinetobacter baumannii*, and *Candida auris* [8–10,22,23]. Higher patient severity, longer length of device use, as well as COVID-19-related IPC activities and their impact on insertion and maintenance practices of central lines could have contributed to the increases in BSI rates [9]. Fortunately, in line with our results, more recent reports have found that these trends did not last beyond pandemic waves [24]. The stable HAI prevalence among non-COVID-19 patients found in this study could also suggest that IPC practices were maintained or at least resumed to pre-pandemic levels in 2022, as also found by another large study conducted in the USA [11]. Further, our results in terms of AMU prevalence could indicate a positive impact of regulatory initiatives such as the Italian National action plan to contrast AMR and local stewardship efforts [25].

In our study, COVID-19 patients had a significantly higher crude HAI risk of 20% compared to non-COVID-19 patients, in line with results from the literature, and adding to the complexity of their care [11,26]. In fact, Sands *et al.* found that the increase in HAIs recorded though their retrospective analysis of US inpatients could be entirely due to HAIs occurring among COVID-19 patients [11]. After matching for severity of underlying clinical conditions, age, and sex, the odds for HAI did not remain significantly higher among COVID-19 patients in our study; different distributions in these characteristics among COVID-19 and non-COVID-19 patients could therefore explain the higher susceptibility among COVID-19 patients. COVID-19 patients were also more significantly exposed to care practices associated with higher HAI risk: COVID-19 patients in our study had longer hospital stays, and were more frequently exposed to multiple invasive devices compared to non-COVID-19 patients. Sands *et al.* also suggested that patient management could have been affected by altered workflows and resource limitations, especially concerning personnel caring for COVID-19 patients, with implications on HAI risk [11]. However, as also observed by Sands *et al.* and Schwaber *et al.*, patient care management improved over the course of the pandemic, which could explain why in our study, conducted in late 2022, we did not see a residual impact attributable to this element [11,26].

Concerning AMU prevalence, crude AMU prevalence was significantly higher among COVID-19 patients prior to matching; however, after propensity score matching AMU prevalence was significantly lower, with an OR of 0.77. These results suggest that the significant difference seen in the crude comparison could be due to measured confounders, but the crude results are nonetheless striking. Since the early stages of the pandemic, antibiotics have frequently been empirically prescribed to COVID-19 patients due to diagnostic uncertainty, to treat bacterial co-infections, or to prevent super-infections [27]. In our study, COVID-19 patients were more frequently prescribed antibiotics for treatment indications compared to non-COVID-19 patients; HAI treatment was almost 60% more prevalent among COVID-19 patients, almost three times the difference in HAI prevalence. In line with our results, previous reports have found high AMU rates (50–75%) but generally low to moderate rates of bacterial co- and super-infections (5% and 18% respectively) among COVID-19 patients [27,28]. Additionally, results of this study indicate that COVID-19 patients were often exposed to broad-spectrum agents, with four out of five

Table IV
Prevalence and characteristics of antimicrobial use (AMU) among included patients according to COVID-19 status

Characteristic	Unmatched ($N = 60,403$)			Matched ($N = 3770$)		
	Non-COVID-19 patients ($N = 58,506$)	COVID-19 patients ($N = 1897$)	PRR (95% CI)	Non-COVID-19 patients ($N = 2745$)	COVID-19 patients ($N = 1025$)	PRR (95% CI)
No. of patients undergoing AMU	24,290	880	–	1310	422	–
AMU prevalence (95% CI)	41.52% (41.12–41.92)	46.39% (44.13–48.66)	1.21% (1.11–1.32)**	47.72% (45.86–49.59)	41.17% (38.2–44.21)	0.86% (0.79–0.94)**
No. of antibiotic prescriptions	31,654	1154	–	1661	564	–
Reason for AMU documented in patient chart/notes (% of antibiotic prescriptions)	25,070 (79.20%)	908 (78.68%)	0.97 (0.85–1.11)	1435 (86.39%)	434 (76.95%)	0.64 (0.54–0.75)**
Indication for AMU (% over all indications)						
Treatment						
Intended for community infection	12,609 (39.83%)	547 (47.40%)	1.35 (1.2–1.51)**	923 (55.57%)	170 (30.14)	0.45 (0.38–0.52)**
Intended for HAI	5565 (17.58%)	295 (25.56%)	1.57 (1.38–1.79)**	294 (17.70%)	205 (36.35%)	1.98 (1.72–2.27)**
Intended for infection acquired in LTCF	546 (1.72%)	42 (3.64%)	2.07 (1.54–2.79)**	67 (4.03%)	17 (3.01%)	0.79 (0.52–1.22)
Prophylaxis						
Medical	4437 (14.02%)	110 (9.53%)	0.65 (0.54–0.8)**	127 (7.65%)	75 (13.30%)	1.54 (1.26–1.97)**
Surgical	5498 (17.37%)	31 (2.69%)	0.14 (0.1–0.19)**	162 (9.75%)	22 (3.90%)	0.40 (0.3–0.67)**
Other	1662 (5.25%)	53 (4.59%)	0.87 (0.67–1.15)	26 (1.57%)	36 (6.38%)	2.38 (1.9–2.98)**
Unknown	1337 (4.22%)	76 (6.59%)	1.57 (1.25–1.96)**	62 (3.73%)	39 (6.91%)	1.56 (1.21–2.02)*

CI, confidence interval; HAI, healthcare-associated infection; LTCF, long-term care facility; PRR, prevalence rate ratio.
Matched controls were obtained among non-COVID-19 patients for each COVID-19 patient according to age, sex, and severity of underlying conditions according to the McCabe score.
*$P < 0.05$; **$P < 0.001$.

most frequently prescribed agents classified as Watch and one out of five as Reserve (WHO AWaRe categorization) [29]. A recent systematic review found a high prevalence of AMR organisms among secondary infections in COVID-19 patients, highlighting the risk of increasing selective pressure and the need for additional stewardship efforts among these patients, particularly relevant to our highly endemic setting [2,28].

During the initial stages of the COVID-19 pandemic, hospital outbreaks caused a serious threat to patient safety due to the close proximity of vulnerable individuals, exposed to high intensity of care, and may have played an important role in overall SARS-CoV-2 circulation, by amplifying transmission [30,31]. A German study found that over the course of the pandemic, the number and size of nosocomial outbreaks progressively decreased, which could be due to several factors including heightened surveillance, improvements in patient management and IPC practices, and higher immunity rates due to natural infection or vaccination. In fact, Suwono *et al.* found that at the beginning of 2022, the increased infectious pressure in the community due to the Omicron variant did not translate into surges of nosocomial outbreaks [31].

The HA COVID-19 category was introduced in the ECDC PPS protocol in 2021 and defined by the ECDC based on days from admission, with both symptomatic and asymptomatic COVID-19 cases occurring seven days after admission falling within this category [14]. Genomic surveillance data indicate the Omicron subvariant BA.5 was predominant in the country at the beginning of November 2022 (91.55%), with BF.7 accounting for 14.7% of analysed sequences [32]. Shortening serial intervals have been associated with emerging variants; however, incubation times have been found to differ according to patient characteristics such as age and comorbidities, with mean incubation times of 7.43 days (95% CI: 5.75–9.11) among patients aged >60 years and 6.69 days (95% CI: 4.53–8.85) among patients with severe illness [33,34].

Given the challenge in distinguishing HA COVID-19 cases from community-acquired cases due to the incubation period distribution and the difficulty in determining the precise moment of infection, and in order to allow comparisons with previous and future PPSs, the Italian national coordination centre did not include HA COVID-19 in this analysis [30]. Further, the objectives of the ECDC PPS include raising awareness and increasing surveillance skills [14]; our experience as National coordinating team has led us to believe that the PPS provides an important platform for educational initiatives regarding HAIs and IPC. Therefore, it is important that messaging remains consistent: introducing an HAI category that includes asymptomatic infections could lead to confusion in other categories, such as UTIs and asymptomatic bacteriuria.

Among the strengths of this study is the reporting of national-level, hospital-wide data from one-third of national hospital beds. Due to the multi-level governance of the Italian National health system, with implications on the provision of care, particular attention was dedicated to representing all Italian Regions in the study sample. The involvement of the Italian Ministry of Health and National Health Institute enabled the high degree of participation seen in this study. However, this study had several limitations that should be considered. First, as the study design only allowed a direct estimate of COVID-19 status and HAI and AMU prevalence on the day of the survey, therefore we make no claim of causality. Also due to study design, length bias could have affected our estimates. Further, we cannot exclude a certain degree of misclassification of COVID-19 patients. At the end of November 2002, >24,000,000 COVID-19 cases had been reported in Italy since the beginning of the pandemic; the weekly incidence was 371.9 cases per 100,000, with >2% of cases requiring hospital admission [20]. Based on incidence data from the Integrated national surveillance system for COVID-19, and assuming a duration of disease of 5–10 days, the expected number of patients with COVID-19 requiring hospitalization in enrolled hospitals would be between 1092 and 1504 [20,35]. Based on our defined criteria, we identified 1897 COVID-19 patients, 509 of whom were asymptomatic, which supports the accuracy of our method of classification. Finally, in our study patients were only matched based on age, sex, and McCabe score, but not based on other known risk factors for HAI (such as length of stay and invasive device use) or antibiotic use (such as ward specialty, hospital type and size) [36]. We also did not investigate differences in terms of AMR rates between the two populations, which could have impacted results and which warrants further study.

In conclusion, this study suggests that COVID-19 patients could be at higher HAI risk due to underlying clinical conditions and to the intensity of healthcare needs, and no longer to altered workflows and resource limitations affecting patient care management. Our results concerning IPC practices are encouraging; however, further efforts should be dedicated to antimicrobial stewardship among COVID-19 patients. From a methodological perspective, the HA COVID-19 category was relevant during the initial stages of the pandemic, due to the serious threat to patient safety and to the number and size of nosocomial outbreaks, but may not remain so in future editions of the ECDC PPS.

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Conflicts of interest statement
None declared.

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Data sharing statement
All data collected within the CCM project 'Sostegno alla Sorveglianza delle infezioni correlate all'assistenza anche a supporto del PNCAR', including those reported in this study, are owned by the Italian Ministry of Health. Datasets will be made available by the corresponding author upon reasonable request.

Ethics statement
The institutional framework of the national PPS was an infectious disease surveillance and quality improvement programme promoted by the Italian National Health Institute (ISS), the Italian Centre for Disease Control (CCM), and Ministry of Health; therefore, written consent of patients was waived. However, patients were provided with an information sheet notifying them of their participation in the PPS and explaining the study and its objectives. The study received the Institutional review board approval of the Bioethics Committee of the University of Turin (protocol number 0421518, 29/07/2022).

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