



Quality indicators for appropriate inpatient antibiotic use: results from two national surveys in Italy, 2016–2022

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SUMMARY

Background: To address its high antimicrobial resistance (AMR) and antibiotic consumption rates, Italy introduced a national action plan to contrast AMR (PNCAR) in 2017. **Aim:** To investigate trends in antibiotic use, prescribing practices, and AMR rates in Italy through indicators of appropriate antibiotic use.

Methods: Two point prevalence surveys (PPSs), according to The European Centre for Disease Prevention and Control (ECDC) methods and definitions, were conducted in 2016 and 2022. Indicators of appropriate antibiotic use were defined and measured. Antibiotic use prevalence and AMR rates for specific pathogen–drug combinations were calculated. To account for potential confounding factors, a propensity score matching approach was applied to compare the results of the two PPS editions using prevalence rate ratio (PRR).

Results: Overall, 28,991 patients from 140 hospitals and 60,403 patients from 325 hospitals were included in 2016 and 2022, respectively. Patient characteristics remained stable, but patients were increasingly exposed to invasive procedures. The overall prevalence of antibiotic use decreased from 43.51 to 41.52 (PRR 0.95, 95% confidence interval, CI 0.94–0.97, $P<0.001$). Improvements in some prescribing practices were identified: the proportion of surgical prophylaxis lasting >1 day decreased from 55.99% to 52.15%, (PRR 0.94, 95% CI 0.90–0.98, $P<0.001$) and the proportion of culture-guided hospital infection treatments increased from 33.68% to 48.57% (PRR 1.30, 95% CI 1.22–1.38, $P<0.05$). Conversely, a significant rise in the proportion of last line/broad-spectrum agents was recorded for most indications.

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Conclusion: This study provided a mapping of prescribing activity at national level, and defined measurable quality indicators, through which strengths and areas for improvement in prescribing practices were identified.

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Introduction

The World Health Organization (WHO) has recognized the spread of antimicrobial resistance (AMR) as one of the world's top 10 public health concerns [1]. In fact, in 2019, worldwide deaths related to AMR were estimated at about 4.95 million, and those actually attributed to the occurrence of resistant bacterial strains were estimated to be approximately 1.27 million [2].

A recent study revealed how infections with selected AMR bacteria that occurred during 2015 across the European Union/European Economic Area accounted for 170 disability-adjusted life years per 100,000 population, with 75% of the total burden of infections due to AMR bacteria being healthcare associated [3].

Antibiotic over- and misuse have been identified among the main promoters of AMR, and as such are recognized as a crucial element to target to reduce AMR rates [1–3]. Programmes to improve antimicrobial prescribing (i.e., to promote the use of the right drug, dose, duration, and route of administration when antibiotics are needed) have led to improved clinical outcomes and reduced adverse effects (i.e., toxicity, pathogen selection, and occurrence of resistance) [4].

Italy is one of the European countries with the highest rates of AMR and overall antibiotic consumption: in 2022, the total antibiotic consumption in both outpatient and inpatient settings was 21.2 daily defined doses/1000 population days, representing an increase from the previous year [4,5]. The observed increase in antibiotic use aligns with global trends reported during the COVID-19 pandemic, where a rise in antimicrobial consumption and resistance has been documented [6,7]. To address these critical issues, Italy introduced a national action plan to contrast AMR (PNCAR) in 2017, which was updated in its current version in 2022 (PNCAR 2022–2025) [8,9]. The national strategy is built on three vertical pillars with a one health approach, including: integrated surveillance and monitoring of AMR, antibiotic use, healthcare-associated infections (HAIs), and the environment; prevention of HAIs in hospital and infectious diseases and zoonoses in community settings; appropriate use of antibiotics for both human and veterinary health. Aiming to reduce the incidence and impact for infections caused by AMR pathogens, the PNCAR 2022–2025 set six comprehensive targets: (1) to enhance HAI prevention and surveillance in hospital and community settings; (2) to reinforce the One Health approach, including the development of coordinated national surveillance of AMR and antibiotic use, and prevent the spread of AMR in the environment; (3) to promote the appropriate use of antibiotics and reduce the rate of infections due to resistant micro-organisms in human and animal health; (4) to foster innovation and research in prevention, diagnosis and treatment of AMR infections; (5) to strengthen national cooperation and Italy's participation in international initiatives to combat AMR; (6) to improve public

awareness and promote health and environmental professionals' training on tackling AMR.

The European Centre for Disease Prevention and Control (ECDC) has promoted five-yearly point prevalence surveys (PPSs) of HAIs and antibiotic use across Europe since 2011. The most recent PPSs in which Italy participated were, respectively, held in October–November 2016 (PPS2) and November 2022 (PPS3).

The aim of this study was to investigate and describe trends in antibiotic use prevalence, antibiotic prescribing practices, and AMR rates in Italy. Monitoring antibiotic consumption provides important information, but it does not allow for an assessment of the quality of prescribing practices [10–13]. In this study, we identified and evaluated trends in indicators of appropriate antibiotic use, providing an outline of prescribing activity at national level. To ensure comparability between the two different editions, we excluded COVID-19 patients from the PPS3 sample. This decision was made to avoid confounding factors, as including COVID-19 patients could have distorted cross-edition comparisons and compromised the validity of our results.

Methods

Study design

A PPS was conducted among Italian acute-care hospitals during October–November 2016 (PPS2) and November 2022 (PPS3).

Sampling and participants

According to the ECDC PPS protocols for both PPS editions [14,15], a sample size for Italy of 55 acute-care hospitals was established, based on expected HAI prevalence and average acute-care hospital size. Hospitals participated in PPS2 on a voluntary basis. For PPS3, the national sample was distributed among Italian regions, in order to reflect the regionalized structure of the Italian National health system. Each region was assigned a minimum number of hospitals and patients to enrol, based on overall population, number of acute-care hospital bed-days, and discharges from acute care facilities; beyond this minimum number of hospitals and patients, Regions could enrol a greater number of hospitals to reflect their surveillance needs. For the current analysis, both community-acquired and hospital-acquired COVID-19 patients enrolled in PPS3 (3.14% of total patients) were excluded [16].

Protocol and definitions

Standardized protocols were developed by the ECDC and used across European nations: namely, the ECDC PPS2 Protocol Version 5.3 and the ECDC PPS3 Protocol Version 6.1 [17,18]. The

protocols include HAI definitions from European (Hospitals in Europe Link for Infection Control through Surveillance, HELICS) and US (National Healthcare Safety Network, NHSN) frameworks.

Adapted versions of these protocols were employed for the Italian PPSs [14,15]. In particular, the HAI category healthcare-acquired COVID-19 (HA COVID-19) was not considered in the Italian PPS3, as explained in detail elsewhere [16].

Data collection

The University of Turin's Department of Public Health and Paediatrics was the national coordinating centre for both editions of the study in Italy, which were promoted by the Italian national health institute (Istituto Superiore di Sanità, ISS) within projects financed by the Italian CDC (Centro nazionale per la prevenzione e il controllo delle malattie, CCM), Ministry of Health.

The methodology for data collection has been described in detail [16–19]. Briefly, data were collected by trained local hospital staff on a single day per ward. Except for emergency departments, the survey was carried out in all wards of participant hospitals, and included all patients admitted to the ward before 08:00 on the day the survey took place and not discharged at the time of the PPS.

The survey involved hospital, ward and patient-level data collection. Patient-level data included demographic characteristics, presence of invasive devices, surgery since admission, and severity of underlying medical conditions assessed through the McCabe score (i.e., rapidly fatal, ultimately fatal and non-fatal disease) according to the ECDC protocol [14]. Concerning invasive devices, our analysis excluded peripheral venous catheters as data regarding their use was collected in PPS2 but not in PPS3 [17,18]. For patients receiving antimicrobials on the day of the survey (or in the previous 24 h for surgical prophylaxis, SP), further information was collected: antimicrobial agent, administration route, indication (i.e., treatment, SP, or medical prophylaxis, MP), site of infection, reason for prescription documented in the patient chart/notes, and any changes since start of prescription. In accordance with the ECDC protocol, escalation occurred when antibiotic therapy was intensified, either by adding another antibiotic or switching to a broader-spectrum drug, including a change from oral to parenteral administration. De-escalation was recorded when therapy was adjusted to a narrower-spectrum or first-line antibiotic due to microbiological susceptibility or clinical improvement if an antibiotic was discontinued, de-escalation was applied to the remaining ones. The IV-to-oral switch was defined as a change in administration route from parenteral to oral for the same antibiotic or within the same class. Each antibiotic was recorded individually, thus if only one of multiple antibiotics was switched from IV to oral, the change was registered only for that specific drug and not for the others. Additionally, therapy modifications due to observed or expected side effects were classified as adverse effects [14]. Finally, in line with the updated ECDC protocol for PPS3, some variables related to antibiotic use, such as the start date of therapy, start date of the first antibiotic, and daily dosage (posology, duration, and unit of measurement) were removed. However, all other variables remained unchanged, ensuring consistency in the parameters collected between the two surveys [14]. For active HAIs, microbiological test results were collected if

available on the day of the PPS, including susceptibility to selected AMR markers. The PPS3 protocol updated antimicrobial susceptibility definitions to the 2019 European Committee on Antimicrobial Susceptibility Testing (EUCAST) terminology, in particular the terms 'susceptible' and 'intermediate' were revised and substituted with 'susceptible, standard dosing regimen' and 'susceptible, increased exposure' [18]. For the current analysis, the proportions of resistant isolates were compared, as this definition remained unchanged.

Data were collected using a REDCap-based online platform, which was previously described [20]. Within the platform, the ECDC PPS data collection instruments were adapted into data collection forms by the national coordinating team in collaboration with software engineers. In compliance with the EU General Data Protection Regulation (GDPR), only authorized users could access the platform and insert/extract data. The national coordinating centre trained personnel involved in data collection regarding study design, protocol, and definitions, as well as on the use of the online platform.

Ethics

Because the survey's aims were the surveillance of diseases and the improvement of healthcare quality and as the program was coordinated by public entities (namely ISS, CCM, and Italian Ministry of Health), the written consent of patients was waived. Patients were provided with an information sheet to notify them of their participation in the PPS. Only anonymized data were collected and sent to the national coordinating centre, between December 2016 and June 2017 (PPS2) and between December 2022 and March 2023 (PPS3). For PPS2, within each region, approval from at least one local health unit's ethics committee was obtained. PPS3 received the Institutional Review board approval of the Bioethics Committee of the University of Turin (protocol number 0421518, 29/07/2022).

Indicators of appropriate inpatient antibiotic use

To assess prescribing practices, we considered the following indicators: most frequently prescribed antibiotic categories; proportion of broad-spectrum and/or last-line agents (BS/LLAs), as defined by the 2017 ECDC, European Food Safety Authority and European Medicines Agency Joint Scientific Opinion [21]; proportion of SP longer than one day over all SP indications; proportion of treatments for hospital infections with an available microbiology result over all hospital infection treatment indications (considered as proxy for targeted therapy) [13,22]; proportion of antimicrobials with a recorded change over all agents (for reasons including escalation, de-escalation, IV–oral switch, adverse events).

Statistical analysis

Descriptive statistics were used to summarize hospital-level and patient-level data. Antibiotic use prevalence was defined as the percentage of patients receiving at least one antimicrobial agent on the day of the survey. AMR rates for specific pathogen–drug combinations were calculated as the proportion of resistant isolates over available results at time of PPS. Results of the two PPS editions were compared using

prevalence rate ratio (PRR), with 95% confidence intervals (CIs) obtained with Taylor series approximations.

Analyses were run on the overall samples and repeated after performing ‘fuzzy’ propensity-score matching, to account for changes in case-mix between the two editions of the PPS. Matched controls were obtained based on age (exact), sex, and McCabe score, in a 1:1 ratio among PPS2 and PPS3 patients. Analyses were run using IBM SPSS Version 28.0 (IBM Corp., Armonk, NY, USA) and the FUZZY extension command (available from: <https://github.com/IBMPredictiveAnalytics/FUZZY>).

Results

Overall, 28,991 patients from 140 hospitals were included in PPS2. The third edition of the PPS saw the participation of 325 hospitals, totalling 60,403 patients. PPS2 and PPS3 included, respectively, over 16% and 34% of all beds, including non-acute beds, in Italian acute-care hospitals [23]. For the current analyses, 1897 COVID-19 patients from PPS3 were excluded. Figure 1 shows participation among Italian Regions in both editions.

Hospital-level characteristics are summarized in Table I and, as shown, PPS3 saw the participation of a higher proportion of small hospitals, private facilities, and facilities providing primary or secondary levels of care.

Table II summarizes patient-level demographic characteristics and risk factors for HAI, before and after propensity-score matching. It was possible to obtain PPS3 matches for 28,905 out of 28,991 patients in the PPS2 sample.

Considering the unmatched sample, patients participating in PPS3 were more frequently exposed to all considered invasive devices, in particular multiple devices (all $P < 0.001$). These differences remained significant in the matched sample, and a significant difference emerged regarding the proportion

Table I

Characteristics of Italian hospitals participating in the second and third editions of the point prevalence survey of healthcare-associated infections and antimicrobial use in European acute-care facilities (PPS2 and PPS3)

Characteristic	PPS2 (N = 140)	PPS3 (N=325)
Hospital size, n (%)		
<200 beds	63 (45)	173 (53.23)
200–500 beds	55 (39.28)	102 (31.38)
≥500 beds	22 (15.72)	50 (15.38)
Administrative type, n (%)		
Public	130 (92.85)	279 (85.85)
Private	7 (5)	42 (12.92)
Other/unknown	3 (2.15)	4 (1.23)
Level of care		
Primary	31 (22.14)	83 (25.54)
Secondary	45 (32.14)	139 (42.77)
Tertiary	49 (35)	74 (22.77)
Specialized	15 (10.72)	28 (8.62)

of patients receiving surgery since admission, which was higher in the PPS3 sample.

Prior to matching, in the PPS2 sample, 12,614 received at least an antimicrobial on the day of the survey (in total 17,030 prescriptions were recorded), resulting in a prevalence of antibiotic use of 43.51% (95% CI 42.76–44.27). In the PPS3 sample, 24,290 received at least an antimicrobial on the day of the survey (in total 31,654 prescriptions were recorded), resulting in a prevalence of antibiotic use of 41.52% (95% CI 41.12–41.92). A significant decrease in prevalence of antimicrobial use was recorded between the two editions: PRR 0.95 (95% CI 0.94–0.97, $P < 0.001$). The ratios of antimicrobial prescriptions over all patients and of antimicrobial prescriptions over patients receiving an antimicrobial both decreased

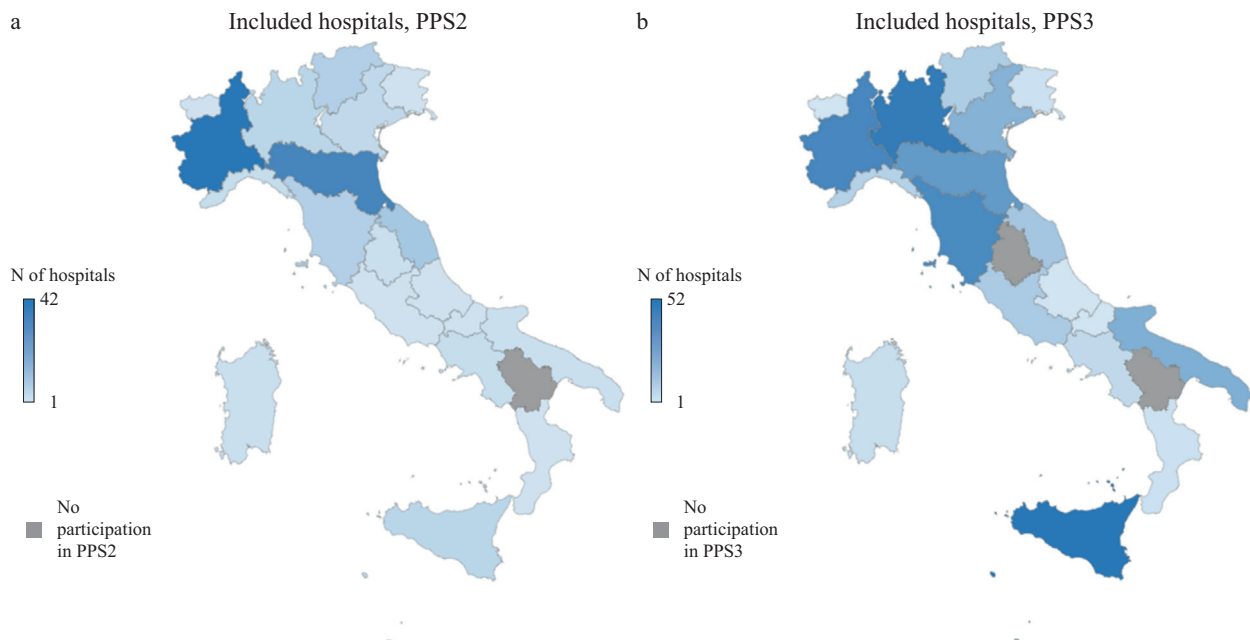


Figure 1. Participation among Italian Regions in the second and third editions of the point prevalence survey of healthcare-associated infections and antimicrobial use in European acute-care facilities (PPS2 and PPS3).

Table II
 Characteristics of patients and prevalence rate ratios (PRRs) with 95% confidence intervals (CIs) participating in the second and third editions of the point prevalence survey of healthcare-associated infections and antimicrobial use in European acute-care facilities (PPS2 and PPS3) in Italy

Characteristic	Unmatched sample			Matched sample		
	PPS2 (N = 28,991)	PPS3 (N = 58,506) ^a	Prevalence rate ratio (95% CI)	PPS2 (N = 28,905)	PPS3 (N = 28,905) ^a	Prevalence rate ratio (95% CI)
Age group, n (%)						
0–14 years	2193 (7.56)	4512 (7.71)	1.02 (0.97–1.07)	2193 (7.59)	2444 (8.46)	1.11 (1.06–1.18) ^c
15–64 years	9903 (34.16)	19399 (33.16)	0.97 (0.95–0.99) ^c	9902 (34.26)	9648 (33.38)	0.97 (0.95–1) ^b
>65 years	16811 (57.99)	33073 (56.53)	0.97 (0.96–0.99) ^b	16810 (58.15)	16813 (58.16)	1 (0.99–1.01)
Unknown	84 (0.29)	1522 (2.60)	8.98 (2.17–11.18) ^b	–	–	–
Sex, n (%)						
Female	14495 (50)	28435 (48.60)	0.97 (0.96–0.99) ^b	14463 (50.04)	13877 (48.01)	0.96 (0.94–0.98) ^c
Male	14450 (49.84)	29947 (51.19)	1.03 (1.01–1.04) ^b	14398 (49.81)	15018 (51.96)	1.04 (1.03–1.06) ^c
Unknown	46 (0.16)	124 (0.21)	1.34 (0.95–1.88)	44 (0.15)	10 (0.03)	0.23 (0.11–0.45) ^c
Days from hospital admission to PPS, median (IQR)	6 (2–13)	6 (2–12)	NS	6 (2–13)	6 (2–12)	NS
McCabe score, n (%)						
Non-fatal	20063 (69.20)	40122 (68.58)	0.99 (0.98–1)	19987 (69.15)	20220 (69.95)	1.01 (1.00–1.02) ^b
Ultimately fatal	5380 (18.56)	10783 (18.43)	0.99 (0.96–1.02)	5373 (18.59)	5361 (18.55)	1 (0.96–1.03)
Rapidly fatal	2026 (6.99)	3786 (6.47)	0.92 (0.88–0.98) ^c	2025 (7)	1768 (6.12)	0.87 (0.82–0.93) ^c
Unknown	1522 (5.25)	3815 (6.52)	1.24 (1.17–1.32) ^b	1520 (5.26)	1556 (5.38)	1.02 (0.96–1.1)
Invasive device use, n (%)						
Central vascular catheter	3902 (13.46)	8926 (15.26)	1.13 (1.10–1.17) ^b	3889 (13.45)	4921 (17.02)	1.27 (1.22–1.32) ^b
Urinary catheter	8322 (28.71)	20127 (34.40)	1.20 (1.17–1.22) ^b	8315 (28.77)	9895 (34.23)	1.19 (1.16–1.22) ^b
Intubation	903 (3.11)	2132 (3.64)	1.17 (1.08–1.26) ^b	902 (3.12)	1180 (4.08)	1.31 (1.20–1.42) ^b
>1 device	2305 (7.95)	5722 (9.78)	1.23 (1.17–1.29) ^b	2301 (7.96)	3135 (10.85)	1.36 (1.29–1.43) ^b
Surgery since admission, n (%)	9033 (31.16)	18516 (31.65)	1.02 (1–1.04)	9025 (31.2)	9742 (33.70)	1.08 (1.05–1.11) ^b

IQR, interquartile range; NS, not significant. Matched controls were obtained among non-COVID-19 PPS3 patients for each patient included in PPS2 using propensity score matching according to age, sex, and severity of underlying conditions according to the McCabe score, with tolerance set at 0 for age and 0.2 for age and McCabe score.
^a Excluding COVID-19 patients.
^b *P* < 0.05.
^c *P* < 0.001.

between the two surveys: from 0.59 in PPS2 to 0.52 PPS3, and from 1.35 in PPS2 to 1.3 in PPS3, respectively.

Following propensity-score matching, 12,589 patients of the PPS2 matched sample received a total of 16,992 agents, resulting in a prevalence of antimicrobial use of 43.6% (95% CI 43.0–44.1). In total, 12,935 patients of the PPS3 matched sample received 17,116 agents, resulting in a prevalence of antimicrobial use of 44.8% (95% CI 44.2–45.3). Conversely to the crude sample, matching revealed a slight but significant increase in prevalence of antimicrobial use between the two editions: PRR 1.03 (95% CI 1.01–1.05, *P* = 0.004). Characteristics pertaining to antimicrobial use prior to and following propensity-score matching are reported in [Table III](#).

Considering the unmatched sample, PPS3 saw a significant increase in ceftriaxone, piperacillin and beta-lactam inhibitors (BLIs), cefazolin, and meropenem prescriptions compared with PPS2. Ceftriaxone surpassed piperacillin and BLIs as the most frequently prescribed agent in PPS3. Conversely, a significant reduction in prescriptions of amoxicillin and BLIs was recorded between PPS2 and PPS3. The same trends were identified in the matched sample.

Concerning indications for antibiotic use, a significant increase in treatment and other indications was found in the crude PPS3 sample, whereas overall prophylaxis indications

decreased compared with PPS2. Matching revealed a significant increase in indications intended for hospital infections.

Both in the unmatched and matched samples, a significant rise in the proportion of last line or broad-spectrum agents (LL/BSAs) was recorded. Considering the proportion of LL/BSAs per indication, only SP saw a decrease between PPS2 and PPS3 (significant following matching). Improvements in prescribing quality for SP were also found considering the proportion of SP lasting >1 day over SP indications: a significant reduction was found both prior to and following matching. The proportion of treatments for hospital infection with an available microbiology result over all hospital infection treatment indications significantly increased by over 10 percentage points in PPS3 compared with PPS2, both prior to and following matching. Conversely, the proportion of antimicrobials with changes recorded for escalation, de-escalation, and IV–oral switch generally decreased between PPS2 and PPS3, whereas the proportion of agents that were unchanged since the initial prescription significantly increased in the crude sample.

Among patients included in PPS2, 2302 HAIs were recorded with an HAI prevalence of 7.36 (95% CI 7.06–7.66). Of the total HAIs, 2087 had undergone microbiology testing and for 1547 a result was available at the time of the survey. Overall, 5119 HAIs were recorded in PPS3 with an HAI prevalence of 8.01 (95%

Table III

Characteristics of antimicrobial use and prevalence rate ratios (PRRs) with 95% confidence intervals (CIs) in the second and third editions of the point prevalence survey of healthcare-associated infections and antimicrobial use in European acute-care facilities (PPS2 and PPS3) in Italy

	Unmatched sample			Matched sample		
	PPS2 (N of prescriptions = 17,030)	PPS3 ^a (N of prescriptions = 31,654)	Prevalence rate ratio (95% CI)	PPS2 (N of prescriptions = 16,992)	PPS3 ^a (N of prescriptions = 17,116)	Prevalence rate ratio (95% CI)
Most frequently prescribed antimicrobial agents, n (% over all agents)						
Ceftriaxone	1996 (11.72)	5108 (16.13)	1.38 (1.31–1.45) ^b	1995 (11.74)	2540 (16.24)	1.26 (1.20–1.33) ^b
Piperacillin and beta-lactam inhibitors	2226 (13.07)	5038 (15.92)	1.22 (1.16–1.28) ^b	2225 (13.09)	2780 (16.24)	1.24 (1.18–1.31) ^b
Cefazolin	1290 (7.57)	2873 (9.07)	1.2 (1.13–1.28) ^b	1289 (7.59)	1462 (8.54)	1.13 (1.05–1.21) ^c
Amoxicillin and beta-lactam inhibitors	1480 (8.69)	1915 (6.05)	0.70 (0.65–0.74) ^b	1473 (8.67)	1027 (6)	0.69 (0.64–0.74) ^b
Meropenem	888 (5.21)	1903 (6.01)	1.15 (1.07–1.25) ^b	888 (5.23)	1064 (6.22)	1.19 (1.09–1.30) ^b
Indication for antimicrobial use, n (% over all agents)						
Treatment						
Intended for community infection	6428 (37.75)	12609 (39.83)	1.06 (1.03–1.08) ^b	6422 (37.79)	6510 (38.03)	1.01 (0.98–1.03)
Intended for HI	2975 (17.47)	5565 (17.58)	1.01 (0.97–1.05)	2970 (17.48)	3942 (23.03)	1.32 (1.26–1.38) ^b
Intended for infection acquired in an LTCF	330 (1.93)	546 (1.72)	0.89 (0.78–1.02)	330 (1.94)	317 (1.85)	0.95 (0.82–1.11)
Treatment total	9733 (57.15)	18720 (59.14)	1.04 (1.02–1.05) ^b	9722 (57.22)	10769 (62.92)	1.1 (1.08–1.12) ^b
Prophylaxis						
MP	3661 (21.50)	4437 (14.02)	0.65 (0.63–0.68) ^b	3641 (21.43)	2045 (11.95)	0.56 (0.53–0.59) ^b
SP	2872 (16.86)	5498 (17.37)	1.03 (0.99–1.08)	2868 (16.88)	2633 (15.38)	0.91 (0.87–0.96) ^b
Prophylaxis total	6533 (38.36)	9935 (31.39)	0.82 (0.80–0.84) ^b	6509 (38.31)	4678 (27.33)	0.71 (0.69–0.74) ^b
Other	128 (0.76)	1662 (5.25)	6.99 (5.84–8.35) ^b	128 (0.76)	941 (5.50)	7.30 (6.01–8.77) ^b
Unknown	636 (3.73)	1337 (4.22)	1.13 (1.03–1.24) ^c	636 (3.73)	684 (4)	1.07 (0.96–1.19)
Indicators of appropriate antibiotic use						
Proportion of LL/BSA, n (% over respective indication)						
Treatment of community infection	4228 (65.78)	8573 (67.99)	1.03 (1.01–1.06) ^c	4200 (65.4)	4344 (66.73)	1.02 (1–1.05)
Treatment of HI	1976 (66.42)	3763 (67.62)	1.02 (0.99–1.05)	2031 (68.38)	2722 (69.05)	1.01 (0.98–1.04)
MP	2000 (54.63)	2455 (55.33)	1.01 (0.97–1.05)	1992 (54.71)	1084 (53.01)	0.99 (0.92–1.02)
SP	816 (28.41)	1517 (27.59)	0.97 (0.9–1.04)	572 (19.94)	468 (17.77)	0.89 (0.8–0.99) ^c
All indications	9807 (57.59)	18962 (59.9)	1.04 (1.02–1.06) ^b	9698 (57.07)	10154 (59.32)	1.04 (1.02–1.06) ^b
SP lasting >1 day, n (% over all SP indications)	1608 (55.99)	2885 (52.15)	0.94 (0.90–0.98) ^c	1607 (56.03)	1290 (48.99)	0.87 (0.83–0.92) ^b
HI treatments with an available microbiology result, n (% over all HI treatment indications)	1002 (33.68)	2703 (48.57)	1.30 (1.22–1.38) ^b	1000 (33.67)	2218 (56.27)	1.43 (1.34–1.52) ^b
Antimicrobials with a recorded change, n (% over all agents)						
Escalation	1714 (10.06)	2792 (8.82)	0.88 (0.83–0.93) ^b	1713 (10.08)	1664 (9.72)	0.96 (0.90–1.03)
De-escalation	446 (2.62)	792 (2.50)	0.96 (0.85–1.07)	446 (2.62)	505 (2.95)	1.12 (0.99–1.28)

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Table III (continued)

	Unmatched sample			Matched sample		
	PPS2 (N of prescriptions = 17,030)	PPS3 ^a (N of prescriptions = 31,654)	Prevalence rate ratio (95% CI)	PPS2 (N of prescriptions = 16,992)	PPS3 ^a (N of prescriptions = 17,116)	Prevalence rate ratio (95% CI)
IV–oral switch	241 (1.42)	234 (0.74)	0.52 (0.44–0.62) ^b	241 (1.42)	153 (0.89)	0.63 (0.52–0.77) ^b
Adverse events	66 (0.39)	90 (0.28)	0.73 (0.53–1.01)	65 (0.38)	53 (0.31)	0.81 (0.56–1.16)
Unknown reason	262 (1.54)	361 (1.14)	0.74 (0.63–0.87) ^b	261 (1.54)	361 (2.11)	1.37 (1.17–1.61) ^b
No change	12557 (73.73)	25151 (79.46)	1.08 (1.07–1.09) ^b	12539 (73.79)	12750 (74.49)	1.01 (0.99–1.02)
Unknown/not reported	1744 (10.24)	1884 (5.95)	0.58 (0.55–0.62) ^b	1727 (10.16)	1808 (10.56)	1.04 (0.98–1.11)

HI, hospital infection; IQR, interquartile range; LL/BSA, last-line or broad-spectrum agents [14]; LTCF, long-term care facility; MP, medical prophylaxis; SP, surgical prophylaxis. Matched controls were obtained among non-COVID-19 PPS3 patients for each patient included in PPS2 using propensity score matching according to age, sex and severity of underlying conditions according to the McCabe score, with tolerance set at 0 for age and 0.2 for age and McCabe score.

^a Excluding COVID-19 patients.
^b P<0.05.
^c P<0.001.

CI 7.79–8.23). Among these, 4995 had undergone microbiology testing and for 3197 a result was available at the time of the survey. Before matching, PRR for HAIs between the two editions was 1.09 (95% CI 1.04–1.14, $P<0.001$). After matching, the PRR increased to 1.47 (95% CI 1.39–1.55, $P<0.001$). Table IV shows results of antibiotic susceptibility testing for selected pathogen–drug combinations.

In both the matched and unmatched samples, significant decreases were found in the proportion of resistant isolates in PPS3 compared with PPS2 for the following: carbapenem-resistance and third-generation cephalosporin resistance among *Klebsiella pneumoniae* isolates, and third-generation cephalosporin resistance among *Escherichia coli* isolates. The only measured increase, albeit non-significant, was found considering carbapenem resistance among *Acinetobacter baumannii* isolates, which reached 95% in PPS3.

Discussion

This study reports national-level data from two subsequent editions of the Italian PPS, allowing assessment of trends in patient characteristics, inpatient antibiotic use, prescribing practices, and AMR rates.

First, concerning the former, even though the Italian population is increasingly elderly and frail [24], characteristics of acute-care hospital inpatients remained relatively stable in terms of age, sex, and McCabe score. However, particularly in the matched sample, increasing trends in the proportion of patients undergoing surgical procedures and exposed to one or more invasive devices were found. Notably, the prevalence of patients with >1 invasive device increased from around 8%–10% of all patients. This finding could reflect a trend towards a broadening of indications for invasive procedures. A Dutch analysis of 10 years of surveillance through repeated PPSs also found a similar pattern of stable patient characteristics and increased invasive device use, leading the authors to question whether the McCabe score is the most accurate classification system to measure patient case-mix [25].

Second, in the overall sample a trend towards reduced inpatient antibiotic use was identified, both in terms of patients exposed to antibiotics and of level of exposure per patient. The prevalence of inpatient antibiotic use decreased from 44% to 42%, with a reduction in the ratio of prescriptions per patient. These results are encouraging and could indicate the effectiveness of national policies such as the PNCAR, particularly considering no significant trend had emerged comparing results of the two previous editions of the Italian PPS, both conducted prior to the publication of the Plan [19]. However, in the matched comparison a slight but significant increase in prevalence of antimicrobial use emerged, which could suggest patients with similar case-mix are in fact being increasingly more exposed to antibiotics. The increased use of invasive devices may have contributed to the higher percentage of antibiotic use observed after propensity matching. These devices are well-established risk factors for HAIs, often leading to greater antimicrobial prescribing, as demonstrated by studies conducted in both acute-care hospitals and long-term care facilities [26,27]. In particular, a significant increase in indications for the treatment of hospital infections was found, which warrants further investigation.

Third, quality indicators identified improvements in some prescribing practices. SP in particular saw reductions both in the proportion of LL/BSAs and in the proportion of

Table IV

Susceptibility to selected antimicrobial agents among micro-organisms isolated from healthcare-associated infections (HAIs) and prevalence rate ratios (PRRs) with 95% confidence intervals (CIs) in the second and third editions of the point prevalence survey of HAIs and antimicrobial use in European acute-care facilities (PPS2 and PPS3) in Italy

Antimicrobial agents and micro-organisms	Unmatched sample							Matched sample						
	PPS2			PPS3 ^a				PPS2			PPS3 ^a			
	N of tested isolates	N of resistant isolates ^b (%)	95% CI	N of tested isolates	N of resistant isolates ^b (%)	95% CI	Prevalence rate ratio (95% CI)	N of tested isolates	N of resistant isolates ^b (%)	95% CI	N of tested isolates	N of resistant isolates ^b (%)	95% CI	Prevalence rate ratio (95% CI)
Oxacillin														
<i>Staphylococcus aureus</i>	147	71/144 (49.3)	40.9–57.8	318	106/303 (35)	29.6–40.6	0.78 (0.61–1.01)	145	71/142 (50)	41.5–58.5	303	104/288 (36.1)	30.6–42	0.80 (0.62–1.02)
Glycopeptides														
<i>Enterococcus faecalis</i>	82	5/78 (6.4)	2.1–14.3	200	10/185 (5.4)	2.6–9.7	0.85 (0.30–2.41)	82	5/78 (6.4)	2.1–14.3	179	9/165 (5.5)	2.5–10.1	0.86 (0.30–2.48)
Carbapenems														
<i>Pseudomonas aeruginosa</i>	126	43/122 (35.3)	26.8–44.4	329	76/314 (24.2)	19.6–29.3	0.75 (0.54–1.04)	124	42/120 (35.3)	26.8–44.4	312	71/299 (23.8)	19–29	0.74 (0.53–1.03)
<i>Acinetobacter baumannii</i>	41	38/46 (82.6)	68.6–92.2	110	94/99 (95)	88.6–98.3	1.08 (0.82–1.42)	41	38/46 (82.6)	68.6–92.2	106	91/96 (94.8)	88.3–98.3	1.08 (0.82–1.42)
<i>Escherichia coli</i>	199	8/192 (4.2)	1.8–8	443	16/410 (3.9)	2.3–6.3	0.94 (0.41–2.16)	197	8/190 (4.2)	1.8–8.1	411	15/381 (3.9)	2.2–6.4	0.94 (0.40–2.17)
<i>Klebsiella pneumoniae</i>	145	70/141 (49.7)	41.1–58.2	449	121/425 (28.5)	24.2–33	0.67 (0.52–0.86) ^c	144	69/140 (49.3)	40.7–57.9	419	107/394 (27.2)	22.8–31.8	0.65 (0.50–0.84) ^c
Third-generation cephalosporins														
<i>E. coli</i>	212	81/208 (38.9)	32.3–45.9	456	117/433 (27)	22.9–31.5	0.76 (0.59–0.97) ^c	210	80/206 (38.8)	32.1–45.9	436	109/413 (26.4)	22.2–30.9	0.75 (0.58–0.96) ^c
<i>K. pneumoniae</i>	146	101/144 (70.1)	62–77.5	452	209/426 (49.1)	44.2–53.9	0.80 (0.66–0.96) ^c	145	100/143 (69.9)	61.7–77.3	430	199/405 (49.1)	44.2–54.1	0.80 (0.66–0.97) ^c

CI, confidence interval. Matched controls were obtained among non-COVID-19 PPS3 patients for each patient included in PPS2 using propensity score matching according to age, sex, and severity of underlying conditions according to the McCabe score, with tolerance set at 0 for age and 0.2 for age and McCabe score.

^a Excluding COVID-19 patients.

^b Resistant isolates over available results at time of PPS.

^c $P < 0.05$.

prescriptions lasting over one day, from 56% to 52%. Still, considering no advantages have been found in administering SP for >24 h in terms of preventing postoperative infections [28], prolonged SP remains frequent in Italy and requires further corrective efforts. It must be noted that PPSs tend to overestimate the duration of SP due to length-biased sampling; even though this indicator may not accurately reflect the precise rate of prolonged SP, it remains of value to set targets and guide improvement [10].

Improvements were also identified in culture-guided treatments for hospital infection, suggesting an increased use of laboratory diagnostics. A significant increase by over 10 percentage points was found in both the unmatched and matched samples, with PPS3 levels comparing favourably to results of a global study (49% vs 20–44%) [29].

Other areas for improvement in prescribing practices were identified. The shift from narrow spectrum towards LL/BSAs seen in recent years in most Southern European countries appears uninterrupted in Italy, apart from SP indications [30]. This result is notable as AMR levels for all considered pathogens (apart from carbapenem-resistance in *A. baumannii* isolates) were stable or decreased over the considered period. The use of carbapenems in particular remains high, with meropenem ranking fifth among the most frequently prescribed agents in PPS3.

Further, inpatient antibiotic use in Italy appears highly static, with unchanged prescriptions reaching 80% in PPS3. This result suggests a lack of proactive IV to oral switching and de-escalation protocols, highlighting the need for stewardship interventions such as routine post-prescription review [31].

Fourth, as previously stated, AMR rates among isolates from HAs showed mostly stable or decreasing trends. In particular, AMR levels and trends in oxacillin resistance among *S. aureus* isolates, glycopeptide-resistance among *E. faecalis* isolates, and third-generation cephalosporin-resistance among *E. coli* and *K. pneumoniae* isolates identified through PPS surveillance were in line with data from the Italian national surveillance system for AMR (AR-ISS) [32]. The only increasing trend (however non-significant) was identified for carbapenem resistance among *A. baumannii* isolates, which reached 95% in PPS3, consistent with AR-ISS data [32]. As AR-ISS includes invasive isolates from both HAs and community infections, these results suggest strains of bacteria with similar resistance levels are circulating in hospitals and the community.

Strengths and limitations of this study should be considered when interpreting results. Both PPSs were conducted at national level, with a strong institutional mandate. Participation was high and increased importantly between the two editions, also with a wider variety of hospitals participating in PPS3. In particular, the latest PPS saw the enrolment and training of around 750 local hospital and regional health authority staff, improving surveillance capacity and awareness towards HAs, inpatient antibiotic use, and AMR. Standardized definitions and methods proposed by the ECDC were applied, allowing the assessment of national trends over time and international comparisons. In both editions, the national coordinating centre opted to conduct patient-based, rather than unit-based surveillance [17,18]. One of the major strengths of this study is the use of propensity score matching. By balancing the characteristics of the groups, propensity matching strengthens the validity of our findings, making the results more robust and reflective of the true relationship

between the variables under investigation. Limitations inherent to PPS study design apply: PPS captures data at a single point in time, making it impossible to assess the duration or outcomes of infections and antimicrobial use; since data is collected at one time point, it does not allow for causal inferences between risk factors and outcomes. In PPS2, hospitals participated on a voluntary basis, which may have introduced volunteerism bias and limited the representativeness of the sample relative to Italy's overall hospital population. For PPS3, measures were taken to improve representativeness, but full elimination of selection bias could not be ensured: two regions did not participate; the heterogeneity and potential regional disparity in antimicrobial resistance patterns and healthcare practices, which may be influenced by underlying socio-economic conditions, may have influenced the comparability between the two editions. Due to data protection requirements, it was not possible to ascertain whether the same hospitals participated in both editions of surveillance. Further, indicators of prescribing appropriateness were selected based on expert opinion and data availability. As it was not the aim of this study, their applicability in clinical practice remains to be determined. Finally, we make no claim of any direct impact of the PNCAR or any specific action on trends identified in this study.

Results of this study underline the importance of national, regularly conducted, patient-level surveillance efforts. Even though PPSs are resource-intensive, other methods such as notification systems may not offer similar representativeness and completeness of information. The level of context and detail provided through PPS surveillance has made it possible to provide a mapping of acute-care hospital prescribing activity at national level. In addition, this study defined measurable quality indicators, through which strengths and areas for improvement in prescribing practices were identified. Surveillance activities should not be seen only as a formal requirement but as a tool for quality improvement. In particular, the indicators defined in this study could be used to set targets and guide the implementation of appropriate corrective actions at local and national level.

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Conflict of interest statement

The authors have no conflicts of interest relevant to this manuscript to declare, including relevant financial interests, activities, relationships, and affiliations.

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Appendix A. Supplementary data

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