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Impact of hospital-related indicators on healthcare-associated infections and appropriateness of antimicrobial use according to a national dataset

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Healthcare-associated infections (HAIs) represent a major threat in Europe. Infection prevention and control (IPC) measures are crucial to lower their occurrence, as well as antimicrobial stewardship to ensure appropriate use of antibiotics. Starting from Italian national data, this study aimed at: (i) describing IPC indicators, prevalence of HAIs, antimicrobial use and appropriateness of antibiotic use in Italy; (ii) estimating effects of IPC variables on HAI prevalence and on the proportion of antibiotics without specific reason. Based on data collected for Italy during the ECDC PPS-2 Point Prevalence Survey, descriptive statistics were computed at national and macro-regional level. Causal assumption-informed regression models were then built to estimate the impact of structural determinants, staffing parameters and IPC-related variables on HAI prevalence and percentage of antibiotic prescriptions with no reason detailed on medical records, after adjusting for relevant confounders. The Italian frame showed substantial heterogeneity for both outcomes between macro-regions. The percentage of single-bed rooms was the only structural determinant with significant, positive impact on HAI prevalence (OR = 0.91 for every + 5%, $p < 0.001$), while the prevalence of antimicrobial agents without specified reason was lower in the presence of one more IPC nurse (OR = 0.78, $p < 0.001$) or one more antibiotic stewardship consultant (OR = 0.67, $p < 0.001$) per 100 beds. Both outcomes were reduced in the presence of routinely filed IPC plans and reports ($p < 0.001$), HAI prevention measures ($p < 0.001$) and post-prescription review ($p < 0.01$). Our model confirmed the pivotal role of IPC measures and antimicrobial stewardship in contrasting HAIs and inappropriate antibiotic prescriptions. Post-prescription review appeared to be a valuable indicator of antimicrobial stewardship policies.

Keywords Healthcare-associated infections (HAIs), Point Prevalence Survey (PPS), Infection Prevention and Control (IPC), Antibiotic use, Antimicrobial stewardship, Surveillance indicators

Healthcare-Associated Infections (HAIs) represent a major public health threat in Europe, with an average prevalence around 5.7–6.5%[1] and an incidence rate around 3.7 HAI cases per 100 admissions[2]. Antimicrobial resistance (AMR) is an additional issue concerning HAIs, especially in the case of multi-drug resistant (MDR) organisms, as every year around 670,000 AMR infections occur in Europe, causing approximately 33,000 deaths[3]. One of the main drivers of AMR is intensive and inappropriate antibiotic use: according to a previous European study, 35% of admitted patients were treated with antibiotics, most frequently systemic antibacterial agents (92.5%), and medical records detailed a specific reason for administering antimicrobial drugs only in 79.4% of prescriptions[1].

In the frame of HAIs and antimicrobial use, Italy outstands the European average, with higher prevalence values both for HAIs (8.0%) and antibiotic use (44%)[2]. Percentages of infections due to antibiotic-resistant

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bacteria are also generally higher than in Central-Northern Europe, especially for some species (e.g. *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Staphylococcus aureus*)[3].

The problem of HAIs and antimicrobial use in Europe has been monitored by the European Centre for Disease Prevention and Control (ECDC) through a series of Point Prevalence Surveys (PPSs): the first (PPS-1) was conducted in 2011–2012[1], the second (PPS-2) in 2016–2017[2], and the third is currently being performed (2022–2023). These studies, besides describing patients, invasive procedures and prescribed antibiotics, also aimed at harmonizing data collection and analysis, to overcome issues in data pooling or even simple trans-national comparison due to heterogeneity between study protocols[4].

A secondary purpose of these surveys was also to identify consistent key indicators, i.e. essential parameters helping to monitor specific aspects of health care, for appropriate decision-making and priority setting. Performing targeted surveillance and providing detailed feedback is paramount in the field of healthcare-associated infections, not only to conduct trans-national comparisons[5], but also to correctly implement an effective infection prevention and control (IPC) programme, as already pointed out in the literature[6]. Reports are a commonly used tool in public health, yet consensus is often limited concerning indicators to be reported or strategies to be adopted in the reporting procedure itself[7].

The third ECDC prevalence survey (PPS-3, 2022–2023) was conducted in Italy in November 2022, with an updated protocol (version 6.1) mostly replicating the former version's items, but also including some elements such as, for example, indicators related to healthcare-associated COVID-19, automated HAI surveillance, and the IPC Assessment Framework based on the World Health Organization (WHO) Guidelines for IPC programmes[8].

In this frame, therefore, starting from Italian national PPS-2 data, our study was designed with two aims: first, to provide a descriptive analysis at a national and macro-regional level of IPC indicators (including structural and staffing variables), prevalence of HAIs and antimicrobial use, and appropriateness of antibiotic prescriptions in Italian hospitals; second, to estimate causal effects of IPC indicators on HAI prevalence and on the proportion of antibiotics prescribed with no specific reason detailed on medical records, thereby investigating which variables might significantly determine these outcomes at a hospital level.

Materials and methods

Data framework

The study is based on the Italian national data from the PPS-2, coordinated at the national level by the Department of Public Health Sciences and Paediatrics of the University of Turin and conducted in Italy in October-November 2016: data were collected by IPC nurses on the hospital, ward and patient data forms provided by the ECDC, which investigated specific questions at respective levels[9].

As specified in another study[10], the PPS-2 was part of a programme coordinated by public entities (namely, the ECDC and the University of Turin at a European and Italian level, respectively) and aimed at HAI surveillance and healthcare quality improvement, in which data were collected and sent to the national coordinating centre in anonymised form only. Therefore, written informed consent was waived, in accordance with the World Health Organisation's Guideline 12 regarding Ethical Issues in Public Health Surveillance[11], even though patients were notified of their participation in the PPS through an information sheet. Ethical board approval was obtained by the relevant local health authorities for each region[10], and the whole study methodology was approved by the Liguria Regional Ethical Committee (3 November 2016, protocol n. 2016/465), the Central Ethical Committee IRCCS Lazio (19/10/2016, protocol n. 2016/12196) and Local Health Authority ASL 1 Sassari (4 October 2016, protocol n. 2016/2415) as representatives.

All the research was performed in accordance with relevant guidelines and regulations: in fact, for this study, hospitals were taken as statistical units (see details in §Database building), hence patient data were drawn from the PPS-2 database in an aggregate form only, which ensured full conformity with the Helsinki Declaration and with the Italian (Law 2003/196) and European Regulations (EC/2016/679) concerning data protection and privacy.

Database building

This study was based on data from all the Italian acute-care hospitals voluntarily responding to the invitation to participate in the PPS-2.

Outcomes considered for the present analysis were HAI prevalence, antibiotic use prevalence, and the proportion of antimicrobial agent prescriptions without a reason specifically stated in medical records, as a proxy measure of inappropriate antibiotic use. HAI cases were defined according to the European (Hospitals in Europe Link for Infection Control through Surveillance) and US (National Healthcare Safety Network) case definitions[1]. Antibiotic use prevalence was defined as the proportion of patients receiving at least 1 antimicrobial agent during the day of the survey. All outcomes were retrieved from the patient-level questionnaire forms and then aggregated to the hospital level.

Among the variables monitored by the PPS-2 study and related to the hospital's structure, personnel and organization of IPC activities, we selected the ones potentially acting as determinants of the aforementioned outcomes[12]. A review of the available literature led to considering the following candidate determinants: percentage of single-bed rooms[13–16], percentage of airborne-infection isolation rooms[14,17], annual alcohol-based hand rub (ABHR) consumption[18,19], proportion of healthcare workers carrying a portable ABHR dispenser (e.g. a bottle)[20] (dichotomized into $\leq 25\%$ vs. $> 25\%$ as per the multiple choices provided by the PPS-2 form), number of blood cultures per 100 beds[21], number of full-time equivalent (FTE) IPC nurses[22–24], IPC physicians[25–27] and antibiotic stewardship consultants per 100 beds[28], routine production of an IPC plan[29] and an IPC report[6,7], number of HAI surveillances[30–32] and of HAI prevention measures[33], presence of antimicrobial stewardship programmes[25,34] and routine performance of a post-prescription review of antibiotic therapies[35,36]. Data for all these determinants were retrieved from the hospital-level questionnaire form of the PPS-2, except for the

proportion of single-bed rooms and ABHR consumption, which were based on data provided through the ward-level forms.

Furthermore, general hospital characteristics were also retrieved, including hospital type (distinguishing between hub hospitals with their own hospital management, hospitals belonging to the territory-based healthcare system, scientific research centres and other healthcare facilities), size (i.e. total number of beds) and geographic region (according to the Nomenclature of Territorial Units for Statistics, NUTS-1).

Statistical analysis

Descriptive statistics were reported in the form of absolute frequencies and percentages for categorical variables and, following the result of the Shapiro-Wilk normality test, as medians and interquartile ranges for quantitative variables.

For all models, we hypothesized that general characteristics - such as hospital location, type and size - could act as confounders by affecting both the explanatory variable and the outcome. A causal-like framework was developed according to the directed acyclic graph (DAG) shown in Supplementary Figure A1, which was closed after adjusting for these confounders. The outcome was in turn represented by HAI prevalence (for the first set of regressions) and by the proportion of antimicrobial prescriptions not followed by reason on medical records (for the second set), and the main determinant was represented by each of the plausible variables at a time. After considering the expected relationships between determinants and outcomes, some structural determinants (ABHR consumption data, proportion of single-bed or airborne-infection isolation rooms) were considered for the first set of regressions but excluded from the second.

For the analyses in which HAI prevalence was the main outcome, the number of blood cultures per 100 beds was added to the model as a potential interactor in the relationship between determinants and outcome, after considering this indicator as a proxy of HAI detection capability and influence on the measured prevalence. However, sensitivity analyses were also performed by considering this variable as a confounder or by removing it at all.

According to the available methodological evidence[37], models were built through maximum a-posteriori Bayesian binomial regressions (R package "arm", version 1.11-2, "bayesglm" function)[38]. The choice of the adjustment set was performed according to the DAG drawn through the DAGitty application (version 0.3-1)[39]. The presence of possible collinearity between variables included in models was checked through the analysis of variance inflation factors (VIFs). All analyses were performed using the R statistical software (R Foundation for Statistical Computing, Vienna, Austria, version 4.0.2)[40].

Results

A total of 135 Italian hospitals took part in the PPS-2 study, with 30,467 patients enrolled in the surveillance. Representative healthcare facilities were present for all Italian areas, even though most participating hospitals (95/135, 70.4%), and consequently of enrolled patients (23,023/30,467, 75.6%) were located in Northern regions (detail by NUTS-1 region is reported in Supplementary Table A1).

Table 1 summarizes all descriptive characteristics and outcomes of included hospitals. Participating hospitals were of various sizes (range: 8-1040 beds), but mostly small-medium (100–500 beds) and belonging to the territory-based healthcare system.

Generally, ABHR consumption was low, with a median consumption around 14.1 L per 100 beds. A higher number of blood cultures was recorded in Northern Italy compared to the South (median 900–1100 vs. 705 per 100 beds respectively).

IPC personnel showed differences between regions, yet with numbers seldom exceeding 2–3 IPC nurses (North-West), and one IPC physician (Centre), per 500 beds. A higher proportion of hospitals with at least one antibiotic stewardship consultant was recorded in the North (57–61%).

Concerning IPC activities, more than 80% of included facilities routinely filed an IPC plan and nearly 80% an annual report of IPC activities at the time of the survey. Approximately 85% of hospitals provided for at least one HAI surveillance and almost all facilities operated HAI prevention measures. Antibiotic stewardship was reported in over 78% of hospitals, but routine post-prescription review procedures were performed in 33.6% only.

Regarding outcomes, HAIs were present in 7.5% of patients (median prevalence at a hospital level: 5.8%, IQR 3.5–8.7%), with appreciably lower values in the South and Isles (below 5%). Almost half (43.5%) of enrolled patients were under treatment with at least one antimicrobial agent, and the proportion of antibiotics prescribed with no reason specified in medical records showed values close to 20% in the North, 30% in the Centre, and 35–40% in South and Isles.

Adjusted regression models showed that the only variable having a significant impact on HAI prevalence was the proportion of single rooms, with a 9% reduction in HAI risk for every 5% increase in that proportion ($p < 0.001$). No significant effect on HAI prevalence could be detected by other structure and resource-related variables (proportion of airborne-infection isolation rooms, ABHR consumption data or IPC personnel in relation to beds): the only exception holds for a borderline-significant reduction by one third in HAIs for every antibiotic stewardship consultant hired per 100 beds ($p = 0.055$).

Conversely, IPC activities appeared to be much more impactful: adjusted results suggested that HAI risk was halved in the presence of appropriate drafting of an IPC plan, as well as with the production of a routine report of performed activities ($p < 0.001$). A significant reduction in HAI prevalence was associated with the presence of HAI prevention measures (-84%, $p < 0.001$), the effect being more relevant as the number of implemented measures increased. Significant results were also obtained for antimicrobial stewardship, with a reduction in HAI prevalence by over 50%, and for the presence of routinely operated post-prescription review (-27%, $p = 0.037$). Table 2 shows full detail of model coefficients concerning HAI determinants, while corresponding coefficients

	North-West (*N* = 52)	North-East (*N* = 43)	Centre (*N* = 19)	South/Isles (*N* = 21)	Overall Italy (*N* = 135)
Baseline characteristics					
Hospital type					
Local Health Authority hospitals (included in the territorial system)	33/52 (63.5)	30/43 (69.8)	12/19 (63.2)	11/21 (52.4)	86/135 (63.7)
Hub hospitals	13/52 (25.0)	8/43 (18.6)	5/19 (26.3)	10/21 (47.6)	36/135 (26.7)
Research hospitals	5/52 (9.6)	3/43 (7.0)	2/19 (10.5)	0/21 (0.0)	10/135 (7.4)
Others	1/52 (1.9)	2/43 (4.6)	0/19 (0.0)	0/21 (0.0)	3/135 (2.2)
Size (beds)	242 (158–418)	242 (72–520)	284 (157–350)	195 (104–385)	244 (114–417)
Proportion of single-bed rooms [%]	16.8 (10.1–22.9)	16.5 (11.6–22.0)	14.6 (9.2–22.8)	15.0 (10.1–19.5)	15.8 (10.1–22.4)
Hospitals with airborne-infection isolation rooms [%]	30/51 (58.8)	17/41 (41.5)	9/19 (47.4)	9/20 (45.0)	65/131 (49.6)
Number of airborne- infection isolation rooms per 100 beds*	0.85 (0.43–1.64)	2.23 (0.80–2.56)	1.22 (0.68–1.92)	0.97 (0.56–2.48)	1.12 (0.51–2.33)
Alcohol-based hand rub consumption [L/100 beds]	1.34 (0.60–2.27)	1.56 (1.03–3.30)	0.73 (0.58–1.39)	1.21 (0.62–1.75)	1.41 (0.63–2.27)
Proportion of HCW carrying portable ABHR dispenser [%]	18.7 (2.8–38.5)	32.7 (5.0–63.6)	2.8 (0.0–20.4)	0.0 (0.0–4.1)	11.6 (0.0–39.1)
Number of blood cultures performed per 100 beds	921 (507–1849)	1071 (759–2072)	1097 (554–1600)	705 (360–1554)	938 (511–1723)
Number of IPC nurses (FTE) per 100 beds	0.56 (0.42–0.80)	0.35 (0.19–0.48)	0.28 (0–0.47)	0 (0–0.51)	0.41 (0.18–0.67)
Number of IPC physicians (FTE) per 100 beds	0.21 (0.09–0.48)	0.08 (0.02–0.15)	0.24 (0–0.53)	0 (0–0.17)	0.12 (0–0.29)
Hospitals with ≥ 1 antibiotic stewardship consultant	29/51 (56.9)	25/41 (61.0)	5/16 (31.3)	4/20 (20.0)	63/128 (49.2)
Number of FTE antibiotic stewardship consultants per 100 beds†	0.26 (0.20–0.56)	0.09 (0.05–0.18)	0.31 (0.28–0.33)	0.77 (0.47–1.17)	0.21 (0.08–0.41)
Hospitals routinely providing IPC plan	49/52 (94.2)	32/40 (80.0)	13/18 (72.2)	14/20 (70.0)	108/130 (83.1)
Hospitals routinely providing IPC report	43/50 (86.0)	34/40 (85.0)	11/17 (64.7)	12/20 (60.0)	100/127 (78.7)
Hospitals performing ≥ 1 HAI surveillance	48/52 (92.3)	36/43 (83.7)	13/19 (68.4)	17/21 (81.0)	114/135 (84.4)
Number of performed HAI surveillances	4 (2–5)	3 (2–5)	2 (0–3)	2 (1–5)	3 (1–5)
Hospitals performing ≥ 1 HAI prevention measure	52/52 (100)	39/43 (90.7)	16/19 (84.2)	19/21 (90.5)	126/135 (93.3)
Number of HAI prevention measures	26 (18–31)	19 (12–30)	10 (5–22)	35 (6–49)	21 (12–34)
Hospitals performing antibiotic stewardship	49/52 (94.2)	34/43 (79.1)	10/19 (52.6)	13/21 (61.9)	106/135 (78.5)
Number of antibiotic stewardship measures	8 (4–9)	4 (2–7)	1 (0–3)	1 (0–6)	4 (1–8)
Hospitals providing for antibiotic review procedures	12/42 (28.6)	16/32 (50.0)	3/17 (17.6)	5/16 (31.3)	36/107 (33.6)
Outcomes					
HAIs					
Patients with HAIs (crude prevalence)	940/11,352 (8.3%)	743/9746 (7.6%)	290/3971 (7.3%)	160/3383 (4.7%)	2133/28,452 (7.5%)
HAI prevalence [unit = hospital]:					
Median (Q1-Q3)	6.4% (4.6–8.4%)	6.6% (3.7–10.0%)	5.6% (2.8–8.1%)	4.4% (3.1–5.7%)	5.8% (3.5–8.7%)
Mean	6.6%	7.2%	6.9%	4.8%	6.6%
Antimicrobial usage					
Patients with ≥ 1 antimicrobial agent (crude prevalence)	4783/11,352 (42.1%)	4134/9746 (42.4%)	1834/3971 (46.2%)	1631/3383 (48.2%)	12,382/28,452 (43.5%)
Prevalence of antimicrobial usage [unit = hospital]:					
Median (Q1-Q3)	41.3% (36.1–48.1%)	40.4% (35.2–46.8%)	48.0% (44.5–51.8%)	44.2% (41.2–52.7%)	42.4% (38.0–49.2%)
Mean	41.2%	40.1%	48.6%	46.6%	42.7%
Antimicrobials with no reason specified on medical records					
Prescriptions with no reason specified (crude prevalence)	1195/6488 (18.4)	1280/5723 (22.4)	717/2482 (28.9)	772/2182 (35.4)	3964/16,875 (23.5)
Percentage of agents prescribed without a specified reason [unit = hospital]:					
Median (Q1-Q3)	15.1% (5.8–33.4%)	12.5% (6.9–19.7%)	30.2% (8.0–35.8%)	35.7% (25.4–57.1%)	17.6% (7.8–35.7%)
Mean (SD)	20.4%	17.7%	29.9%	39.8%	23.9%

Table 1. Baseline characteristics and outcomes, by NUTS-1 macro-region and at a national level. Values are expressed as numbers and percentages (for categorical variables) or medians and Q1-Q3 ranges (for quantitative ones). For outcomes, data presentation indices are specified in the first cell of each line. *considering only hospitals with at least one airborne-infection isolation room. †considering only hospitals with at least one antibiotic stewardship consultant.

Variable	OR (95% CI)	*p*-value
Proportion of single-bed rooms	0.91 [0.87–0.95] (for every + 5%)	< 0.001
Number of airborne-infection isolation rooms per 100 beds	1.00 [0.95–1.05] (+ 1 per 100 beds)	0.968
Alcohol-based hand rub consumption [L/100 beds]	0.99 [0.94–1.05] (+ 1 L/100 beds)	0.787
Proportion of HCW carrying portable ABHR dispenser	0.91 [0.71–1.17] (≥ 25% vs. < 25%)	0.458
Number of IPC nurses (FTE) per 100 beds	0.92 [0.84–1.02] (+ 1 per 100 beds)	0.110
Number of IPC physicians (FTE) per 100 beds	1.04 [0.93–1.16] (+ 1 per 100 beds)	0.481
Number of antibiotic stewardship consultants (FTE) per 100 beds	0.67 [0.44–1.01] (+ 1 per 100 beds)	0.055
Routinely provided IPC plan	0.49 [0.37–0.65]	< 0.001
Routinely provided IPC report	0.47 [0.37–0.61]	< 0.001
≥ 1 HAI surveillance performed	1.37 [0.96–1.96]	0.082
Nr of performed HAI surveillances	1.02 [0.97–1.07]	0.485
≥ 1 HAI prevention measure	0.16 [0.08–0.31]	< 0.001
Nr of HAI prevention measures	0.992 [0.986–0.998]	0.006
Antibiotic stewardship performed	0.48 [0.34–0.66]	< 0.0001
Nr of antibiotic stewardship measures	0.97 [0.95–0.99]	0.006
Post-prescription review procedures	0.73 [0.54–0.98]	0.037

Table 2. Effect of different variables on HAI prevalence in multivariable models, adjusted for geographic region, hospital type and size (number of beds). These models account for the possible interaction of the proxy variable "number of blood cultures per 100 beds".

Variable	OR (95% CI)	*p*-value
Number of IPC nurses (FTE) per 100 beds	0.78 [0.71–0.86]	< 0.001
Number of IPC physicians (FTE) per 100 beds	1.00 [0.96–1.05]	0.867
Number of antibiotic stewardship consultants (FTE) per 100 beds	0.79 [0.68–0.92]	0.001
Routinely provided IPC plan	0.79 [0.71–0.88]	< 0.001
Routinely provided IPC report	0.76 [0.70–0.83]	< 0.001
Antibiotic stewardship performed	1.33 [1.20–1.47]	< 0.001
Nr of antibiotic stewardship measures	1.02 [1.01–1.03]	0.003
Post-prescription review procedures	0.68 [0.62–0.75]	< 0.001

Table 3. Effect of different variables on the proportion of antibiotics prescribed with no reason specified on medical records, according to multivariable models adjusted for geographic region, hospital type and size (number of beds).

of confounding variables are reported in Supplementary Table A2. The models appeared to be quite robust as sensitivity analyses performed without considering the interaction term or the number of blood cultures yielded very similar results, in terms of coefficients and statistical significance (Supplementary Tables A3-A4). No collinearity issues were detected in any model.

When evaluating antibiotic appropriateness, the model showed a reduction by over 20% in the proportion of antibiotics prescribed with no reason on medical records as an effect of the availability of one more IPC nurse per 100 beds (OR = 0.78, $p < 0.001$), and suggested a similar improvement in consequence of the presence of one more antibiotic stewardship consultant per 100 beds (OR = 0.79, $p = 0.001$); conversely, no significant effects were observed for the number of IPC physicians ($p = 0.867$). Routine production of an IPC plan and IPC reporting showed a potentially protective effect on the percentage of antimicrobial agents without a reason on medical records. The same outcome seemed to be positively correlated with the presence of antibiotic stewardship procedures in the corresponding healthcare facility (OR = 1.33): however, if a more specific variable - such as the presence of post-prescription review - is taken into account, the outcome appears to be reduced (OR = 0.68, $p < 0.001$). Table 3 shows full detail of model coefficients concerning determinants of the proportion of antibiotics with no specified reason, while corresponding coefficients of confounding variables are reported in Supplementary Table A5.

Discussion

This study included, among its aims, a description of the Italian frame in relation to HAI prevalence and antimicrobial use. Interestingly, the area of Southern Italy showed a considerably lower HAI prevalence (even below 5%): however, this data come from many smaller-sized hospitals (Table 1), which may have played a confounding role since HAIs occur more frequently in bigger hospitals, with higher care complexity. Moreover, the reduced participation in the survey (Supplementary Table A1) and the relatively lower amount of blood cultures annually performed (Table 1) in this area allow speculating that, probably, less attention is paid to HAI diagnosis and surveillance, with a tendency to under-notification, as already spotted in previous national surveys[41]. As a result, the detection of fewer HAIs might have been a drive towards lower attention to IPC, with consequently lesser achievements regarding IPC indicators.

The main aim of this study was to identify variables with a potential role as determinants of HAI prevalence and proportion of antibiotics prescribed with no specified reason. As expected, a greater proportion of single-bed rooms seems to lead to a reduction in HAIs: this agrees with results obtained in high-risk settings, where a reduction in infections by methicillin-resistant *Staphylococcus aureus* (MRSA) was observed after introducing new single-bed rooms[42], even though some studies about direct contact infections (*Clostridium difficile*) failed to show significant improvement in incidence rates in single-bed compared to multiple-bed rooms[13].

Remarkably, HAI prevalence did not appear to be impacted by any other structural determinants, including indicators related to ABHR consumption, which represents a provenly effective measure in HAI prevention[43]. Nevertheless, it is important to consider possible issues of this indicator, mainly linked to problems in measuring healthcare workers' actual compliance to hand hygiene practice, and in making comparisons between diverse contexts (with extremely different hand hygiene requirements, e.g. intensive-care units vs. low-intensity wards)[44]. Furthermore, the effect of hand hygiene on HAI transmission has been shown to be non-linear[45], thus some relationships - albeit existent - might have remained undetected by the regression model.

Having one more antibiotic stewardship consultant in the IPC staff per 100 beds appears to reduce HAI prevalence by 33% and antimicrobials with no specified reason by 21%: hence, activities performed by these professionals seem to have a positive impact, reasonably due to their bridging role between scientific evidence and routine clinical practice[28].

Also, the presence of IPC nurses can lower both HAIs and antimicrobial agents with no specified reason (−8% and −22%, respectively), although a fully significant result is obtained in the latter outcome only. This finding agrees with previous studies underlining the substantial role of IPC nurses[22–24] and the importance of fulfilling the international standard that would require the presence of at least one IPC nurse per 250 beds[46]: indeed, having this threshold reached - in almost all Italian macro-regions - by less than half of the included hospitals might represent a partial limitation of the model on this variable. Hence, training the model on a higher number of hospitals would be advisable, to include more healthcare facilities with higher values for this variable, and thus to provide more precise estimates for effect sizes.

Analysis of both outcomes' determinants demonstrates that surveillance is paramount, but setting up a systematic IPC programme is all the more important: as already pointed out in previous studies, drafting an appropriate plan[29] is crucial to involve all stakeholders required for the creation of a suitable patient safety climate aimed at HAI prevention. Equally, producing adequate reports is essential to give precise feedback to all involved operators, providing them with a tool for evaluation and improvement of good practice implementation[6,7].

A systematic IPC activity - of which the production of a plan and a report could represent a proxy indicator - is probably the ground for establishing appropriate surveillance for HAIs and antimicrobial use, which have proved to effectively reduce both the overall HAI incidence (for example in Germany[30], the Netherlands[31] or South Korea[32]), and the incidence of specific HAI subgroups, such as surgical site infections[47] and central line-associated bacteraemia[48].

The establishment of a patient safety environment within healthcare facilities leads to improved application of prevention measures[49], which retain a major role in HAI control (-84% according to our model, Table 2): as shown in the literature, applying simple bundles, for example, in monitoring ventilated patients[50], or adequate training for correct use of central lines[51], can contribute to reducing respective infections even by 66%. Unsurprisingly, the greatest results are obtained by combining several prevention measures, as suggested by multimodal prevention strategies, whose effects have been widely demonstrated, especially for MRSA, central line-related and lower respiratory tract infections[12].

Regarding antibiotic use, the model output suggests that the presence of a stewardship programme could potentially halve HAI prevalence in a hospital, and its effectiveness significantly improves with an increasing number of stewardship measures (Table 3): this confirms that antimicrobial stewardship can improve antibiotic use - and reduce healthcare costs - without jeopardizing the quality of assistance[52]. However, the presence of antibiotic stewardship seems to be positively correlated with a higher share of antimicrobial drugs prescribed with no reason specified on medical records. However, this apparent paradox disappears if a specific stewardship indicator – i.e., presence of routine post-prescription review – is considered: a positive impact of this element is recorded on both HAI prevalence (-27%) and antimicrobials prescribed with no specified reason (-32%).

The seeming contradiction is probably explained by the fact that "antimicrobial stewardship" can be considered an umbrella term[53], i.e. a cross-functional word encompassing all evidence-based strategies aimed at improving healthcare quality through optimization of antimicrobial use. Monitoring healthcare quality through wide-scope indicators undoubtedly represents a valuable resource, since it provides an overall view on many different management features, but must be interpreted very carefully, considering also more specific indicators[54]. Moreover, the available PPS database includes data on the provision of antimicrobial stewardship advice in the hospitals, but not on its correct implementation in the everyday clinical practice. For instance, no data are available on the presence and impact of the stewardship round and on the level of synergy between

antibiotic stewardship consultants and clinical team, which is crucial to promote reduction of inappropriate antibiotic use.

Not coincidentally, routine execution of post-prescription review is often used as specific antibiotic stewardship indicator[35], first because this is an element effectively reducing antimicrobial prescriptions[36], and also because this intervention has proved to be successful both in modifying physicians' behaviour towards antibiotic prescription[55] and in creating a relationship of confidence and co-operation among teams handling patients' therapies[56], thus working as an actual drive for stewardship.

Among the strengths of this research, the study design must be mentioned: the analysis has been projected by using national-level data, and by reviewing what was a priori known about possible relationships among variables involved, to investigate the relationship between the potential determinants monitored by the European PPS and two of the main outcomes of the surveillance. This acquires further importance, as relating determinants to outcomes is key to performing appropriate healthcare evaluations.

Nevertheless, some limitations must be acknowledged: a first shortcoming comes from the fact that healthcare facilities participated in the surveillance on a voluntary basis, after responding to regional coordinators' requests. Hence, this convenience sampling may have suffered from selection biases and lack of representativeness[57], especially considering the great heterogeneity between healthcare services in different Italian regions and the reduced participation of hospitals from Southern Italy (where some hospitals may have opted for not participating due to organisational issues): for instance, the proportion of medium- and high-size hospitals in our sample is slightly higher than the true proportion among Italian hospitals. However, although such a sampling might slightly alter local prevalence estimates and comparisons between Northern and Southern regions, it is very unlikely to bias the relationships between determinants and outcomes, particularly considering that these were evaluated via adjusted models.

The final 55-hospital subsample tried to provide a solution to the issue of the representativeness of data provided to the ECDC for the European prevalence computation[58]: however, unluckily, the model proposed in this study would be hardly reproducible on that subsample, since there would not be a sufficient sample size to obtain estimates with sufficient statistical power. Repeating this study on a larger group of hospitals, possibly from several countries, would help to obtain more robust (and less setting-dependent) estimates of the actual effect of various determinants on examined outcomes.

Another possible limitation lies in the fact that this analysis proposes a causal inference model based on data from a prevalence survey, and therefore attempts to detect cause-effect relationships (whose development needs a latency period) starting from point data. However, the conditions for building an aetiological hypothesis starting from available prevalence data are almost all apparently met, such as stable patient population and lack of effect of the investigated variables on the duration of HAIs once acquired[59]. Instead, our study is rooted in the assumption that the evaluated hospital IPC strategies are not directly affected by the HAI prevalence observed during the study (inverse causation). Although not testable, this assumption can be based on the low probability that the great majority of participating hospitals changed their IPC strategies in response to an increase in HAI prevalence close to the time of the PPS. Instead, it is reasonable to suppose that changes in the IPC strategies were distributed over the years and there was enough time for HAI prevalence to return to the expected steady state, given the strategies in place. Eventually, the survey was conducted with a prevalence design (i.e. within a maximum of 2 days in each wards), and data collection between different wards/hospitals was performed within a maximum time lag of some weeks between one facility and another, so the impact of temporal effects can be assumed to be negligible.

Conclusions

The latest PPS was the first prevalence survey for HAIs and antibiotic use since the SARS-CoV-2 pandemic, which has brought disruptive effects on all healthcare systems, and consequently also on HAIs and IPC procedures. A correct interpretation of the results of this study could have implications for planning and re-organizing adequate measures to prevent and control HAIs and antimicrobial resistance. The results of this study might represent an interpretation tool for healthcare workers and policy-makers, possibly helpful to effectively translate PPS data into organizational and behavioural changes[49,60], encouraging efforts at a local and national level to improve major indicators in those hospitals identified as lacking.

Specifically, our study and relevant comparisons with the previous papers highlight the importance of the following elements: routine production of IPC plans and reports, implementation of adequate HAI prevention measures, routinely performed post-prescription review, and presence - within the staff - of an appropriate number of IPC nurses and professionals (consultants) specifically devoted to antibiotic stewardship. These variables proved to be associated with reducing HAIs and potentially inappropriate antimicrobial use, but they also showed to work as specific indicators, to be reasonably considered for targeted and evidence-based surveillance. Moreover, the proportion of single-bed rooms in the hospital is the only structural determinant with a significant (positive) impact on HAI prevalence.

The other indicators, at least in their current form, appear not to be associated with significant variations in the outcomes. This result does not automatically reduce the value of such indicators, nor does it imply that their monitoring is unnecessary: however, it may suggest that such indicators need a revision, or at least particular attention is required while interpreting and using them to evaluate healthcare facilities or health systems.

Data availability

The datasets used and/or analysed during the current study, as well as the relevant codes, are available from the corresponding author on reasonable request.

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Disclaimer

The views and opinions expressed herein are the authors' own and do not necessarily state or reflect those of ECDC. ECDC is not responsible for the data and information collation and analysis and cannot be held liable for conclusions or opinions drawn.

Author contributions

AD, CV, FQ and CMZ conceptualised the study; AD, CV and FQ were involved in data curation; JG, AD and CV performed the formal analysis, and JG and AD developed software codes. JG, CV, FQ and CMZ con-

tributed to validation and visualisation of the results achieved. CMZ supervised the work and co-ordinated the project. All the authors participated in the writing, both for the original drafting and for the review and editing. All the authors read and approved the final manuscript and agreed to the final submission.

Declarations

Ethics approval and consent to participate

Ethical board approval was obtained by the hospital institutions and local health authorities for each region, as specified in a previous paper[10].

Competing interests

The authors declare no competing interests.

Additional information

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