ORIGINAL ARTICLE

Determinants of Implementation of Isolation Precautions Against Infections by Multidrug-Resistant Microorganisms: A Hospital-Based, Multicenter, Observational Study

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OBJECTIVES. We aimed to ascertain the factors associated with lack of isolation precautions (IP) in patients infected or colonized by third-generation cephalosporin-resistant *Enterobacteriaceae* (3GCR-E) and methicillin-resistant *Staphylococcus aureus* (MRSA) in hospital settings.

DESIGN. Prospective surveillance and audit of practices.

SETTING. The study included 4 university hospitals in Lyon, France.

PARTICIPANTS. All patients hospitalized between April and June in 2013 and 2015 were included. Case patients had ≥1 clinical sample positive for MRSA and/or 3GCR-E.

METHODS. Factors associated with the lack of IP implementation were identified using multivariate logistic regression. The incidence of MDRO infections was expressed per 10,000 patient days.

RESULTS. Overall, 57,222 patients accounting for 192,234 patient days of hospitalization were included, and 635 (1.1%) MDRO cases were identified. MRSA incidence was 2.5 per 10,000 patient days (95% confidence interval [95% CI], 2.1–3.0) and 3GCR-E incidence was 10.1 per 10,000 patient days (95% CI, 9.2–11.0), with no crude difference between 2013 and 2015 ($P = .15$ and $P = .11$, respectively). Among 3GCR-E, the main species were *Escherichia coli* (43.8%) and *Klebsiella pneumoniae* (31.0%). Isolation precautions were implemented in 78.5% of cases. Lack of IP implementation was independently associated with patient age, year, specialty, hospital, colonization compared with infection, and lack of medical prescription for IPs (adjusted odds ratio, 17.4; 95% CI, 8.5–35.8; $P < .001$).

CONCLUSIONS. MRSA and 3GCR-E infections and/or colonizations are frequent in healthcare settings, and IPs are implemented in most cases. When IPs are lacking, the main factor is the absence of medical prescription for IPs, underscoring the need for alerts to physicians by the microbiological laboratory and/or the infection control team.

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Multidrug-resistant microorganisms (MDROs) are a major concern in infection control.[1] The 2 most prevalent MDRO in hospital settings are third-generation cephalosporin-resistant *Enterobacteriaceae* (3GCR-E), typically represented by extended spectrum β-lactamase–producing *Enterobacteriaceae* (ESBL-E) and methicillin-resistant *Staphylococcus aureus* (MRSA).[2] These bacteria induce substantial morbidity and mortality in hospital settings. MRSA bacteremia has been associated with 2-fold increased mortality compared to sensitive strains,[3] whereas ESBL-E bacteremia has been linked by meta-analysis to 1.85-fold augmented relative risk of death.[4] MRSA incidence has decreased in many European countries in recent years,[5,6] and 3GCR-E incidence has increased during the same period.[7,8] Similar trends have been observed in the United States[9,10] and Asia.[11]

Contact precautions against MDRO are a major component of most infection control strategies.[12] They are effective in controlling MDRO transmission during hospital outbreaks,[13] despite repeated discussion of efficacy, compared to consistent implementation of standard precautions or other measures.[14,15] While it has been described in some settings, compliance with isolation precautions (IPs) has been assessed in a nonoutbreak context less frequently. Factors associated with lack of IP implementation could guide future strategies to improve

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compliance with IPs and limit MDRO spread. Barriers to IP implementation may be related to patient characteristics, type of infection (ie, urinary tract vs other infections) or organizational factors (ie, specialty or medical prescription for IPs). To the best of our knowledge, these factors have rarely been reported, and the relationships between them have been poorly investigated in a nonoutbreak context.[16,17]

In view of the changing epidemiology of MDRO in hospitals and the dearth of knowledge of IPs against MDRO infections, we conducted a multicenter, hospital-based, observational study and an audit of practices at our university center in France. Our primary study objective was to identify factors associated with lack of IP implementation in patients infected or colonized with MRSA and 3GCR-E. The secondary objectives were to estimate the incidence of infections and/or colonizations with MRSA and 3GCR-E and to report IP compliance in 2015 compared to 2013.

METHODS

Standardized monitoring of IPs and epidemiological surveillance were undertaken for all patients hospitalized between April 1, 2013, and June 30, 2013, and between April 1, 2015, and June 30, 2015, in 4 Lyon University hospitals in France: Hôpital de la Croix-Rousse, Hôpital Edouard Herriot, Hôpital Gériatrique, and Hôpital Lyon-Sud. Surveillance of a local section of the MDRO Surveillance Network in southeastern France was based on standardized definitions.[18] Implementation of IPs was based on a local protocol (Table 1); patients with MRSA nasal carriage without any site of infection or respiratory sign do not necessitate isolation precautions. Information on new positive culture results for MRSA and 3GC-E are normally reported in the electronic medical record, and microbiological staff orally inform practitioners. In addition, an automatic daily e-mail was sent to infection control practitioners. Overall, 3,713 and 3,454 hospital beds were monitored in 2013 and 2015, respectively.

Each MDRO case patient had at least 1 positive clinical sample of MRSA or 3GCR-E after culture. The exclusion criterion was MRSA or 3GCR-E detection by rectal, nasal, or cutaneous screening. A standardized data collection form was completed for each case, with information on demographic characteristics, microbiological results, infections or colonizations, and acquisition type (hospital-acquired or imported). Colonization was defined as identification of MRSA or a 3GCR-E from a clinical sample, without clinical and therapeutic consequences for the patient, at a level below microbiological threshold. Infection was clinically defined as identification of MRSA or a 3GCR-E above the microbiological threshold, with clinical and/or radiological signs. This information was validated by an infection control practitioner, and uncertain cases were discussed with the physician in charge of the patient. For each patient, a new MDRO event was counted if (1) another clinical sample was positive from the same patient during study period but with different species or (2) another clinical sample from the same patient identified the same species with different antibiogram. An additional questionnaire concerning IPs was completed for type of isolation measures recommended and observed, prescription, and personal protective equipment available (Table 1). This form was filled out either by observation (30.0%) or by telephone contact (70.0%) with a healthcare worker from the unit.

Bacteria were identified using biochemical strips (Vitek 2 or Vitek Compact System, bioMérieux, Marcy l'Étoile, France) or matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry (Vitek MS System, bioMérieux). For *Enterobacteriaceae*, 3GCR-E was analyzed by broth dilution (Vitek 2 System, bioMérieux) or diffusion with antibiotic (ceftazidim, ceftriaxone, and cefotaxim) discs (SIRScan System, i2a, Perols Cedex, France). MRSA was recognized by cefoxitin testing with broth dilution (Vitek 2 System, bioMérieux), diffusion with cefoxitin disc (SIRScan System, i2a), *mecA* gene detection with "homemade" polymerase chain reaction, or PLP2a (PBP2a Culture Colony Test, Alere, Waltham, MA).

TABLE 1. Recommended Measures in Cases of Methicilin-Resistant *Staphylococcus aureus* (MRSA) or Cultures Positive for Third-Generation Cephalosporin-Resistant *Enterobacteriaceae* (3GCR-E) in University of Lyon Hospitals

Characteristics	Microorganism					
	Positive for MRSA			Positive for 3GCR-E		
Clinical site	Nasal[a]	Pulmonary	Blood, Urinary, or Other	Rectal[a]	Pulmonary	Blood, Urinary, or Other
Type of isolation						
No isolation	Yes	No	No	No	No	No
Contact precautions	No	Yes	Yes	Yes	Yes	Yes
Droplet precautions	No	Yes[b]	No	No	Yes[b]	No
HCW responsible for starting isolation	MD	MD	MD	MD	MD	MD
Medical prescription for isolation precautions	Yes	Yes	Yes	Yes	Yes	Yes
Automated post-discharge reminder	No	No	No	No	No	No

NOTE. HCW, healthcare worker; MD, medical doctor.
[a]Site not included in the present study.
[b]If respiratory signs are present.

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A descriptive analysis was conducted. Incidence was calculated per 10,000 patient days of hospitalization. Incidences were compared with a mid-*P* exact test, and crude incidence ratios were calculated according to the type of unit. Categorical variables were reported as numbers and percentages and were compared using the χ^2 test. Continuous variables were described as mean (± standard deviation) and were compared using the Student *t* test. The following factors were potentially associated with lack of IP implementation: gender, age (<50 years, 50–59 years, 60–69 years, 70–79 years, ≥80 years), study year (2015 vs 2013), specialty (acute care, intensive care, rehabilitation, extended stay facility, nursing home, or psychiatric facility), hospital center (A, B, C, and D), microorganism, infection versus colonization, hospital-acquired versus imported infection, anatomical site (blood, deep wound, pulmonary protected or nonprotected samples, urine, other), time between admission and onset of infection (day 0, days 1–2, days 3–9, days 10–29, ≥ day 30), type of isolation indicated (contact only, contact and droplets, or other), and medical prescription for IPs. After univariate logistic regression analysis of factors associated with lack of IP implementation, variables with *P* values <.10 were entered in the initial multivariate model. Variables then underwent backward stepwise deletion with the Wald test until all *P* values were <.05. Major relevant interactions were also tested; no interaction was finally retained in the multivariate model. All tests were 2-tailed, and $P < .05$ was considered significant. Analyses were conducted with Stata 13.0 software (StataCorp LP, College Station, TX). The study did not require ethics committee approval because it drew from an observational surveillance database approved under French national regulations (*Comité National Informatique et Liberté*). The data were analyzed anonymously, and patient care was not affected.

RESULTS

Overall, 57,222 patients were included in the study (29,136 in 2013 and 28,386 in 2015), accounting for 505,947 patient days of hospitalization (257,351 patient days in 2013 and 248,616 patient days in 2015). A total of 635 MDRO cases occurred overall, for a global attack rate of 1.3 (95% confidence interval [95% CI], 1.0–1.2) per 100 patients and an incidence of 12.5 (95% CI, 11.6–13.6) MDRO infections per 10,000 patient days. Crude incidence rates were somewhat stable in 2013 and 2015 for MRSA ($P = .28$) and 3GCR-E ($P = .14$; Table 2). The highest incidence of MDRO was found in intensive care units (ICUs) compared with extended-stay facilities and nursing homes. Among MDRO case patients, the male:female ratio was 1.3, and the mean age was 68.2 years (±19.3). Moreover, 268 infections (42.2%) were acquired in a hospital, and 348 infections (54.8%) were imported. Overall, 126 MRSA cases (19.8%) and 509 3GCR-E cases (80.2%) comprised the MDRO burden. The main 3GCR-E species were *Escherichia coli* (n = 223; 43.8%), *Klebsiella pneumoniae* (n = 158; 31.0%), *Enterobacter cloacae* (n = 60; 11.8%), *Citrobacter freundii* (n = 20; 3.9%), and *Enterobacter aerogenes* (n = 16; 3.1%). Urinary tract infections accounted for almost half of MDRO cases (n = 316; 49.8%). The other most prevalent infection sites were blood culture (9.9%) and pulmonary (protected) samples (8.5%) and pulmonary (nonprotected) samples (7.1%). Among 3GCR-E, 20 of 509 (2.8%) were also resistant to carbapenems. Table 3 reports the 3GCR-E and MRSA cases encountered. MRSA differed from

TABLE 2. Incidence of Methicilin-Resistant *Staphylococcus aureus* (MRSA) and Third-Generation Cephalosporin-Resistant *Enterobacteriaceae* (3GCR-E) Infections by Specialty and Year in University of Lyon Hospitals, 2013 and 2015 (n = 57,222)

	2013		2015				Overall	
Characteristics	No. of Infections/No. of Patient Days	Incidence (95% CI)[a]	No. of Infections/No. of Patient Days	Incidence (95% CI)[a]	Crude IRR[b]	*P* Value[b]	No. of Infections/No. of Patient Days	Incidence (95% CI)[a]
MRSA infections								
Overall	73/257,331	2.8 (2.2–3.5)	53/248,616	2.1 (1.6–2.8)	0.82 (0.57–1.20)	.28	126/505,947	2.5 (2.1–3.0)
Short stay	40/159,759	2.5 (1.8–3.4)	35/153,954	2.3 (1.6–3.1)	0.91 (0.56–1.47)	.68	75/313,713	2.4 (1.9–3.0)
Intensive care	15/10,464	14.3 (8.3–23.1)	8/10,198	7.8 (3.6–14.9)	0.55 (0.20–1.37)	.17	23/20,662	11.1 (7.2–16.4)
Rehabilitation	13/43,092	3.0 (1.7–5.0)	6/42,128	1.4 (0.6–3.0)	0.47 (0.14–1.33)	.13	19/85,220	2.2 (1.4–3.4)
Extended-stay facility	4/33,913	1.2 (0.4–2.8)	3/35,157	0.9 (0.2–2.3)	0.72 (0.11–4.28)	.69	7/69,070	1.0 (0.4–2.0)
Nursing home	0/7,383	0.0	1/7,179	1.4 (0.07–6.9)	NE	.49	1/14,562	0.7 (0.03–3.4)
3GCR-E infections								
Overall	242/257,331	9.4 (8.3–10.6)	267/248,616	10.7 (9.5–12.1)	1.14 (0.96–1.36)	.14	509/505,947	10.1 (9.2–11.0)
Short stay	150/159,759	9.4 (8.0–11.0)	170/153,954	11.0 (9.5–12.8)	1.18 (0.94–1.47)	.15	320/313,713	10.2 (9.1–11.4)
Intensive care	53/10,464	50.6 (38.3–65.7)	44/10,198	43.1 (31.7–57.4)	0.85 (0.56–1.29)	.43	97/20,662	46.9 (38.3–57.0)
Rehabilitation	33/43,092	7.7 (5.4–10.6)	44/42,128	10.4 (7.7–13.9)	1.36 (0.85–2.21)	.18	77/85,220	9.0 (7.2–11.2)
Extended-stay facility	6/33,913	1.8 (0.7–3.7)	7/35,157	2.0 (0.9–3.9)	1.13 (0.32–4.05)	.84	13/69,070	1.9 (1.0–3.1)
Nursing home	0/7,383	0.0	1/7,179	1.4 (0.07–6.9)	NE	.49	1/14,562	0.7 (0.03–3.4)

NOTE. CI, confidence interval; IRR, incident rate ratio.

[a]Per 10,000 patient days.

[b]2015 compared with 2013 (reference).

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TABLE 3. Characteristics of Methicilin-Resistant *Staphylococcus aureus* (MRSA) and Third-Generation Cephalosporin-Resistant *Enterobacteriaceae* (3GCR-E) Infections in Lyon University Hospitals, 2013 and 2015 (n = 635)

Characteristics, No. (%)[a]	MRSA (n = 126)	3GCR-E (n = 509)	*P* Value
Gender			.97
Male	72 (57.1)	290 (57.0)	
Female	54 (42.9)	219 (43.0)	
Age, y, mean (SD)	67.3 (22.8)	68.4 (18.3)	.58
Age category			.02
<50 y	24 (19.0)	69 (13.6)	
50–59 y	16 (12.7)	62 (12.2)	
60–69 y	15 (11.9)	99 (19.4)	
70–79 y	17 (13.5)	113 (22.2)	
≥80 y	54 (42.9)	166 (32.6)	
Year			.04
2013	73 (57.9)	242 (47.5)	
2015	53 (42.1)	267 (52.5)	
Specialty			.14
Acute care	65 (57.0)	289 (60.7)	
Intensive care	21 (18.4)	95 (20.0)	
Rehabilitation	19 (16.7)	77 (16.2)	
Extended-stay facility, nursing home, psychiatric facility	9 (7.9)	15 (3.1)	
Hospital centers			.28
Hospital A	25 (19.8)	94 (18.5)	
Hospital B	21 (16.7)	56 (11.0)	
Hospital C	29 (23.0)	144 (28.3)	
Hospital D	51 (40.5)	215 (42.2)	
Type of infection			.25
Colonization	39 (32.5)	130 (27.2)	
Infection	81 (67.5)	348 (72.8)	
Origin			.38
Imported	50 (40.0)	218 (44.4)	
Hospital-acquired	75 (60.0)	273 (55.6)	
Site of infection			<.001
Blood	23 (18.2)	40 (7.8)	
Deep wound	11 (8.7)	34 (6.7)	
Pulmonary, protected	12 (9.5)	42 (8.2)	
Pulmonary, nonprotected	19 (15.1)	26 (5.1)	
Urine	23 (18.2)	293 (57.6)	
Other	38 (30.2)	74 (14.5)	
Time between admission and infection			.28
0 d	30 (23.8)	103 (20.2)	
1–2 d	22 (17.5)	82 (16.1)	
3–9 d	16 (12.7)	104 (20.4)	
10–29 d	26 (20.6)	114 (22.4)	
≥30 d	32 (25.4)	106 (20.8)	

NOTE. IQR, interquartile range; SD, standard deviation.
[a]Unless otherwise specified.

3GCR-E cases by age ($P = .02$), year ($P = .04$), and site of infection ($P < .001$). The proportion of 3GCR-E acquired in hospital decreased from 50.4% in 2013 to 39.2% in 2015 ($P = .01$), whereas MRSA proportion was stable. MDRO cases did not differ regarding main characteristics between 2013 and 2015 (Table 4).

TABLE 4. Characteristics of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Third-Generation Cephalosporin-Resistant *Enterobacteriaceae* (3GCR-E) Infections in Lyon University Hospitals, 2013 and 2015 (n = 635)

Characteristics	2013 (n = 315), No. (%)[a]	2015 (n = 320), No. (%)[a]	*P* Value
Gender			.12
Male	170 (54.0)	128 (40.0)	
Female	145 (46.0)	192 (60.0)	
Age, y, mean (SD)			.10
<50 y	53 (17.8)	37 (11.6)	
50–59 y	36 (11.4)	42 (13.1)	
60–69 y	60 (19.1)	54 (16.9)	
70–79 y	66 (20.9)	64 (20.0)	
≥80 y	97 (30.8)	123 (38.4)	
Microorganism			.04
MRSA	73 (23.2)	53 (16.6)	
3GCR-E	242 (76.8)	267 (83.4)	
Specialty			.50
Acute care	177 (59.0)	177 (61.0)	
Intensive care	66 (22.0)	50 (17.2)	
Rehabilitation	46 (15.3)	50 (17.2)	
Extended-stay facility, nursing home, psychiatric facility	11 (3.7)	13 (4.5)	
Hospital centers			.34
Hospital A	65 (20.6)	54 (16.9)	
Hospital B	37 (11.8)	40 (12.5)	
Hospital C	77 (24.4)	96 (30.0)	
Hospital D	136 (43.2)	130 (40.6)	
Type of infection			.12
Colonization	75 (25.3)	94 (31.1)	
Infection	221 (74.7)	208 (68.9)	
Origin			.07
Imported	142 (47.2)	126 (40.0)	
Hospital-acquired	159 (52.8)	189 (60.0)	
Site of infection			.15
Blood	30 (9.5)	33 (10.3)	
Deep wound	15 (4.8)	30 (9.4)	
Pulmonary, protected	30 (9.5)	24 (7.5)	
Pulmonary nonprotected	20 (6.3)	25 (7.8)	
Urine	157 (49.8)	159 (49.7)	
Other	63 (20.0)	49 (15.3)	
Time between admission and colonization/infection			.20
0 d	58 (18.4)	75 (23.4)	
1–2 d	50 (15.9)	54 (16.9)	
3–9 d	58 (18.4)	62 (19.4)	
10–29 d	69 (21.9)	71 (22.2)	
≥30 d	80 (25.4)	58 (18.1)	

NOTE. SD, standard deviation.
[a]Unless otherwise specified.

Overall, 461 (72.6%) MDRO case patients had an evaluation of IP implementation; the other patients were either discharged or deceased at time of IP evaluation. Among them, IPs were implemented in 76.0% of cases in 2013 and 81.4% in 2015

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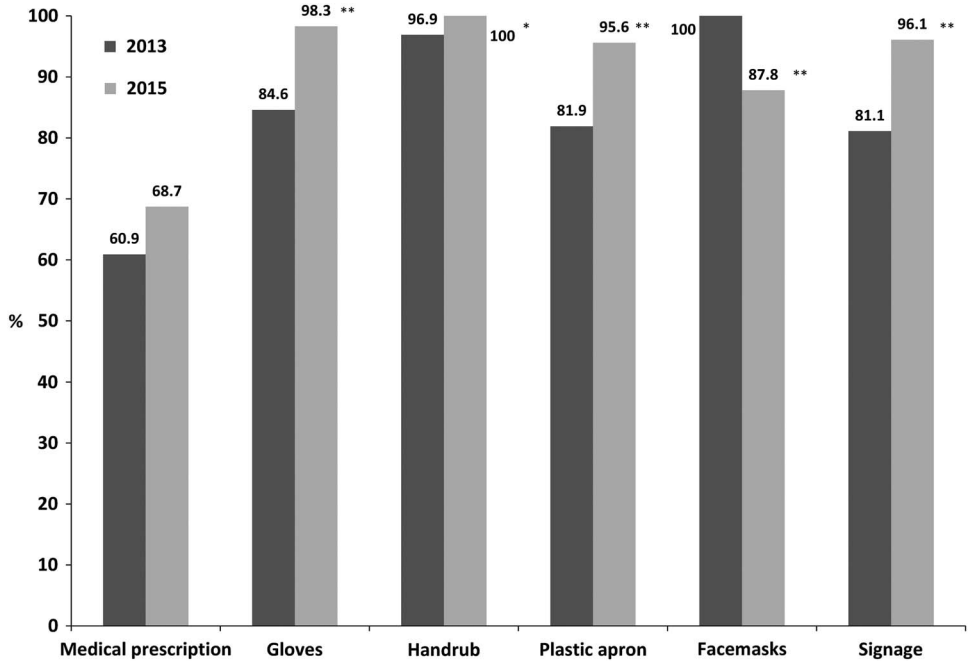


FIGURE 1. Measures implemented in patients infected and/or colonized by multidrug-resistant organisms under isolation precautions, Lyon University Hospitals, 2013 and 2015, (n = 477). *$P < .05$; *$P < .001$.

($P = .16$), with no differences in temporal trends by hospital. However, IP implementation improved from 74.2% in 2013 to 87.1% in 2015 ($P = .01$) for patients with imported MDRO infection and/or colonization. Isolation precautions were implemented for 73% of patients on the day the test results were obtained, and for 91% on the day of medical prescription for IPs. Between 2013 and 2015, global improvement occurred in the presence of protective equipment, signage, and hand-rub solutions in patients with IPs (Figure 1).

Table 5 shows the factors associated with lack of implementation of isolation precautions after univariate and multivariate analysis. The strength of the association between lack of medical prescription and absence of IPs was heterogeneous by specialty: crude odds ratios were respectively 15.4 (95% CI, 6.2–38.1; $P < .001$) in acute care, 9.7 (95% CI, 3.1–31.1; $P < .001$) in intensive care, and 24.8 (95% CI, 5.3–115.4; $P < .001$) in rehabilitation. On multivariate analysis, patient age, year, specialty, hospital, colonization versus infection, and lack of medical prescription for IPs were independent predictors of lack of IP implementation (Table 5). Lack of medical prescription for IPs was strongly associated with the absence of IPs (adjusted odds ratio, 17.4; 95% CI, 8.5–35.8; $P < .001$).

DISCUSSION

The main objective of the study was to assess the determinants of lack of IP implementation in MDRO cases. We found that incidence was stable during this period, but the proportion of nosocomial-acquired MDRO infection and/or colonization decreased. Several factors were associated with the lack of IP implementation, but medical prescription for IPs was the main modifiable, contributing component. Significant differences in MDRO incidence were observed between specialties with higher frequency in ICUs. Our estimates agree with those of earlier French national surveillance, which reported MRSA and ESBL-E incidence rates of 0.40 and 0.39 per 1,000 patient days, with the highest incidence in ICUs.[18] More recently, in Germany, MRSA incidence decreased between 2010 and 2014 (relative risk, 0.88; 95% CI, 0.84–0.91).[5] The increased proportion of imported 3GCR-E infections and/or colonizations underlines the growing importance of community acquisition in the hospital burden of 3GCR-E, caused mainly by international travel and inappropriate antibiotic use but also by community acquisition.[19] We observed similar trends in our study population.

Isolation precautions were applied frequently, sometimes despite a lack of medical prescription for IPs. After adjusting to confounding factors, 30% improvement of IP implementation was seen between the 2 study periods, while no major transversal campaign was instituted during this time. Improvement may be partially due to frequent on-site visits by infection control professionals in recent years in our hospitals, particularly in geriatric units. Continuous, prospective surveillance of MDRO cases is ongoing in all short- and extended-stay geriatric units. Each time a case is identified, an infection control professional calls the unit to establish whether IPs have been applied and whether they are appropriate. Protective equipment is most often present and is the consequence of an institutional campaign for the standardization of supports for patients who need complementary precautions.

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TABLE 5. Factors Associated With Lack of Implementation of Isolation Precautions in Lyon University Hospitals, 2013 and 2015 (N = 461)

Characteristics	Isolation Precautions, No. (%)	No Isolation Precautions, No. (%)	*P* Value	Crude Odds Ratio (95% CI)[a]	Adjusted Odds Ratio (95% CI)[a,b]
Gender			.09		
Female	200 (55.2)	64 (64.6)		1.0 (ref.)	…
Male	162 (44.8)	35 (35.4)		0.7 (0.4–1.1)	…
Age category			.04		
< 50 y	55 (15.2)	12 (12.1)		1.0 (ref.)	1.0 (ref.)
50–59 y	45 (12.4)	21 (21.2)		2.1 (1.0–4.8)	3.9 (1.3–12.1)
60–69 y	57 (15.7)	22 (22.2)		1.8 (0.8–3.9)	1.4 (0.5–4.2)
70–79 y	77 (21.3)	21 (21.2)		1.2 (0.6–2.8)	1.0 (0.3–2.7)
≥80 y	128 (35.4)	23 (23.3)		0.8 (0.4–1.8)	0.9 (0.3–2.6)
Year			.16		
2013	187 (51.7)	59 (59.6)		1.0 (ref.)	1.0 (ref.)
2015	175 (48.3)	40 (40.4)		0.7 (0.5–1.1)	0.7 (0.5–1.0)
Specialty			.01		
Acute care	187 (54.0)	55 (57.9)		1.0 (ref.)	1.0 (ref.)
Intensive care	75 (21.7)	18 (19.0)		0.8 (0.4–1.5)	1.6 (0.7–3.7)
Rehabilitation	72 (20.8)	12 (12.6)		0.6 (0.3–1.1)	1.4 (0.5–3.7)
Extended-stay facility, nursing home, psychiatric facility	12 (3.5)	10 (10.5)		2.8 (1.2–6.9)	27.8 (5.8–133.0)
Hospital centers			<.001		
Hospital A	71 (19.6)	8 (8.1)		1.0 (ref.)	1.0 (ref.)
Hospital B	54 (14.9)	9 (9.1)		1.5 (0.5–4.1)	0.8 (0.1–4.9)
Hospital C	96 (26.5)	17 (17.2)		1.6 (0.6–3.8)	1.7 (0.6–5.1)
Hospital D	141 (39.0)	65 (65.6)		4.1 (1.9–9.0)	4.4 (1.6–11.7)
Microorganism			.50		
MRSA	67 (18.5)	19 (19.2)		1.0 (ref.)	…
Enterobacter cloacae	42 (11.6)	9 (9.1)		0.8 (0.3–1.8)	…
Escherichia coli	121 (33.4)	40 (40.4)		1.2 (0.6–2.2)	…
Klebsiella pneumoniae	95 (26.2)	19 (19.2)		0.7 (0.3–1.4)	…
Other 3GCR-E	37 (10.2)	12 (12.1)		1.1 (0.5–2.6)	…
Type of infection			.02		
Infection	103 (29.4)	17 (17.9)		1.0 (ref.)	1.0 (ref.)
Colonization	247 (70.6)	78 (82.1)		1.9 (1.1–3.4)	3.8 (1.6–8.7)
Origin			.26		
Hospital–acquired	164 (46.2)	51 (52.6)		1.0 (ref.)	…
Imported	191 (53.8)	46 (47.4)		0.8 (0.5–1.2)	…
Site of infection			.28		
Blood	27 (7.5)	9 (9.1)		1.0 (ref.)	…
Deep wound	23 (6.3)	12 (12.1)		1.6 (0.6–4.4)	…
Pulmonary, protected	34 (9.4)	12 (12.1)		1.1 (0.4–2.9)	…
Pulmonary nonprotected	29 (8.0)	5 (5.0)		0.5 (0.2–1.7)	…
Urine	176 (48.6)	46 (46.5)		0.8 (0.3–1.8)	…
Other	73 (20.2)	15 (15.2)		0.6 (0.2–1.6)	…
Delay between admission and infection, category			.31		
0 d	53 (14.6)	18 (18.2)		1.0 (ref.)	…
1–2 d	58 (16.0)	12 (12.1)		0.6 (0.3–1.4)	…
3–9 d	79 (21.8)	18 (18.2)		0.7 (0.3–1.4)	…
10–29 d	76 (21.0)	18 (18.2)		1.1 (0.6–2.2)	…
≥30 d	96 (26.5)	29 (29.3)		0.7 (0.3–1.4)	…
Type of isolation indicated			<.001		
Contact only	323 (91.2)	81 (88.0)		1.0 (ref.)	…
Contact and droplets	23 (6.5)	1 (1.1)		0.2 (0.02–1.3)	…
Other	8 (2.3)	10 (10.9)		5.0 (1.9–13.0)	…
Medical prescription for isolation precautions			<.001		
No	81 (23.2)	77 (81.9)		15.0 (8.4–26.8)	17.4 (8.5–35.8)
Yes	268 (76.8)	17 (18.1)		1.0 (ref.)	1.0 (ref.)

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*; 3GCR-E, third-generation cephalosporin-resistant *Enterobacteriaceae*; ref., reference.
[a]By logistic regression.
[b]Adjusted to the other covariates.

According to our local protocols, IP implementation warrants medical prescription. Despite recent improvements, lack of medical prescription is the main limiting factor in IP implementation, indicating that it is often not recognized as a core component of patient care by some physicians. Contact precautions are, however, widely recommended by international societies.[17]

In addition, other policies call for implementation of IPs by infection control personnel, without a physician order, or mandatory implementation of IPs, which presumably would not require a physician prescription or order when patients are colonized or infected with highly drug-resistant pathogens.[19,20] European guidelines recommend their application

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in hospitalized patients with detected or suspected MDRO infection or carriage, to limit nosocomial spread.[21] Moreover, errors or omission of medical prescription are frequent at hospital admission[22] or during hospital stay,[23,24] and these may be associated with increased risk of various adverse events, such as pressure ulcers.[25]

Other independent factors of IP absence are the medium age category of patients with better practices in younger and older populations. In acute or intensive care, the incidence of MRDO infections is high, but IP practices are good. However, units with lower risk of MDRO infections, namely, extended-stay facilities, nursing homes, and psychiatric facilities may have poorer practices. Particular attention must be given to specialties that are less aware of MDRO but are at risk of outbreaks.[26,27] Moreover, significant heterogeneity was observed between hospitals, even when all settings followed the same protocols and recommendations for IPs. This heterogeneity might be related more to local screening practices and IPs than to the type of study population. In addition, the probability of being isolated was greater in infected than in colonized patients, and their risk of transmission might be also higher.

This study had some limitations. First, screened patients with only positive nasal or rectal tests were excluded, while some of them might have needed contact precautions. However, patients with MRSA nasal carriage did not necessitate contact precautions according to our protocol. Second, although the study was prospective, there was a time lag between the identification of MDRO cases and investigation. Thus, some patients were already discharged at inclusion, and information was less reliable than direct observation. Third, although multivariate models were used to control for main cofounding variables, residual confounding (eg, change in staff who are eligible to write prescriptions for isolation or in training on isolation prescriptions between 2013 and 2015) might persist because such data were not prospectively collected. The study's main strengths were its multicenter design, which increased external validity, and the standardization of data collection.

In conclusion, MRSA and 3GCR-E infections and/or colonizations are frequent in French healthcare settings. Isolation precautions are implemented in most cases. When they are lacking, the main causative factor is the absence of medical prescription for IPs. Despite recurring discussions on the importance of IPs to control the spread of MRDO infections, their utility is demonstrated in both outbreak and nonoutbreak situations. Continuous monitoring with real-time advice from the infection control team and the microbiological laboratory should be promoted and evaluated.

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