Sistema Socio Sanitario
Carlo Poma
Regione Lombardia
ASST Mantova

Tavola rotonda:
STRATEGIAE DI PREVENZIONE E CONTROLLO IN EPOCA COVID

L'EPIDEMIOLOGIA ATTUALE

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ASST Carlo Poma Mantova

Sistema Sanitario Regione Lombardia





Tasso di incidenza di infezioni da SARS-CoV-2 (per 100.000 ab.) segnalate in Italia per Regione/PA di domicilio/residenza
(Periodo: 18 - 24/09/2023)



Casi di COVID-19 diagnosticati in Italia negli ultimi 30 giorni

125.384
Casi negli ultimi 30 giorni***

3.145
Casi tra gli operatori sanitari negli ultimi 30 giorni*

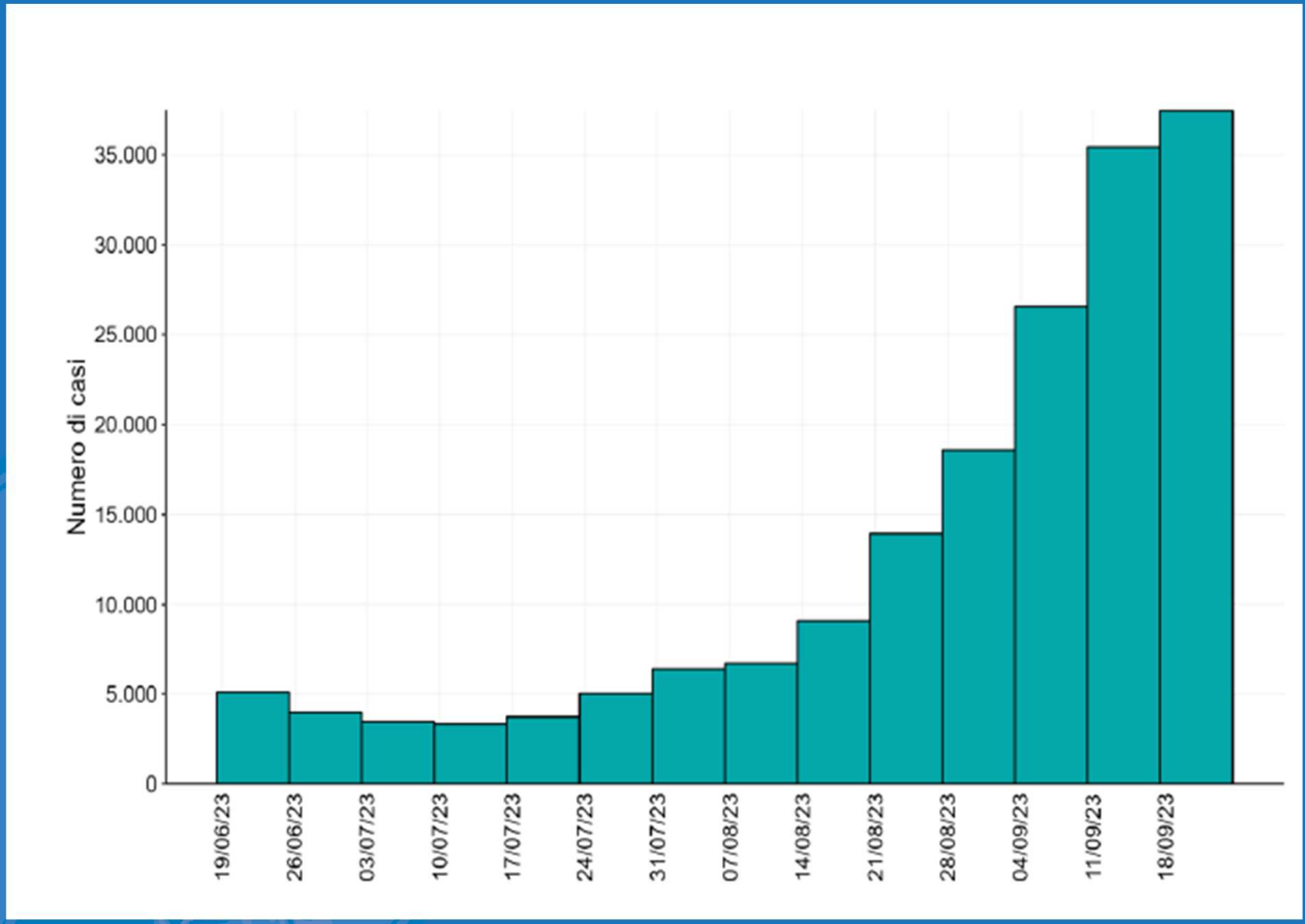
56 anni
Età mediana dei casi negli ultimi 30 giorni

43,2% | 56,8%
Maschi (%) | Femmine (%) negli ultimi 30 giorni

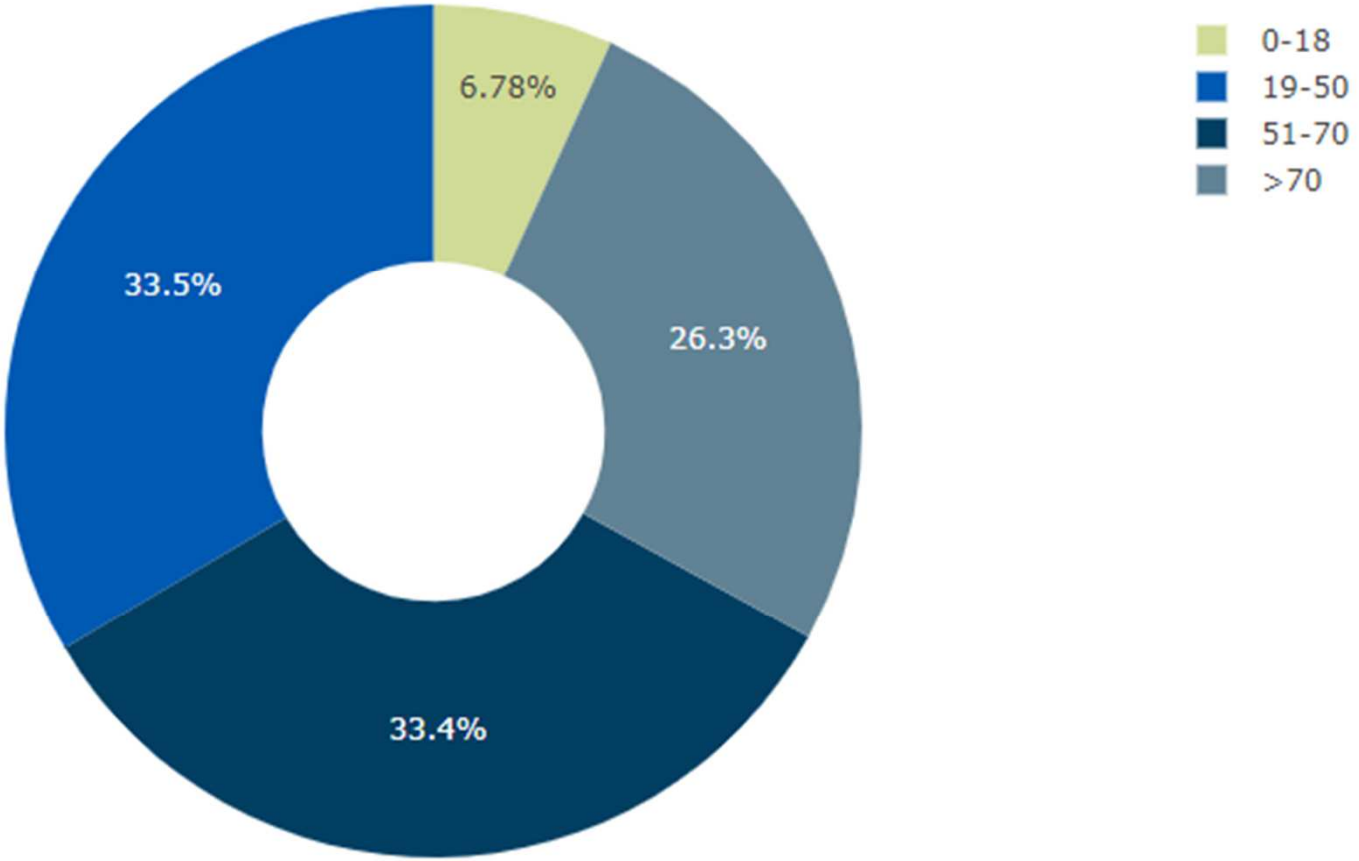
310
Deceduti negli ultimi 30 giorni**

62.854
Guariti negli ultimi 30 giorni**

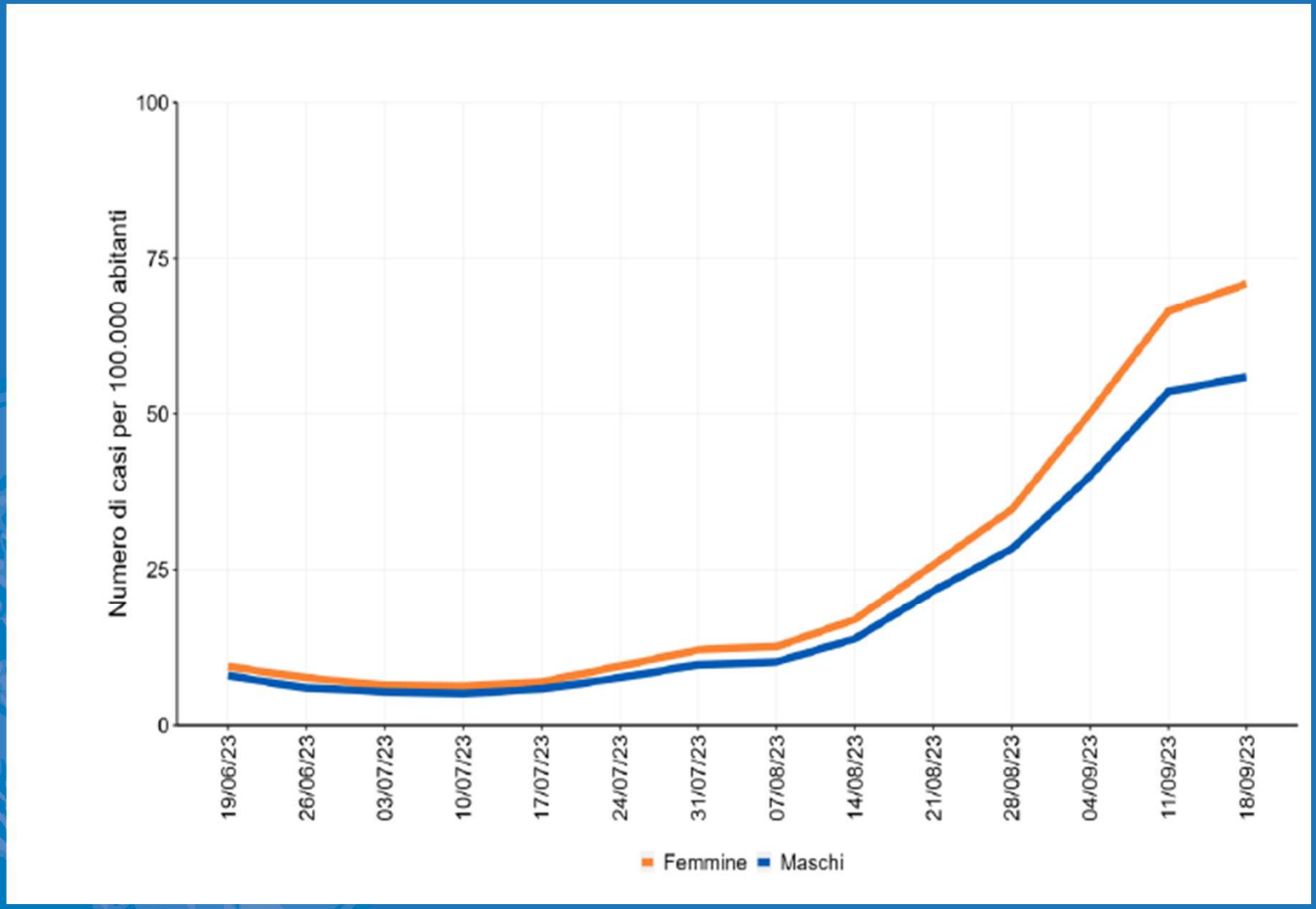
Curva epidemica dei casi di COVID-19 diagnosticati in Italia negli ultimi 30 giorni



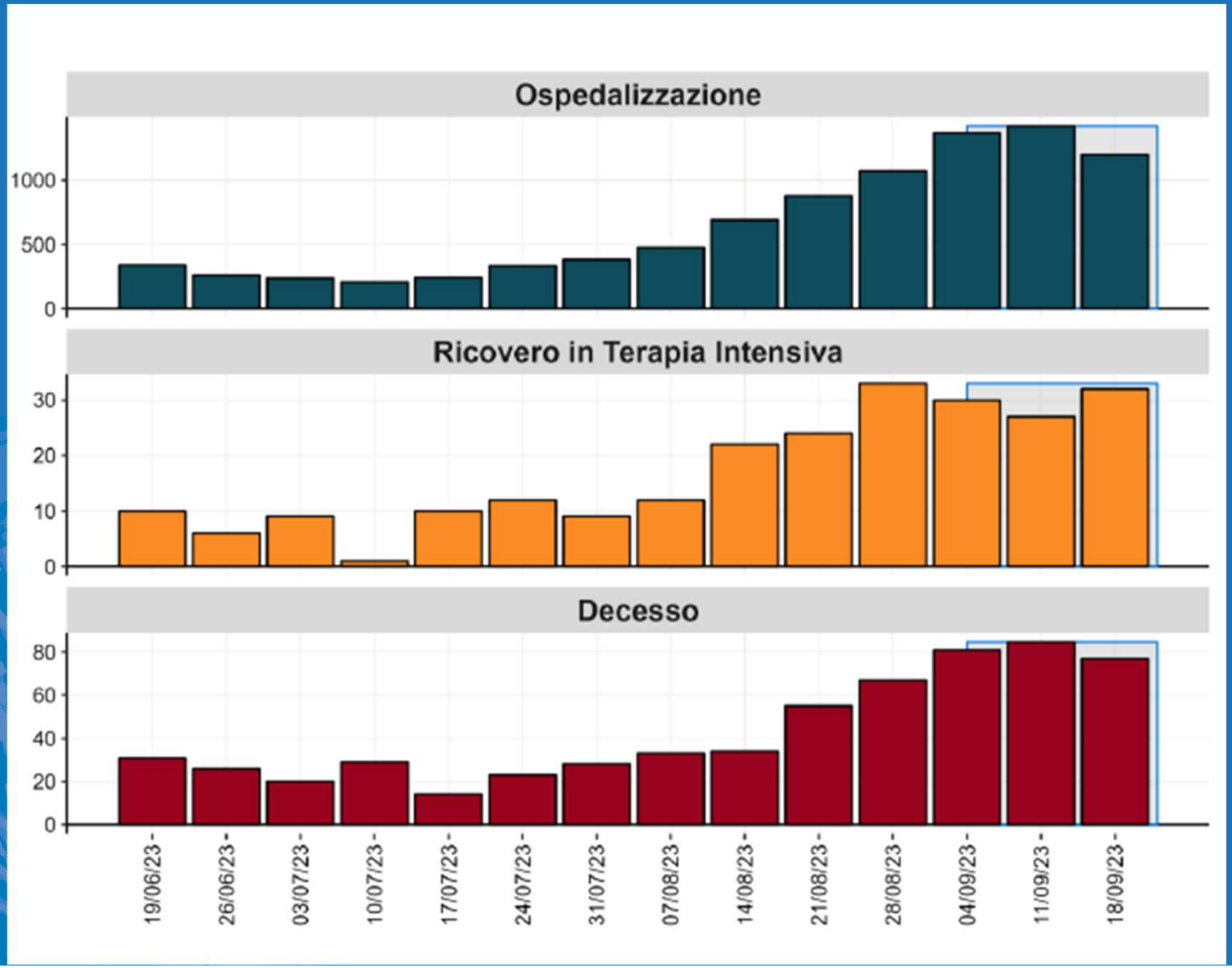
Proporzione (%) di casi di COVID-19 segnalati in Italia negli ultimi 30 giorni per classe di età (dato disponibile per 125.382 casi)



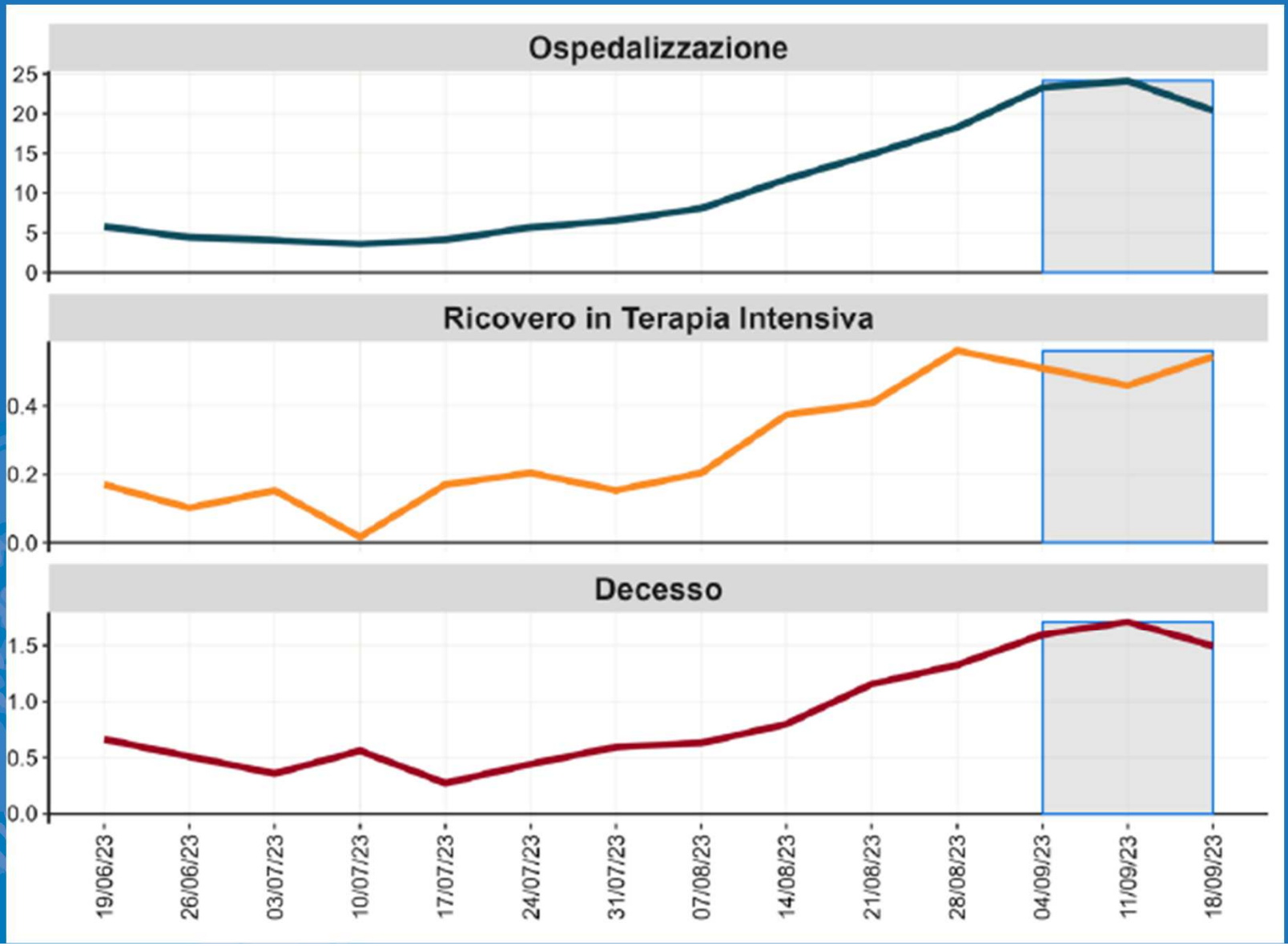
Incidenza settimanale di diagnosi di infezione da SARS-CoV-2 per 100.000 abitanti per sesso a partire dal 19 giugno 2023



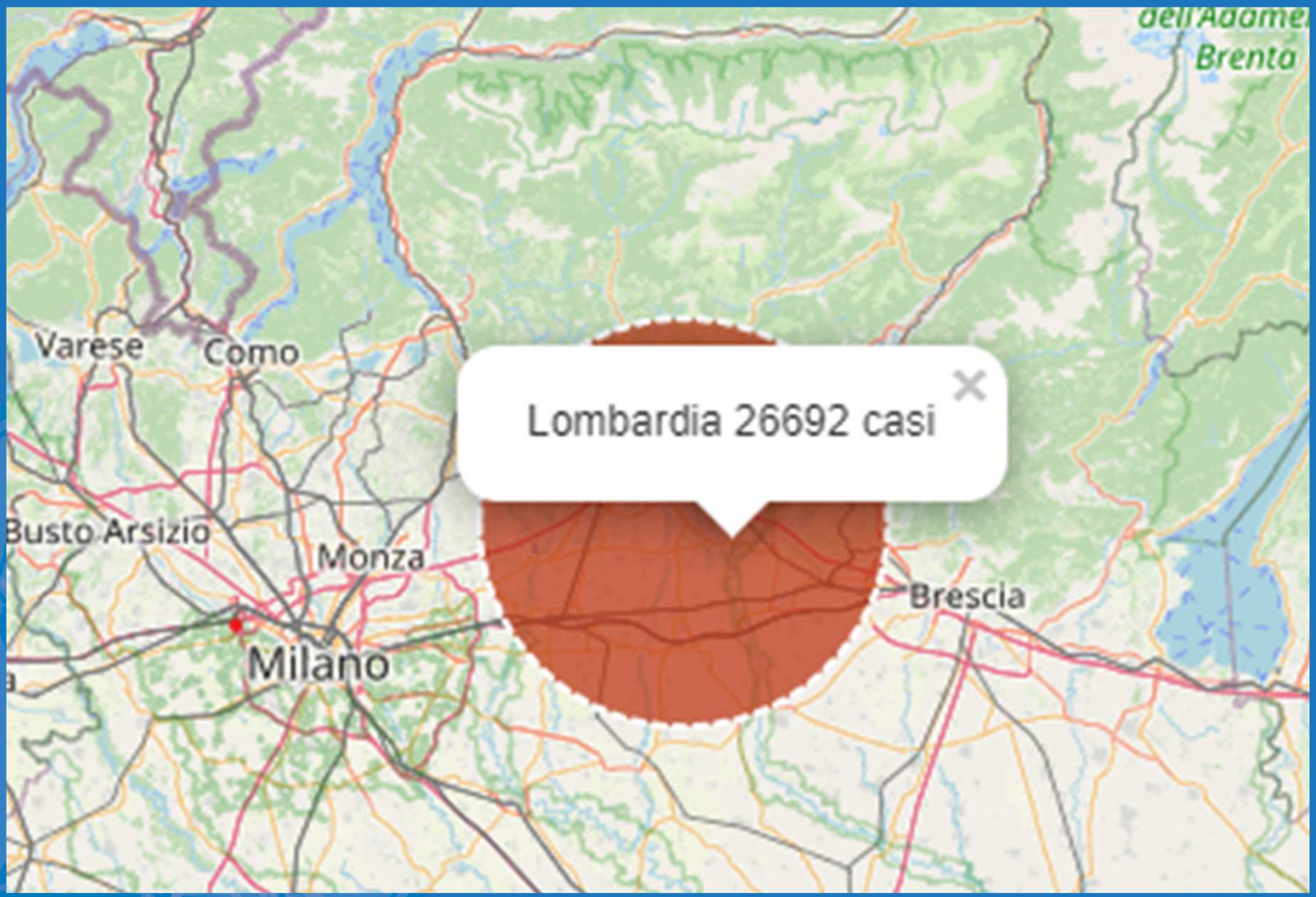
Numero settimanale di ospedalizzazioni, ricoveri in terapia e decessi per settimana dell'evento dal 19 giugno 2023



Tasso settimanale di ospedalizzazione, ricovero in terapia intensiva e decesso in pazienti con diagnosi di infezione da SARS-CoV-2 (per 1.000.000 ab.) dal 19 giugno 2023



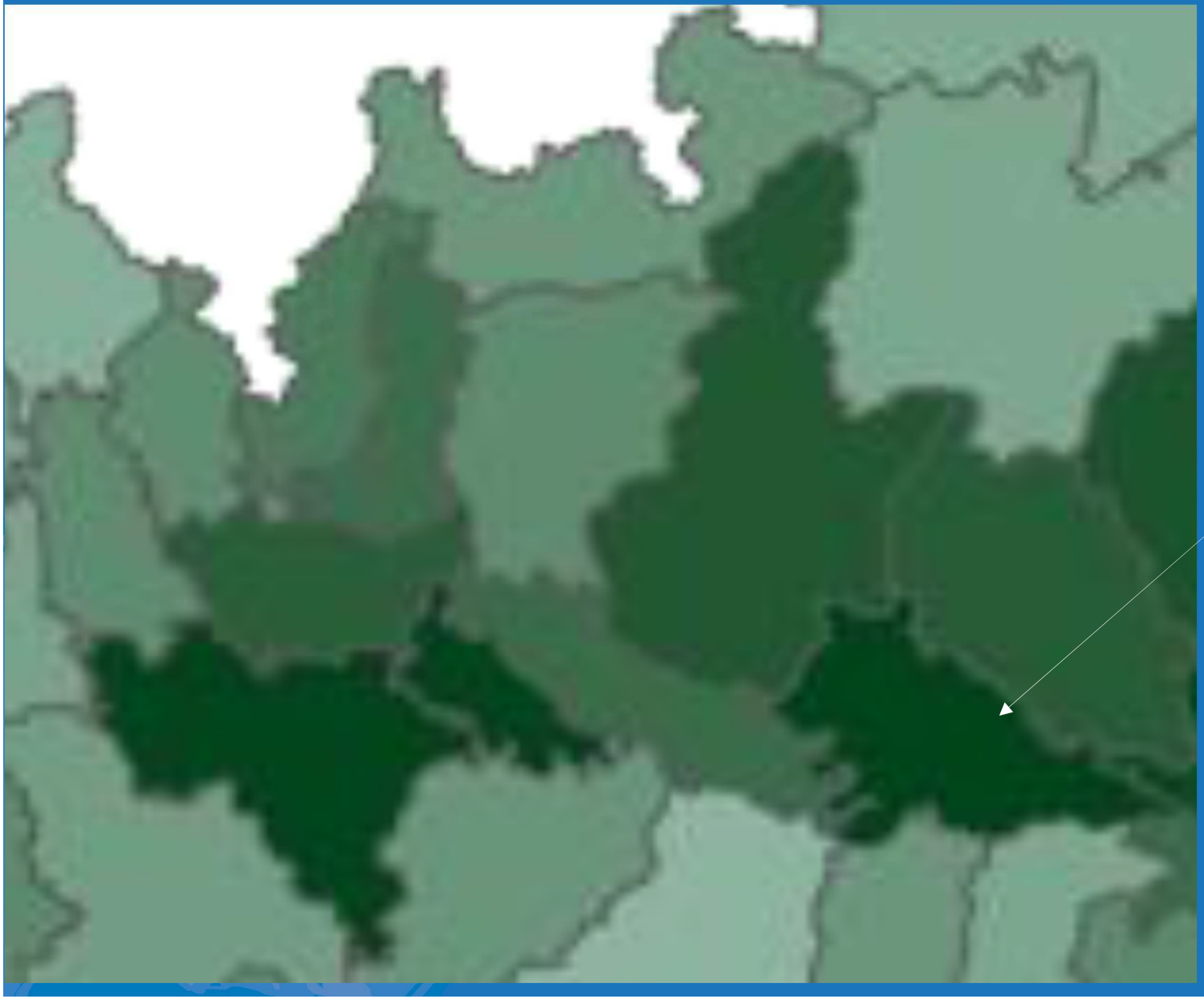
Casi di COVID-19:
-negli ultimi 30 giorni per Regione/Provincia Autonoma di diagnosi (rosso)



Tasso di incidenza di infezioni da SARS-CoV-2 (per 100.000 ab.) segnalate in Italia per provincia

(Periodo: 18 - 24/09/2023)





Provincis
di Mantova

L'antibiotico-resistenza ai tempi della pandemia da COVID-19: nonostante i dati contrastanti, la minaccia resta sempre attuale

Antibiotic resistance at the time of the COVID-19 pandemic: despite conflicting data, the threat still remains current

- ✓ Studio di *The Lancet* fornisce dati allarmanti sulla resistenza agli antibiotici.
- ✓ Nel 2019 si sono registrate, a causa delle infezioni batteriche resistenti agli antibiotici, circa 1,27 milioni di decessi
- ✓ La pandemia di COVID-19 ha avuto un impatto considerevole sui sistemi sanitari a livello globale, con conseguenze importanti nella gestione di altre minacce come la resistenza antimicrobica

Tabella 1. Fattori relativi alla pandemia da COVID-19 che possono influenzare l'antibiotico-resistenza.[9,10]

	Fattori che favoriscono un aumento dell'AMR	Fattori che favoriscono una riduzione dell'AMR
Uso di antibiotici negli ospedali	• Uso di azitromicina (+195%) nei pazienti COVID gravi, nel dubbio di una sovrainfezione batterica, per profilassi o come terapia sperimentale, soprattutto nelle fasi iniziali della pandemia.[11] • Prescrizione potenzialmente inappropriata di antibiotici in pazienti ospedalizzati.[12]	• Riduzione dei ricoveri programmati e degli interventi chirurgici in pazienti ospedalizzati.[12] (es: riduzione di profilassi antibiotica)
Uso di antibiotici nella comunità	• Aumento del trattamento empirico con antibiotici in caso di sintomi respiratori, spesso anche come automedicazione. • Diffusione di consultazioni mediche in via telematica	• Distanziamento sociale, DPI, igiene delle mani e sanificazione ambientale riducono l'incidenza di malattie a trasmissione respiratoria o droplet (con conseguente minor uso di antibiotici)
Pratiche igieniche nella comunità	• Rilascio nell'ambiente di biocidi da detergenti antimicrobici e disinfettanti (più pressione selettiva per i ceppi resistenti)	• Distanziamento sociale, DPI, igiene delle mani e sanificazione ambientale riducono la trasmissione di altre infezioni respiratorie (minor uso di antibiotici)

Tabella 1. Fattori relativi alla pandemia da COVID-19 che possono influenzare l'antibiotico-resistenza.[9-10]

	Fattori che favoriscono un aumento dell'AMR	Fattori che favoriscono una riduzione dell'AMR
Prevenzione e controllo delle infezioni negli ospedali	• Sovraffollamento delle strutture • Carenza di operatori sanitari • Applicazione scorretta delle precauzioni standard (aumento della trasmissione crociata) • Riduzione della capacità di diagnosi dei pazienti MDRO-positivi, isolamento o *cohorting*. • Ricovero prolungato e procedure invasive per i pazienti COVID gravi (più rischio ICA)	• DPI, igiene delle mani, sanificazione ambientale e limitazione dei visitatori in ospedale (riduzione della diffusione dei microrganismi multiresistenti) • Isolamento dei pazienti COVID in reparti specifici con un gruppo di operatori sanitari dedicati (riduzione trasmissione crociata) • Costruzione di nuove strutture COVID-19 senza un serbatoio stabilito di MDRO
Spostamento dei pazienti tra le strutture sanitarie	• Trasferimento dei pazienti fra le terapie intensive con diffusione di diversi germi MDR fra strutture diverse	• Riduzione degli spostamenti dei pazienti da un setting all'altro (meno pressione di colonizzazione per i MDRO)
Diffusione tra Paesi		• Forte diminuzione dei viaggi internazionali (meno diffusione globale di MDRO)
Politiche in materia di sanità pubblica	• Rallentamento delle iniziative di contrasto dell'AMR	• Guadagno dell'attenzione pubblica e politica sulle minacce legate alle malattie trasmissibili, comprese le questioni già endemiche prima del COVID-19 come l'antibiotico-resistenza.

L'antibiotico-resistenza ai tempi della pandemia da COVID-19: nonostante i dati contrastanti, la minaccia resta sempre attuale

Antibiotic resistance at the time of the COVID-19 pandemic: despite conflicting data, the threat still remains current

- ✓ Una metanalisi, condotta su oltre 3.000 pazienti COVID-19 ospedalizzati, ha inoltre mostrato che sebbene solo circa il 7% dei pazienti avesse un'infezione batterica, ben il 70% di loro aveva ricevuto almeno un antibiotico, per profilassi o per trattamento. Gli agenti eziologici più frequenti tra questi pazienti sono risultati essere *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa* e *Haemophilus influenzae*

Figura 1. Categorie di farmaci utilizzati per il COVID-19, serie storica del delta percentuale pre-post COVID-19 rispetto a gennaio 2019 fino a maggio 2020.[11]

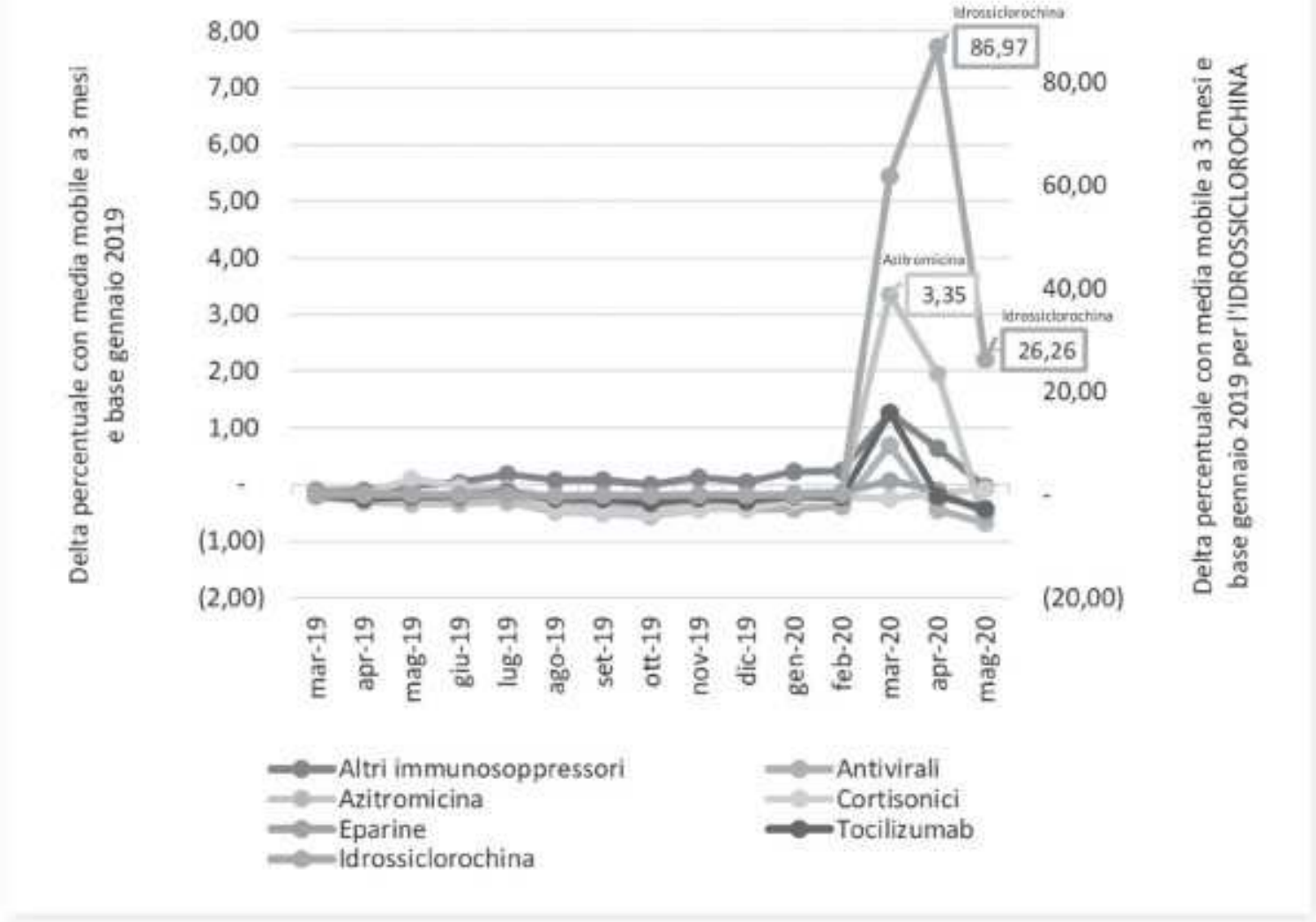
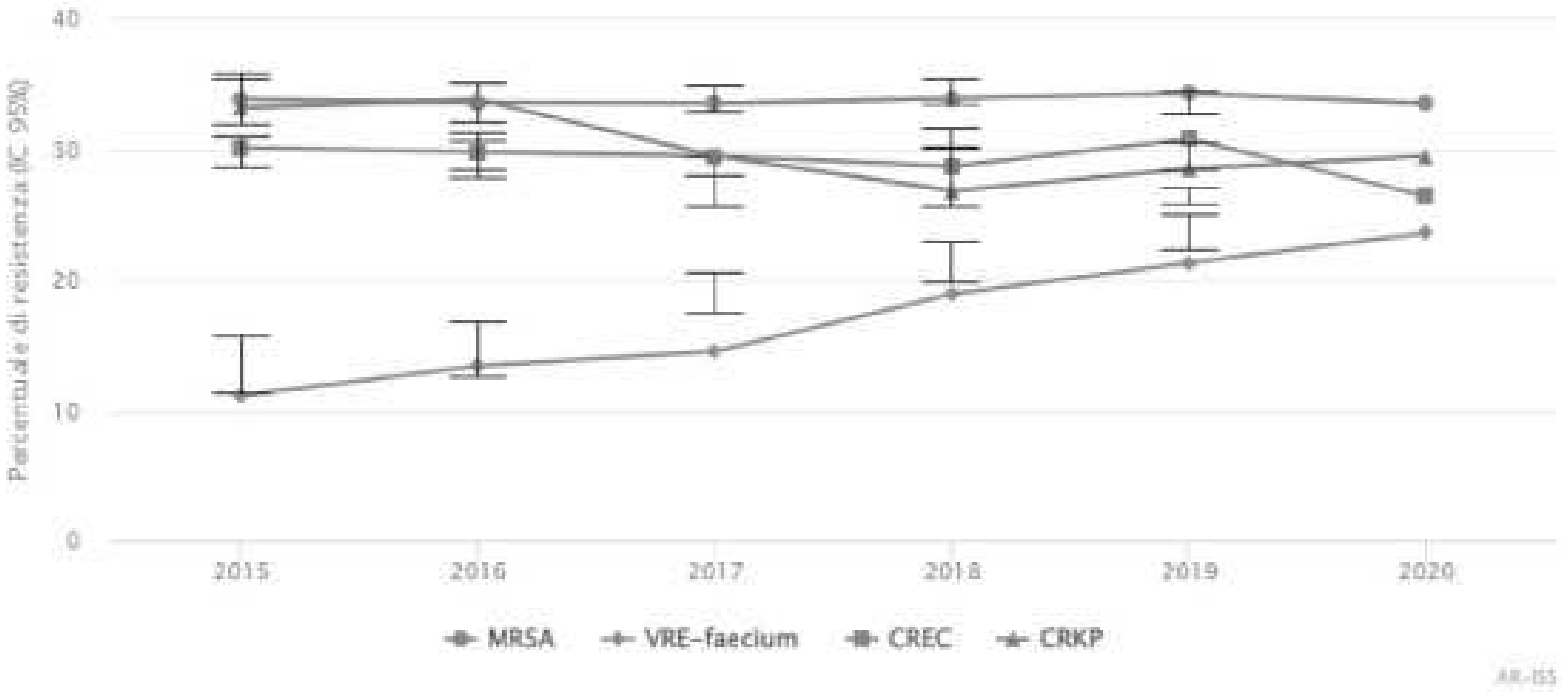


Figura 2. Distribuzione della percentuale di resistenza delle principali combinazioni patogeno/antibiotico nel periodo 2015-2020.[45]



- *MRSA, S. aureus resistente alla meticillina*
- *VRE-faecium, E. faecium resistente alla vancomicina*
- *CREC, E. coli resistente alle cefalosporine di terza generazione*
- *CRKP, K. pneumoniae resistente ai carbapenemi*

Carbapenemase-producing *Enterobacterales* infections in COVID-19 patients

Vicente Pintado[a], Patricia Ruiz-Garbajosa[b], Rosa Escudero-Sanchez[a], Francesca Gioia[a], Sabina Herrera[a], Pilar Vizcarra[a], Jesús Fortún[a], Javier Cobo[a], Pilar Martín-Dávila[a], María Isabel Morosini[b], Rafael Cantón[b] and Santiago Moreno[a]

INFECTIOUS DISEASES, 2021; VOL. 0, NO. 0, 1–10

ABSTRACT

Background: Carbapenemase-producing *Enterobacterales* (CPE) infections have been occasionally described in patients with coronavirus disease-19 (COVID-19). We assess the clinical features and outcome of these infections.

Methods: In this retrospective single-centre, case-control study, we included 54 patients with CPE infection: 30 case-patients (COVID-19) and 24 controls (non-COVID-19), collected between March and May 2020. We compared the epidemiological, clinical features, and outcome between cases and controls.

Results: CPE infection was more frequent in COVID-19 patients than in controls (1.1 *vs.* 0.5%, $p = .005$). COVID-19 patients were younger, had a lower frequency of underlying diseases ($p = .01$), and a lower median Charlson score ($p = .002$). Predisposing factors such as antimicrobial use, mechanical ventilation, or ICU admission, were more frequent in COVID-19 patients ($p < .05$). There were 73 episodes of infection (42 cases and 31 controls) that were more frequently hospital-acquired and diagnosed at the ICU in COVID-19 patients ($p < .001$). Urinary tract was the most common source of infection (47.9%), followed by pneumonia (23.3%). The frequency of severe sepsis or shock ($p = .01$) as well as the median SOFA score ($p = .04$) was higher in cases than in controls. *Klebsiella pneumoniae* (80.8%), *Serratia marcescens* (11%) and *Enterobacter cloacae* (4.1%) were the most common bacteria in both groups (KPC 56.2%, OXA-48 26% and VIM 17.8%). Overall 30-d mortality rate of COVID-19 patients and controls was 30 and 16.7%, respectively ($p = .25$).

Conclusions: COVID-19 patients have an increased risk of CPE infections, which usually present as severe, nosocomial infections, appearing in critically-ill patients and associated with a high mortality.

INFECTIOUS DISEASES, 2021; VOL. 0, NO. 0, 1–10

Vicente Pintado[a], Patricia Ruiz-Garbajosa[b], Rosa Escudero-Sanchez[a], Francesca Gioia[a], Sabina Herrera[a], Pilar Vizcarra[a], Jesús Fortún[a], Javier Cobo[a], Pilar Martín-Dávila[a], María Isabel Morosini[b], Rafael Cantón[b] and Santiago Moreno[a]

Table 1. Baseline characteristics of COVID-19 and non-COVID-19 patients.

Characteristic	All ($N = 54$)	Cases ($N = 30$)	Controls ($N = 24$)	p Value
Age, median (IQR), years	65 (57–74)	62.5 (56–71)	71 (63–76)	.011
Male sex	36 (66.7)	23 (76.7)	13 (54.2)	.081
Charlson comorbidity score, median (IQR)	2 (0–5)	1 (0–3)	4 (2–6)	.002
Comorbidities				
Any	47 (87.0)	23 (76.7)	24 (100)	.011
Hypertension	27 (50.0)	15 (50.0)	12 (50.0)	1.00
Malignancy	17 (31.5)	5 (16.7)	12 (50.0)	.009
Cardiovascular disease	15 (27.8)	7 (23.3)	8 (33.3)	.415
Diabetes	14 (25.9)	6 (20.0)	8 (33.3)	.267
Immunodeficiency state	10 (18.5)	4 (13.3)	6 (25.0)	.273
Obstructive pulmonary disease	7 (13.0)	3 (10.0)	4 (16.7)	.469
Chronic renal disease	7 (13.0)	4 (13.3)	3 (12.5)	.928
Cerebrovascular disease	6 (11.1)	2 (6.7)	4 (16.7)	.245
Chronic liver disease	6 (11.1)	2 (6.7)	4 (16.7)	.245
Other diseases	11 (20.4)	3 (10.0)	8 (33.3)	.034
Predisposing factors to CPE infection[a]				
Antimicrobials	48 (88.9)	30 (100)	18 (75.0)	.004
Urinary catheter	43 (77.8)	27 (90.0)	16 (66.7)	.034
Central venous catheter	39 (72.2)	27 (90.0)	12 (50.0)	.001
Mechanical ventilation	31 (57.4)	25 (83.3)	6 (25.0)	<.001
Parenteral nutrition	10 (18.5)	7 (23.3)	3 (12.5)	.309
Surgery (general anaesthesia)	6 (11.1)	0 (0.0)	6 (25.0)	.004
Renal replacement therapy	1 (1.9)	1 (3.3)	0 (0.0)	.367
Intensive care unit admission	32 (59.3)	25 (83.3)	7 (29.2)	<.001
Previous admission (<3 months)	19 (35.2)	5 (16.7)	14 (58.3)	.001

INFECTIOUS DISEASES,
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Table 2. Clinical features of CPE infections of COVID-19 and non-COVID-19 patients.

Characteristic	All ($N = 73$)	Cases ($N = 42$)	Controls ($N = 31$)	p Value
Acquisition of infection				
Nosocomial	55 (75.3)	39 (92.9)	16 (51.6)	<.001
Healthcare	16 (21.9)	3 (7.1)	13 (41.9)	
Community	2 (2.7)	0 (0.0)	2 (6.5)	
Time from admission[a], median (IQR), days	21 (12–34)	26 (14–33)	12 (7–41)	.116
Ward of hospitalization				
Intensive care unit	37 (50.7)	30 (71.4)	7 (22.6)	<.001
Emergency department	17 (23.3)	4 (9.5)	13 (41.9)	
Medical ward	15 (20.5)	8 (19.0)	7 (22.6)	
Surgical ward	4 (5.5)	0 (0.0)	4 (12.9)	
Type of infection				

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INFECTIOUS DISEASES, 2021; VOL. 0, NO. 0, 1–10

Table 3. Antimicrobial resistance of KPC-, OXA-48 and VIM-producing *Enterobacterales*.

Antimicrobial	All isolates ($N = 73$)	KPC ($N = 41$)	OXA-48 ($N = 19$)	VIM ($N = 13$)
Piperacillin-tazobactam	100% (73/73)	100% (41/41)	100% (19/19)	100% (13/13)
Ceftazidime-avibactam	0% (0/48)	0% (0/36)	0% (0/12)	–
Ceftazidime	93.2% (68/73)	100% (41/41)	73.7% (14/19)	100% (13/13)
Cefepime	93.2% (68/73)	100% (41/41)	73.7% (14/19)	100% (13/13)
Aztreonam	81.6% (40/49)	100% (30/30)	55.6% (5/9)	50% (5/10)
Ertapenem	97.3% (71/73)	100% (41/41)	100% (19/19)	84.6% (11/13)
Imipenem	75.3% (55/73)	100% (41/41)	21.1% (4/19)	76.9% (10/13)
Ciprofloxacin	87.7% (64/73)	97.6% (40/41)	94.7% (18/19)	46.2% (6/13)
Gentamicin	76.7% (56/73)	92.7% (38/41)	42.1% (8/19)	76.9% (10/13)
Amikacin	18.3% (11/60)	11.4% (4/35)	0% (0/14)	63.6% (7/11)
Cotrimoxazole	79.5% (58/73)	95.1% (39/41)	36.8% (7/19)	92.3% (12/13)
Colistin	27.4% (20/73)	24.4% (10/41)	10.5% (2/19)	61.5% (8/13)
Tigecycline	11.9% (7/59)	8.8% (3/34)	14.3% (2/14)	18.2% (2/11)
Fosfomycin	23.7% (9/38)	9.1% (2/22)	53.8% (7/13)	0% (0/3)

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In conclusion, COVID-19 patients have an increased risk of infections due to highly resistant CPE, which usually appear in critically-ill patients. UTI and pneumonia were the most common infections and were associated with a severe clinical presentation and a high mortality. KPC-producing *K. pneumoniae* was the most frequently isolated bacteria, reflecting the current institutional ecology of the hospital. Given the progressive expansion of the COVID-19 pandemic, institutions and regions with a high prevalence of CPE should be prepared for a significant increase in the prevalence of these infections. Implementation of increased surveillance and antimicrobial stewardship programmes focussed on CPE infections should be an essential component of management strategies for COVID-19 patients.

antibiotics

MDPI

Article

Carbapenemase-Producing *Klebsiella pneumoniae* in COVID-19 Intensive Care Patients: Identification of IncL-VIM-1 Plasmid in Previously Non-Predominant Sequence Types

Javier E. Cañada-García [1,2,†], Eva Ramírez de Arellano [1,2,†], Miguel Jiménez-Orellana [1], Esther Viedma [3], Aida Sánchez [4], Almudena Alhambra [5], Jennifer Villa [3], Alberto Delgado-Iribarren [6], Verónica Bautista [1], Noelia Lara [1], Silvia García-Cobos [1], Belén Aracil [1,2], Emilia Cercenado [7,8], María Pérez-Vázquez [1,2,*,‡] and Jesús Oteo-Iglesias [1,2,‡]

Durante la pandemia di COVID-19, le unità di terapia intensiva (ICU) hanno avuto un numero di pazienti superiore al normale e di conseguenza le infezioni da microrganismi nosocomiali sono aumentate. Questo studio vuole individuare la popolazione e i meccanismi di resistenza della Klebsiella pneumoniae (CP-Kpn) produttrice di carbapenemasi proveninte dai pazienti COVID-19 e confrontarli con le popolazioni pre-pandemiche di CP-Kpn.

antibiotics

MDPI

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Abstract: During the COVID-19 pandemic, intensive care units (ICUs) operated at or above capacity, and the number of ICU patients coinfected by nosocomial microorganisms increased. Here, we characterize the population structure and resistance mechanisms of carbapenemase-producing *Klebsiella pneumoniae* (CP-Kpn) from COVID-19 ICU patients and compare them to pre-pandemic populations of CP-Kpn. We analyzed 84 CP-Kpn isolates obtained during the pandemic and 74 CP-Kpn isolates obtained during the pre-pandemic period (2019) by whole genome sequencing, core genome multilocus sequence typing, plasmid reconstruction, and antibiotic susceptibility tests. More CP-Kpn COVID-19 isolates produced OXA-48 (60/84, 71.4%) and VIM-1 (18/84, 21.4%) than KPC (8/84, 9.5%). Fewer pre-pandemic CP-Kpn isolates produced VIM-1 (7/74, 9.5%). Cefiderocol (97.3–100%) and plazomicin (97.5–100%) had the highest antibiotic activity against pandemic and pre-pandemic isolates. Sequence type 307 (ST307) was the most widely distributed ST in both groups. VIM-1-producing isolates belonging to ST307, ST17, ST321 and ST485, (STs infrequently associated to VIM-1) were detected during the COVID-19 period. Class 1 integron Int1-bla_{VIM-1}-*aac*(6′)-1*b*-*dfrB*1-*aadA*I-*catB*2-*qacE*Δ1/*sul*1, found on an IncL plasmid of approximately 70,000 bp, carried bla_{VIM-1} in ST307, ST17, ST485, and ST321 isolates. Thus, CP-Kpn populations from pandemic and pre-pandemic periods have similarities. However, VIM-1 isolates associated with atypical STs increased during the pandemic, which warrants additional monitoring and surveillance.

CURRENT OPINION

Antimicrobial resistance in ICUs: an update in the light of the COVID-19 pandemic

REVIEW

Rafael Cantón[a,b], *Desirèe Gijón*[a,b], *and Patricia Ruiz-Garbajosa*[a,b]

Purpose of review

To describe current antimicrobial resistance in ESKAPE Gram-negative microorganisms and their situation in the ICUs, the implication of the so-called high-risk clones (HiRCs) involved in the spread of antimicrobial resistance as well as relevance of the COVID-19 pandemic in the potential increase of resistance.

Recent findings

Extended-spectrum and carbapenemase producing *Enterobacterales* and multidrug and extensive drug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* have increased worldwide. Sequence type (ST)131 *Escherichia coli*, ST258, ST11, ST10, ST147 and ST307 *Klebsiella pneumoniae*, ST111, ST175, ST235 and ST244 *P. aeruginosa* HiRCs are responsible for this increase in the ICUs, and some of them are implicated in the emergence of resistance mechanisms affecting new antimicrobials. A similar situation can be found with European clonal complex 1 and clonal complex 2 of *A. baumannii*. The high use of antimicrobials during the COVID-19 pandemic, particularly in ICUs, might have a negative influence in future trends of antimicrobial resistance.

Summary

The increase of antimicrobial resistance in ICUs is mainly due to the spread of HiRCs and is exemplified with the ESKAPE Gram-negative microorganisms. The COVID-19 pandemic might have a negative impact in the increase of antimicrobial resistance and should be monitored through specific surveillance studies in ICUs.

Gram-negative ESKAPE microorganisms (*Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* spp.)

CURRENT OPINION

Antimicrobial resistance in ICUs: an update in the light of the COVID-19 pandemic

REVIEW

Rafael Cantón[a,b], *Desirèe Gijón*[a,b], *and Patricia Ruiz-Garbajosa*[a,b]

Pro and con reasons of the potential increase of antimicrobial resistance in ICUs due to the COVID-19 pandemics

Minor impact on AMR

- Personal hygiene (hand hygiene)
- Use of personal protective equipment (PPE)
- Air and surface decontamination
- Social distancing (even in patient management!)
- Early antibiotic use in hospitalization
- Potential lower antibiotic consumption in outpatients



Major impact on AMR

- Potential risk of coinfections and superinfections
- Overcrowding of healthcare systems. Workload of health care workers
- Non trainee staff, including nurses, in the management of COVID-19 infected patients
- Relaxing of measures preventing the spread of MDR organisms
  - decrease of screening cultures of MDR organisms
  - absence of isolation of patients in single rooms or cohorting patients with risk factors for MDR organisms colonization
  - breakdown of antimicrobial stewardship and educational programs
- Increased empiric use of broad spectrum antimicrobials
- Absence of clear guidelines: use of antibacterials (i.e azithromycin) in front line anti-COVID-19 treatment
- Loss of expert support in the use of antimicrobial agents
- Decrease of laboratory capacity on AMR (focused in SARS-CoV-2 diagnosis)
- Absence of use of diagnostic tests for detecting AMR organisms

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MINI REVIEW
published: 17 March 2022
doi: 10.3389/fcimb.2022.823626

The Collateral Effects of COVID-19 Pandemic on the Status of Carbapenemase-Producing Pathogens

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The serious challenge of antimicrobial resistance continues to threaten public health and lingers in the era of the coronavirus disease 2019 (COVID-19), declared pandemic by the World Health Organization. While the pandemic has triggered the importance of infection control practices and preventive measures such as physical distancing, hand hygiene, travel reduction and quarantine, the ongoing alarm of antimicrobial resistance seems to accompany the pandemic too. Antimicrobial resistance has been fostered during COVID-19, possibly due to high rate of empirical antibiotic utilization in COVID-19 patients, increased use of biocides, and the disruption of proper healthcare for other conditions.

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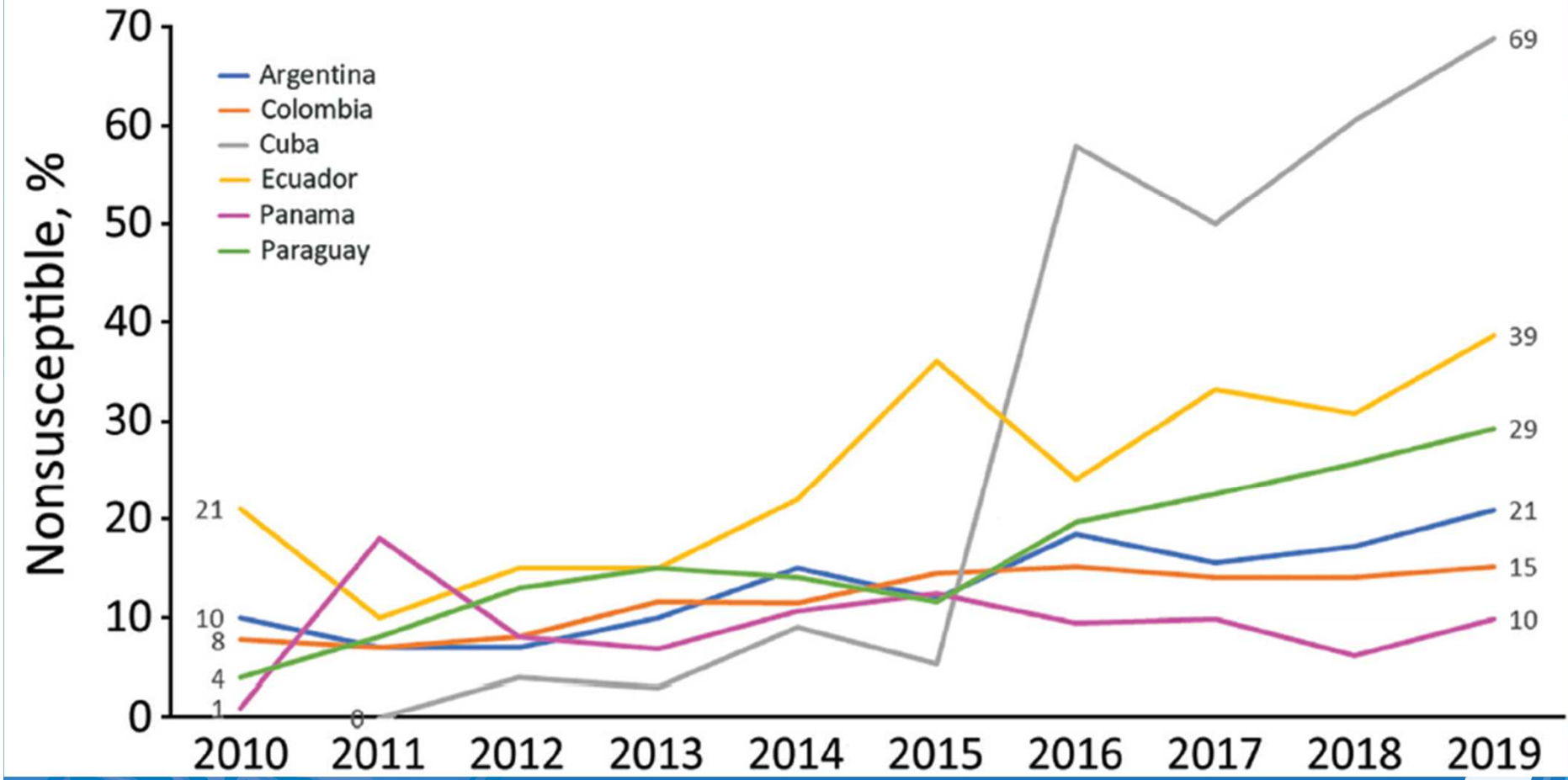
Nosocomial cluster of carbapenemase-producing *Enterobacter cloacae* in an intensive care unit dedicated COVID-19

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Abstract

Concomitant prevention of SARS-CoV-2 and extensively drug-resistant bacteria transmission is a difficult challenge in intensive care units dedicated to COVID-19 patients. We report a nosocomial cluster of four patients carrying NDM-1 plasmid-encoded carbapenemase-producing *Enterobacter cloacae*. Two main factors may have contributed to cross-transmission: misuse of gloves and absence of change of personal protective equipment, in the context of COVID-19-associated shortage. This work highlights the importance of maintaining infection control measures to prevent CPE cross-transmission despite the difficult context and that this type of outbreak can potentially involve several species of *Enterobacterales*.

Increased Detection of Carbapenemase-Producing Enterobacterales Bacteria in Latin America and the Caribbean during the COVID-19 Pandemic



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Specifically, carbapenemase-producing Gram-negative bacteria have shown to cause secondary bacterial infections in patients hospitalized for COVID-19. Clinical and microbiological evidence of such infections is accumulating in different parts of the world. With the resilient nature of carbapenemases, their association with mortality, and the limited treatment options available, concerns regarding this group of antibiotic-hydrolyzing enzymes during the pandemic are expected to upsurge. While the additional burden carbapenemases exert on healthcare is worrisome, it remains hidden or abandoned among the various health consequences of the pandemic. The purpose of