Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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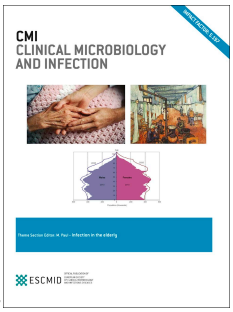

Effect of COVID-19 infection and pandemic period on healthcare-associated infections acquired in intensive care units

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Original article

Effect of COVID-19 infection and pandemic period on healthcare-associated infections acquired in intensive care units

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Abstract

Objectives. To compare the occurrence of healthcare-associated infections acquired in intensive care units (HAI-ICU) in France among COVID-19 patients and non-COVID-19 patients in 2020, and the latter to that in pre-pandemic patients.

Methods. Multicentre HAI-ICU surveillance network (REA-REZO) data were used to identify 3 groups: 2019 patients (2019Control), a 2020Cov group, and a 2020NonCov group. The primary outcome was the occurrence of HAI-ICU (ventilator-associated pneumonia [VAP], bloodstream infections [BSI], catheter-related bacteraemia [CRI/CRB]). Standardised infection ratios (SIR) of VAP were calculated for each quarter in 2020 and compared to those of 2019.

Results. A total of 30105 patients were included in 2020: 23798 in the 2020NonCov group, 4465 in 2020Cov group and 39635 patients in the 2019Control group. The frequency of VAP was strikingly greater in the 2020Cov group: 35.6 [33.4-37.8] episodes/1000days of mechanical ventilation versus 18.4 [17.6-19.2] in the 2020nonCov group. VAP SIR was higher in 2020 patients, particularly during the 2 quarters corresponding to the 2 waves. BSI/1000 days were more frequent in the 2020Cov group (6.4 [6.4-6.4]% versus 3.9 [3.8-3.9] % in the 2020nonCov group). VAP and BSI were also more frequent in the 2020nonCov group compared to the 2019Control group. Microbial epidemiology was only slightly different.

Conclusions. The data presented herein indicate that HAI-ICU were more frequent during the COVID-19 period, whether the patients were admitted for COVID-19 or, to a lesser extent, for another cause. This implies that managing severe patients in a pandemic context carries risks for all patients.

Introduction

In France, and worldwide, intensive care units (ICUs) have been the main battleground to treat patients with severe COVID-19 that is associated with a high risk of death [1]. The pandemic had a major effect on the hospital organisation, with work overload, creation of temporary beds in ICUs, involvement of personnel not usually dedicated to ICUs, and an initial shortage of personal protective equipment [2]. This situation was further complicated by the continuing flow of ICU non-COVID-19 patients. REA-REZO is a nationally active surveillance network dedicated to the epidemiology of ICU-acquired infections as well as the use of antimicrobials and bacterial epidemiology running since 2004 in voluntary French ICUs. [3–5]. During the COVID-19 pandemic period, the ongoing surveillance programme was continued on the same basis with the identification of COVID-19 patients. The objective of the study was to compare first the occurrence of HAI-ICU in 2020 COVID-19 patients to that in 2020 non-COVID-19 patients, and secondly the latter to that in 2019 pre-pandemic patients.

Methods

Surveillance design

The continuous surveillance network includes ICUs on a voluntary basis and is patient-based, including each patient with a length of stay (LOS) ≥ 2 calendar days in an adult ICU. Individual data are prospectively recorded on HAI, with selected antimicrobial resistance and individual risk factors (Table S1). The database has been approved by the national data protection commission (*Commission nationale de l'informatique et des libertés*, Number 919149) and by the IRB (CPP SUD EST—IRB 00009118). The protocol is available on the website of the network [6].

Surveillance data

General patient characteristics.

Age, sex, severity as assessed by the Simplified Acute Physiological Score II (SAPS II) [7], date of ICU admission and discharge, status at ICU discharge (alive or deceased), antibiotic treatment (excluding prophylaxis) ± two days before or after admission day, category of diagnosis (medical, surgical scheduled or emergency, trauma), origin of the patient (community, long-term care, rehabilitation centre, acute care, other ICU), immunosuppression are recorded.

Individual exposure to invasive device.

The dates of insertion and removal of endotracheal tube and central venous catheter (CVC) as well as the site of CVC insertion are recorded.

ICU-HAI.

Pneumonia (including ventilator-associated pneumonia, VAP), catheter-related bacteraemia (CRB), as well as bloodstream infections (BSI) of all origin are recorded

Pulmonary infection data include the date of onset, and the method of diagnosis for pneumonia. For each infection up to 2 microorganisms are recorded, as well as resistance status by tracer phenotypes for bacteria of interest (*S. aureus*, *E. faecalis* and *faecium*, Enterobacterales, *P. aeruginosa*, and *Acinetobacter sp.*; Supplementary data table S1). Susceptibility testing in all the units was done according to EUCAST .[8].

Definitions of ICU-acquired infections (HAI)

HAI are infections occurring > 48 h after admission. Definitions follow European Centre for Disease Control (ECDC) definitions [9].

Briefly, pneumonia is defined by a combination of clinical, radiological, and laboratory criteria. VAP is a lung infection in a patient mechanically ventilated for >48 hours. BSI are defined by the positivity of at least one blood culture for a recognised pathogen or two positive blood cultures for a common skin contaminant. The complete definition set can be found on the ECDC Website [10].

The outcomes are the incidence of HAI expressed as incidence, as well as incidence density per 1000 patient-days for BSI and per 1000 days of device exposure for specific infections (mechanical ventilation for VAP, catheter for CRB).

Surveillance design.

The data collection is performed using a standardised form completed for each patient by the physician in charge in collaboration with the Infection Control Unit; the data collected concerns patient characteristics, devices used, and HAI. they are collected during the ICU stay, and the form is finalised at the end of the ICU stay, for each patient staying 2 or more days.

Statistical plan

Descriptive statistics were expressed by the median and interquartile range [IQR] for quantitative variables and by the number and percentage (%) for qualitative variables. Device utilisation ratio was calculated by dividing the total number of device days by the total number of patient-days during the stay. Differences between groups were estimated using the Wilcoxon rank-sum test for quantitative variables, and the Chi-squared test for qualitative variables or Fisher's exact test when applicable. If heterogeneity between groups was detected, a two-by-two comparison was performed in order to detect the group differences. The statistical threshold for between-group comparisons was set at 0.001.

Standardised infection ratios (SIR) were computed as previously described [11]: the proportion of change (%) in VAP incidence was calculated as follows: [(2020 SIR − 2019 SIR) ÷ 2019 SIR] × 100. Temporal comparisons in VAP incidence between 2019 and 2020 were analysed using SIR, calculated for each calendar quarter by dividing the number of reported infections by the number of predicted infections. A SIR <1 indicates fewer infections observed than predicted; likewise, a SIR >1 indicates that more infections were observed than predicted. The predicted individual probability of occurrence of VAP was estimated using logistic regression: first, a backward stepwise regression was performed to select the best minimal model to explain a VAP using a subset of predefined variables (Table S3). The model fit was maximised using the minimal Akaike information criterion (AIC). The Odds Ratio (OR) and their 95% confidence interval [95% CI] were computed for the variables retained in the final model. Analyses were performed using SAS-Studio (SAS Institute Inc., Cary, NC, US).

Results

Population

The number of participating units was N=110 in 2019 and N=90 in 2020. In 2020, 30105 patients were reported in the surveillance network database: 23798 patients in the non-COVID-19 (2020NonCov) group; 4465 patients in the COVID-19 (2020Cov) group, including 3800 COVID patients diagnosed by PCR and 665 on clinical basis (mainly before complete accessibility of PCR early in the year 2020). The 1842 patients with an unknown COVID status were not included in the present study. In 2019, 39635 patients were included in the surveillance (Fig. 1).

Patient characteristics

The 2019Control and 2020NonCov patients were comparable, except for the proportion of scheduled surgical patients that was lower in the 2020NonCov group. A greater proportion of patients in the 2020Cov group were transferred from a ward or other ICU compared to the 2020NonCov. According to the number of 2020Cov and 2020NonCov admissions each month in 2020, there were 2 waves in France: the first in March, the second in October-November (Supplementary data Fig. S1). The median length of ICU stay, sex ratio, fatality rate were greater in the 2020Cov group than in the 2020NonCov group. Exposure to antibiotics was not different between the 2019Control and the 2020NonCov population, but higher in the 2020Cov group than in the 2020NonCov group (Table 1).

Exposure to invasive devices (endotracheal tube or CVC) were slightly increased in the 2020NonCov group. The exposure duration and the device utilisation ratio were higher in the 2020Cov group. During 2020, the proportion of intubated patients decreased among the 2020Cov patients and remained stable in the 2020NonCov patients (Supplementary data Fig. S2). During the same period, the interval between ICU admission and mechanical ventilation increased during the 2 waves (Supplementary data Fig. S3).

Device-related infection rates

Overall rate of HAI-ICU.

The overall rate of HAI was higher in the 2020Cov group compared to both the 2019Control and 2020NonCov groups. Among the 2020NonCov patients, the increase was partially due to more frequent VAP, but also, at a lesser extent, to more frequent BSI (including CRB) (Table 2).

VAP

At least 1 episode of VAP was diagnosed in 37% of patients in the 2020Cov group, compared to 12.9% in the 2020NonCov group (Table 2). Logistic regression of predicted individual probability of VAP are provided in supplementary material table S3. The greatest change in VAP SIR was found in the second and fourth quarter for the whole 2020 cohort (2020Cov + 2020NonCov); when only 2020NonCov patients were considered, the greatest change was found in the second quarter (Table 4).

BSI

The increase in BSI rate in 2020Cov group as compared to the 2019NonCov group was related to an increase in intra-vascular device origin of infection, particularly from peripheral catheters, but also from pulmonary origin, while bacteraemia of digestive origin were less frequent (Table 3).

Bacterial ecology and resistance

Multidrug resistant bacteria carriage and acquisition

The proportion of patients carrying at least 1 targeted MDRB was not significantly different between the 2020NonCov and 2019Control group; it was more frequent in the 2020Cov group than in the 2020NonCov group. This was particularly the case for the acquisition of extended spectrum betalactamase (ESBL), but also for the initial carriage and acquisition of

carbapenemase-producing enterobacterales (CPE) or ceftazidime-resistant *Pseudomonas aeruginosa* (CRPa) strains (Supplementary material Table S3).

Micro-organisms involved in HAI-ICU and antimicrobial resistance profile

The distribution of the different bacterial species of interest appears to be little different between the 2019Control and 2020NonCov groups. In 2020, only modest differences in bacterial ecology were found between the 2020Cov and 2020NonCov groups, with the exception of non-fermenting Gram-negative bacilli that are more frequent in 2020Cov patients (Supplementary data Tables S4 and S5).

The proportion of patients infected with a MDRB (all infections combined: pneumonia, BSI, CRI, CRB) was greater in both 2020 groups (2020NonCov and 2020Cov) than in the 2019Control group. The proportion of patients infected with MRSA, carbapeneme resistant enterobacteriae (CRe) and ceftazidime-resistant *Pseudomonas aeruginosa* (CRPa) was significantly greater in the 202Cov group than in the 2020NonCov group (Table 5). It should be noted that all the CRe were isolated in VAP, but never in CLABSI.

Discussion.

The main result of the present study is that HAI-ICU, particularly VAP, were more frequent in both ICU populations during 2020 than in 2019, regardless of their COVID status. This is due to extrinsic and intrinsic factors. Among extrinsic factors, the pandemic had a major effect on the hospital and ICU organisation [2]. Breakdown in infection prevention best practices are highly likely, but is probably variable between countries [12] and unit. However, it is not possible to further analyse the responsibility of prevention practice in the present study since this is not recorded in our surveillance programme.

The higher rate of pneumonia and of BSI have different determinants. VAP were at least 3 times more frequent in 2020Cov than 2020NonCov patients; such a high rate of VAP has been reported in several multicentre studies, for example in 2 French cohorts, the rate of VAP was 43% [13] and 52% [14], and the main study on HAI-ICU in COVID-19 patients, conducted in Italy, reported a rate of 50% of VAP in intubated patients (26.0 (95% CI, 23.6-28.8) VAP per 1,000 MV-days). [15]. In addition, during the 2 years of surveillance, no modification in diagnostic practice of VAP were found in the different period and groups (*data not shown*), and the higher SIR of VAP corresponded to the 2 waves of the pandemic in France. The higher rate of VAP in the 2020Cov was related to the lung tropism of SARs-CoV-2 and the resulting lung lesions that are particularly exposed to pulmonary superinfections, as shown, for instance, in a comparison between COVID and influenza [16]. Intrinsic factors related to the disease process itself include lung parenchymal damage, immune dysregulation, and an increased risk of thrombosis [17].

Higher rate of BSI has also been reported elsewhere [18]. It is related to a more frequent intra-vascular device origin of infection, which could be attributed at least partially to the modification of the management of ICU patients [2]. In addition, it is also associated with a

more frequent pulmonary origin (related to the more frequent VAP) and a decrease of digestive origin (fewer surgical patients) in 2020Cov patients.

The surveillance data provide information about several interesting characteristics of the 2020Cov patients. The median age of the 2020Cov cohort is similar to the 2020NonCov and the historical 2019Control cohorts, indicating that very old patients were not necessarily admitted to ICU [19]. In addition, the classical male predominance in COVID-19 patients was found in the 2020Cov cohort [20]. Mortality was more frequent in in the 2020Cov group despite a lower severity score (SAPS II) at admission; this could be explained by the early admission of 2020Cov patients to ICU. Furthermore, there was a reduced direct admission to ICU, which is likely to be explained by a more frequent prior admission to a medical ward. Moreover, scheduled surgical activity was reduced in relation to reorientation of ICU beds towards COVID-19 in European countries [2]. It is also important to note that antibiotic exposure measured around the ICU admission was very high in 2020Cov group, almost 70%. This has been well analysed in an editorial by De Waele [21]: possible co-infections, use of immunomodulating medications, such as corticosteroids and interleukin inhibitors and a longer duration of mechanical ventilation in 2020Cov patients. As the understanding of COVID-19 progressed, the initial overexposure of COVID-19 patients to antibiotics for fear of bacterial co-infection slightly decreased in our study (*data not shown*).

MDRB carriage was more frequent in 2020Cov patients, especially ESBL-producing Enterobacterales and CRPa, a result possibly related to a higher exposure to antibiotics at admission and during a previous stay in a ward. There was no remarkable difference in the distribution of the most frequent bacteria: Enterobacterales were found at the same rate in all groups, and there was a slightly higher rate of *Pseudomonas aeruginosa* in 2020Cov patients. Furthermore, resistance levels were not very different, for instance there was less ceftazidime resistance in Pseudomonas isolated in 2020Cov patients, and only ESBL Enterobacterales were

slightly more frequent in these patients. Taken together, these data lead to deduce that the microbial epidemiology and resistance are not a major problem in COVID-19 infections.

Strengths and limitations

Surveillance network data from the REA-REZO are of value as a large number of patients are included, and, as the network has existed for many years, the quality of the data is therefore high. It also has the advantage of measuring the burden of HAI-ICU in all the ICU populations during the pandemic period, showing that 2020NonCov patients were also concerned by the increase in HAI-IC. However, data are limited to variables collected in the surveillance, not including the comorbidities such as obesity and the treatments potentially associated with the development of HAIs (i.e. corticosteroids, tocilizumab, *etc*.).

Moreover, we need to point-out that nearly 15% of the COVID-19 patients were not diagnosed with the use of PCR due to the lack of availability of this method at the beginning of the pandemic. However, the risk of misclassifying these patients is limited by the strict recommendations from the ministry of health and learned medical societies for case definition.

In conclusion, the data presented herein indicate that HAI-ICU were more frequent during the COVID-19 period, whether the patients were admitted to ICU for COVID-19 or another cause. This implies that besides the specific role of COVID-19, particularly in pulmonary superinfection, the high flow of patients decreases the quality of the care provided to all patients, leading to an increased risk of HAI-ICU for all patients.

Author contributions

Study design: AL, AM, CB, AF, AS; data analysis and interpretation: AM, CV; writing all sections of the manuscript: AL, AM; manuscript revision: AL, CB, AF, CV, AS.

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Table 1: Characteristics of included patients

	2019Control	2020NonCov	2020Cov	p value
	(N = 39635)	(N = 23798)	(N = 4465)	
Age (year), median [IQR]	67.0 [56-75]	66.0 [55-74]	67.0 [58-74]	*NS*
Sex-ratio M/F	1.72	1.84	2.35	*<0.001* $^{\alpha\,\varepsilon}$
Length of ICU stay (days), median [IQR]	6 [4-11]	6 [4-11]	10 [6-19]	*<0.001* $^{\alpha}$
SAPS II, median [IQR]	44 [32-58]	43 [32-57]	38 [30-49]	*<0.001* $^{\alpha\,\varepsilon}$
ICU case fatality, n (%)	6498 (16.4)	3998 (16.8)	1017 (22.8)	*<0.001* $^{\alpha}$
Antibiotics ± 48h around admission, n (%)	22184 (56.1)	13137 (55.3)	3098 (69.6)	*<0.001* $^{\alpha}$
Admission from, n (%)				
Home	21784 (55.1)	13809 (58.1)	1963 (44.0)	*<0.001* $^{\alpha\,\varepsilon}$
Nursing home	574 (1.5)	320 (1.3)	63 (1.4)	NS
Long-term care facility	782 (1.8)	202 (0.9)	66 (1.5)	*<0.001* $^{\alpha\,\varepsilon}$
Rehabilitation	626 (1.6)	305 (1.3)	42 (0.9)	NS
Other wards (acute care)	14201 (35.9)	7892 (33.2)	1973 (44.2)	*<0.001* $^{\alpha\,\varepsilon}$
Other ICU	1653 (4.2)	1225 (5.2)	352 (7.9)	*<0.001* $^{\alpha\,\varepsilon}$
Diagnostic category at admission, n (%)				
Medical	26886 (67.9)	16627 (69.9)	4195 (94.1)	*<0.001* $^{\alpha\,\varepsilon}$
Emergency surgery	7160 (18.1)	4338 (18.2)	189 (4.2)	*<0.001* $^{\alpha}$
Scheduled surgery	5556 (14.0)	2809 (11.8)	75 (1.7)	*<0.001* $^{\alpha\,\varepsilon}$
Trauma, n (%)	2826 (7.2)	1817 (7.6)	155 (3.5)	*<0.001* $^{\alpha}$
Immunosuppression, n (%)	5908 (15.3)	3345 (14.6)	625 (14.2)	NS
Including < 500 PNN/mm^{3,} n (%)	652 (1.7)	360 (1.6)	48 (1.1)	NS
Device exposure, n (%)				
Intubation probe	24109 (60.9)	15131 (63.7)	2628 (58.9)	*<0.001* $^{\alpha\,\varepsilon}$
Central venous catheter	26706 (67.5)	17089 (71.9)	2935 (65.8)	*<0.001* $^{\alpha\,\varepsilon}$
Urinary catheter	33236 (86.0)	20735 (88.1)	3353 (77.6)	*<0.001* $^{\alpha\,\varepsilon}$
Exposure duration (days), median [IQR]				
Mechanical ventilation	4 [2-10]	5 [2-11]	12 [6-22]	*<0.001* $^{\alpha\,\varepsilon}$
Central venous catheter	6 [4-12]	7 [4-12]	12 [7-22]	*<0.001* $^{\alpha}$
Device utilisation ratio, %				
Intubation probe	50.9	55.2	64.0	*<0.001* $^{\alpha\,\varepsilon}$
Central venous catheter	68.5	72.0	72.4	*<0.001* $^{\alpha\,\varepsilon}$

Data are shown as the number of patients n and percentage (%) or median and interquartile range [IQR]. Between-group comparisons with significant p value set at 0.001. NS: not significant, α: Significant difference between 2020Cov and 2020NonCov, ε: Significant difference between 2020NonCov and 2019Control.

Table 2: Healthcare-associated infections acquired in intensive care units (HAI-ICU).

	2019Control 39635	2020NonCov 23798	2020Cov 4465	p value
Patients with at least one infection, n (%)	3698 (9.3 [9.04-9.61])	2680 (11.3 [10.86-11.66])	1160 (26 [24.69-27.27])	<0.001 α ε
Pneumonia (including VAP) , n (%)	2852 (7.2 [6.94-7.45])	2140 (9 [8.63-9.36])	1024 (22.9 [21.70-24.17])	<0.001 α ε
VAP, n (%)	2507 (10.4 [10.01-10.78])	1948 (12.9 [12.34-13.41])	973 (37 [35.18-37.88])	<0.001 α ε
VAP /1000 days of MV	15.4 [14.78-15.97]	18.4 [17.62-19.24]	35.6 [33.42-37.81]	<0.001 α ε
Interval from MV onset to VAP (days), median [IQR]	8 [4-12]	7 [4-12]	8 [5-12]	<0.001 α ε
Bloodstream infection (BSI)	1271 (3.2 [3.03-3.38])	888 (3.7 [3.49-3.97])	388 (8.7 [7.86-9.52])	<0.001 α ε
BSI /1000 days of stay	3.4 [3.33-3.45]	3.9 [3.84-3.88]	6.4 [6.36-6.44]	<0.001 α
Central catheter-related bacteraemia (CRB), n (%)	163 (0.6 [0.52-0.70])	118 (0.6 [0.57-0.81])	36 (1.2 [0.83-1.62])	<0.001 α
Central catheter-related bacteraemia /1000 central catheter-days	0.6 [0.47-0.65]	0.6 [0.58-0.65]	0.6 [0.63-0.63]	NS

Data are shown as the number of patients n and percentage (%) or median and interquartile range [IQR]. Between-group comparisons with significant p value set at 0.001. NS: not significant, α: Significant difference between 2020Cov and 2020NonCov, ε: Significant difference between 2020NonCov and 2019Control. MV: mechanical ventilation, VAP: ventilator associated pneumonia.

Table 3: Origin of bacteraemia of each origin.

	2019Control (N=1271)	2020NonCov (N=1030)	2020Cov (N=466)
Intra-vascular devices n (%)	404 (27.5)	38.4	35.7
Arterial catheter	107 (7.3)	123 (11.9)	43 (9.2)
Peripheral catheter	38 (2.6)	81 (7.9)	48 (10.3)
Central venous catheter	201 (13.7)	146 (14.2)	60 (12.9
PICC	8 (0.5)	8 (0.8)	2 (0.4)
Hemodialysis catheter	26 (1.8)	18 (1.7)	6 (1.3)
Implantable port catheter	13 (0.9)	3 (0.3)	0 (0.0)
ECMO	5 (0.3)	4 (0.4)	3 (0.6)
Midline	-	3 (0.3)	3 (0.6)
Other vascular devices	6 (0.4)	9 (0.9)	2 (0.4)
Lungs n (%)	272 (18.5)	151 (14.7)	114 (24.5)
Urinary tract n (%)	102(6.9)	47 (4.6)	19 (4.1)
Digestive tract n (%)	242 (16.5)	109 (10.5)	26 (5.6)
SSI n (%)	7 (0.5)	4 (0.4)	2 (0.4)
Skin & soft tissues infections n (%)	57 (3.9)	24 (2.3)	3 (0.6)
Other origin n (%)	15 (1.0)	9 (0.9)	5 (1.1)
Unknown n (%)	369 (25.1)	291 (28.3)	130 (27.9)

Table 4: Standardised Infection Ratio (SIR) for VAP.

	SIR 2019 [95% CI]	SIR 2020NonCov	% change SIR [95% CI]	SIR 2020Cov + 2020NonCov	% change SIR [95% CI]
Q1	0.92 [0.86-0.99]	0.97 [0.89-1.05]	4.3 [-0.3; 8.9]	0.95 [0.88-1.03]	3.3 [-1.3; 7.9]
Q2	0.88 [0.81-0.95]	1.32 [1.23-1.41]	50.0 [36.1; 63.9]	1.57 [1.49-1.64]	78.4 [61.1; 95.8]
Q3	0.99 [0.92-1.06]	1.06 [0.97-1.14]	7.1 [1.9; 12.3]	1.11 [1.03-1.19]	12.1 [5.3; 18.9]
Q4	0.91 [0.84-0.99]	1.03 [0.94-1.13]	12.0 [5.2; 18.7]	1.59 [1.52-1.67]	74.7 [57.8; 91.7]

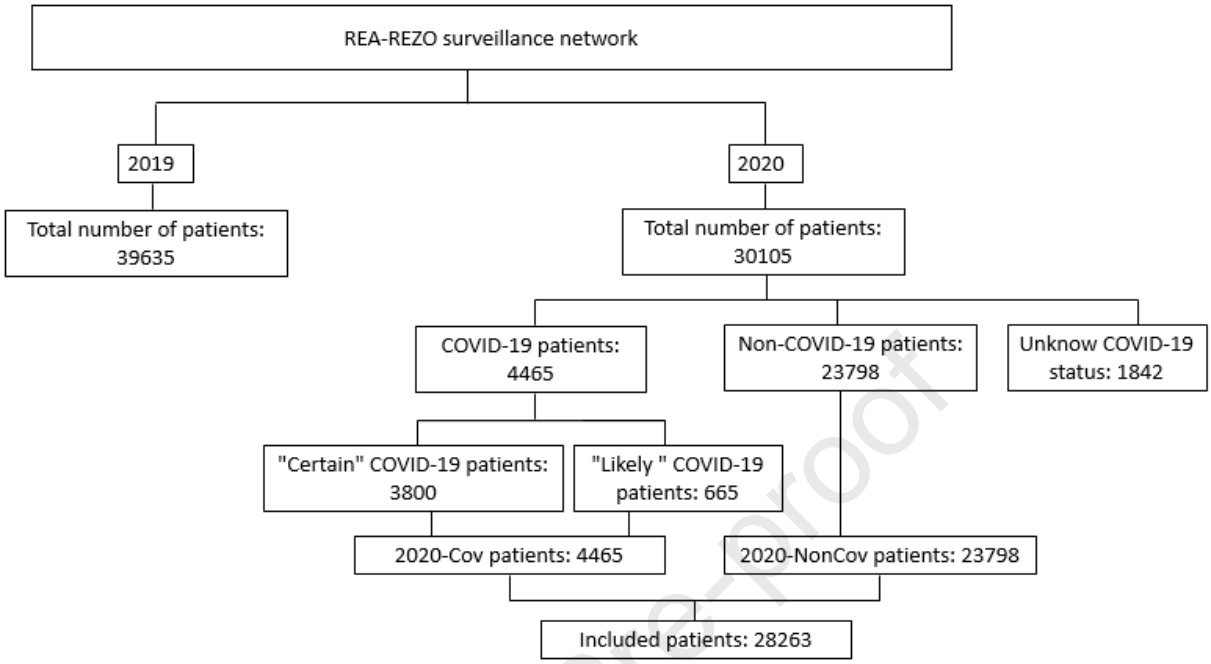
Q: calendar quarter. The proportion of change (%) was calculated as follows: [(2020 SIR − 2019 SIR) ÷ 2019 SIR] × 100. Statistical significance based on 2-tailed $P \leq .05$, reflected in the relative % change in magnitude. The number of predicted infections was obtained using regression models created from the 2019-20 baseline data. A SIR below 1 indicates fewer infections observed than predicted, signalling a reduction; likewise, a SIR above 1 indicates more infections were observed than predicted, signalling an increase.

Table 5: Number of patients infected with a multidrug resistant bacteria (MDRB) during the study period 2019-2020

	2019Control 39635	2020NonCov 23798	2020Cov 4465	p-values
Patients with at least one infection, n (%)	3698 (9.3)	2669 (11.3)	1158 (26)	*<0.001* $^{\alpha\,\varepsilon}$
Patients infected by methicillin resistant ***Staphylococcus***, n (%)	74 (0.2)	51 (0.2)	22 (0.5)	*<0.001* $^{\alpha}$
Patients infected by extended spectrum betalactamase, n (%)	267 (0.7)	201 (0.8)	128 (2.9)	*<0.001* $^{\alpha}$
Patients infected by carbapeneme resistant enterobacteriae, n (%)	20	14	11	*<0.001* $^{\alpha}$
Patients infected by ceftazidime-R *P aeruginosa*, n (%)	166 (0.4)	136 (0.6)	69 (1.5)	*<0.001* $^{\alpha}$

Data are shown as the number of patients n and percentage (%) from the total population of included patients. Between-group comparisons with significant p value set at 0.001. NS: not significant, α: Significant difference between 2020Cov and 2020NonCov, ε: Significant difference between 2020NonCov and 2019Control.

Figure 1 – Flowchart



Supplementary material.

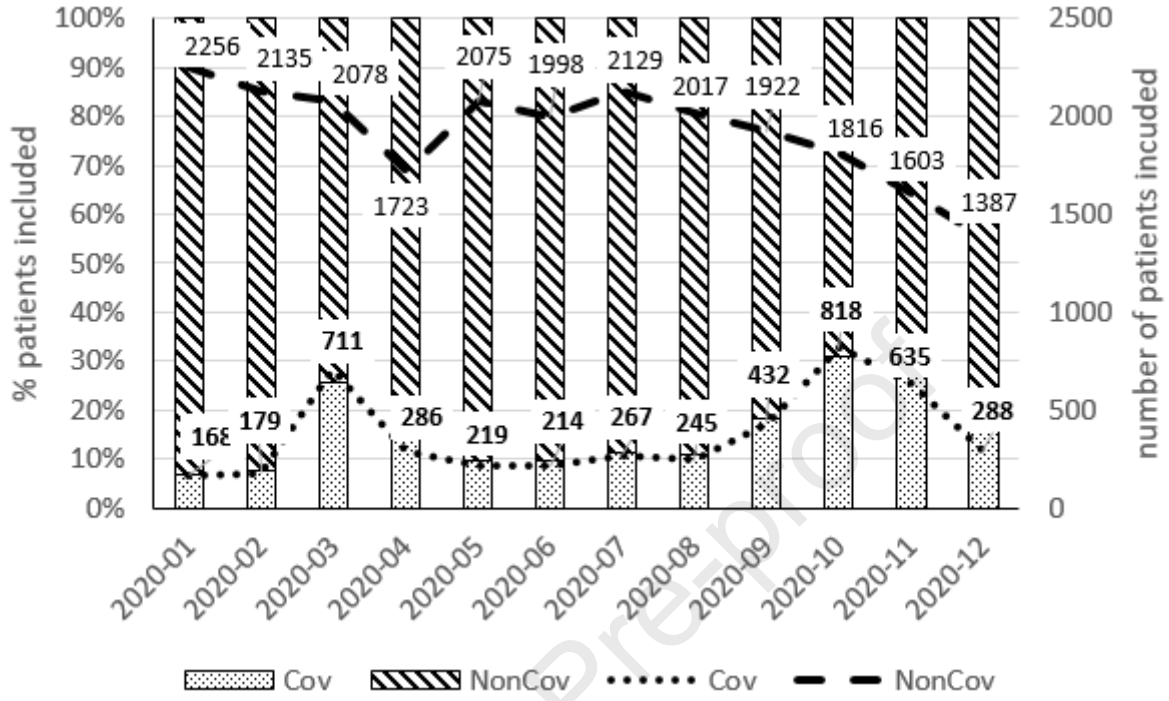


Figure S1 : Monthly evolution in 2020 of the number of patients admitted to ICUs according to COVID status in absolute values (lines) and proportions (histograms)

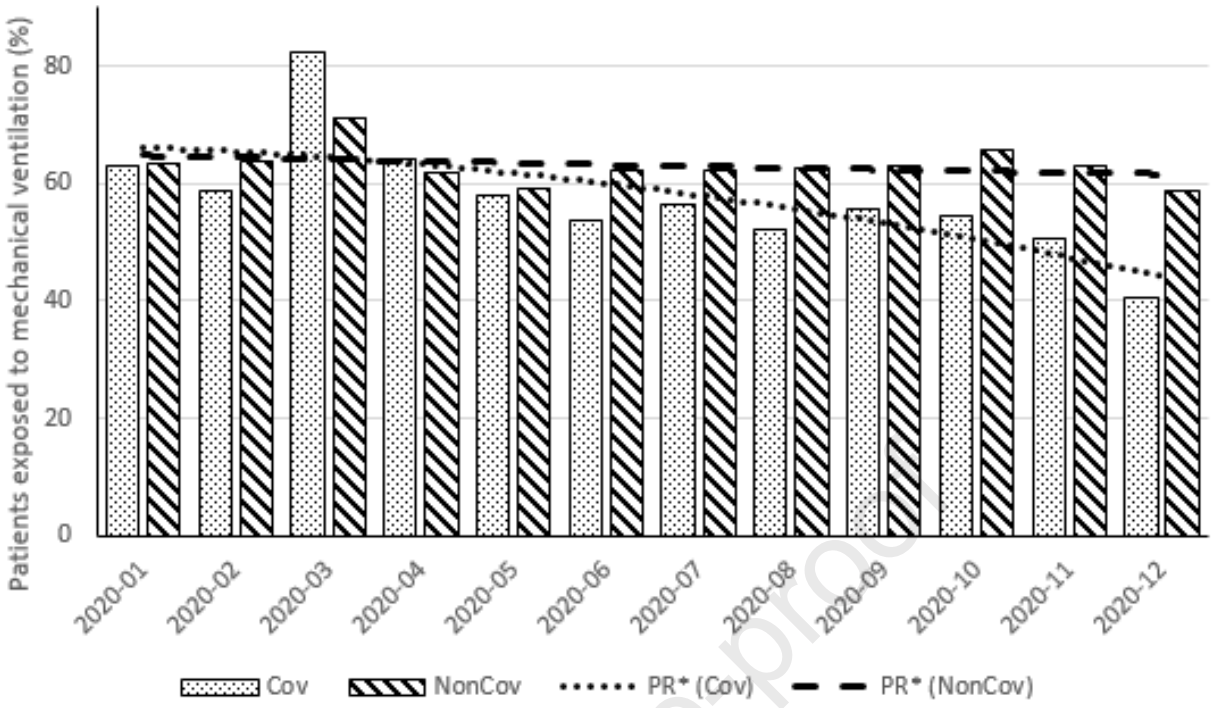


Figure S2: Monthly rate of mechanical ventilation according to the COVID status (REA-REZO 2020) and polynomial regression (PR)

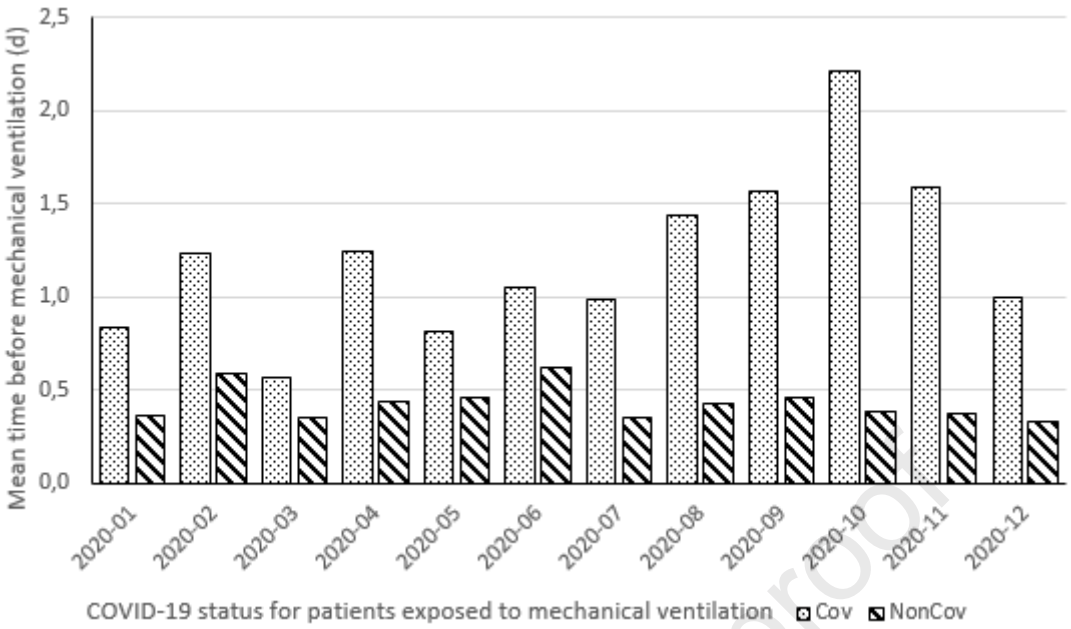


Figure S3 Monthly time to mechanical ventilation (days) since admission according to COVID status.

Table S1: Antimicrobial resistance indicators recorded in the surveillance.

	OXA	AMP	GLY	AMC	3GC	PTZ	CAZ	CAR	COL	ESBL	PanR
Staphylococcus aureus	x		x								X
Enterococcus faecalis and faecium		x	x								X
Enterobacterales				x	X			X		X	X
Pseudomonas aeruginosa						X	X	X	X		X
Acinetobacter baumannii							X	X	X		X

OXA: oxacillin (or meticillin); AMP: ampicillin or amoxicillin; AMC: amoxicillin and clavulanate; ticar: ticarcillin; PTZ: piperacillin-tazobactam 3GC: 3rd generation cephalosporins (cefotaxime or ceftriaxone); CAZ: ceftazidime; CAR: carbapenem (imipenem or meropenem); GLY: glycopeptide (vancomycin or teicoplanin), COL: colistin, ESBL: extended-spectrum beta-lactamase, PANR: non-susceptible to all tested agents.

Table S2**: Logistic regression of predicted individual probability of ventilator-associated pneumonia (VAP).**

			OR	95%CI
Antimicrobials 2 days ± admission			0.83	[0.76 ; 0.92]
Trauma			1.4	[1.18 ; 1.66]
Covid-19			2.78	[2.50 ; 3.10]
SAPSII		0-35		
		36-47	1.25	[1.09 ; 1.43]
		48-61	0.98	[0.86 ; 1.13]
		≥62	0.92	[0.80 ; 1.06]
MV duration (censored for VAP)	1-2			
		3-4	6.89	[5.33 ; 8.91]
		5-10	13.74	[10.77 ; 17.53]
		11-39	13.02	[10.14 ; 16.73]
		≥40	6.64	[4.21 ; 10.47]
Sex		F		
		M	1.5	[1.35 ; 1.65]
Age		15-54		
		55-65	1.05	[0.92 ; 1.20]
		66-76	1.09	[0.95 ; 1.24]
		≥77	0.83	[0.70 ; 0.97]
Patient provenance		home		
		long-stay	0.62	[0.46 ; 0.82]
		short-stay	1	[0.90 ; 1.10]
		other ICU	1.21	[1.04 ; 1.42]
Immunosuppression			0.86	[0.75 ; 0.99]
Reintubation			3.51	[3.14 ; 3.92]

OR: odds ratio, 95%[CI]: 95% confidence interval, MV: mechanical ventilation

Table S3: Multidrug resistant bacteria carriage in ICU patients during the study period 2019-2020

	2019Control	2020NonCov	2020Cov	p-value
ICU patients during the period	39635	23798	4465	
Screening at admission	36338	20321	4013	
Selected MDRB carriers, n (%)	3912 (9.9)	1953 (9.6)	471 (11.7)	*<0.001* $^{\alpha}$
ICU-acquired, n (%)	1215 (3.1)	753 (3.7)	271 (6.8)	*<0.001* $^{\alpha\,\varepsilon}$
Gram positive bacteria				
Methicillin resistant *S aureus*, n (%)	583 (1.5)	280 (1.4)	47 (1.2)	NS
ICU-acquired, n (%)	125 (0.3)	65 (0.3)	26 (0.6)	*<0.001* $^{\alpha}$
Glycopeptide-resistant enterococci, n (%)	112 (0.2)	25 (0.1)	7 (0.2)	NS
ICU-acquired, n (%)	32 (0.1)	11 (0.1)	2 (0.0)	NS
Gram negative bacteria				
Extended spectrum Beta lactamase (ESBL) enterobacterales, n (%)	3005 (7.8)	1618 (7.4)	351 (8.3)	NS
ICU-acquired ESBL, n (%)	856 (2.2)	573 (2.6)	185 (4.4)	*<0.001* $^{\alpha}$
Carbapenem-resistant enterobacterales (CRE), n (%)	143 (0.4)	69 (0.3)	42 (1.0)	*<0.001* $^{\alpha}$
ICU-acquired CRE, n (%)	38 (0.1)	29 (0.1)	27 (0.7)	*<0.001* $^{\alpha}$
Carbapenem-resistant *P aeruginosa* (CRPa), n (%)	392 (1.0)	249 (1.2)	92 (2.3)	*<0.001* $^{\alpha}$
ICU-acquired CRPa, n (%)	231 (0.6)	159 (0.8)	75 (1.9)	*<0.001* $^{\alpha}$

Data are shown as the number of patients n and percentage (%) or median and interquartile range [IQR]. Between-group comparisons with significant p value set at 0.001: NS: not significant, α: Significant difference between 2020Cov and 2020NonCov, ε: Significant difference between 2020NonCov and 2019Control. MDRB: multidrug resistant bacteria.

Table S4: **Microorganisms and selected bacterial resistance.**

	2019Control N=7309 n (%)	2020NonCov N = 5234 n (%)	2020Cov N=2585 n (%)
Gram + micro-organisms	2392 (32.7)	1618 (30.9)	720 (27.9)
Staphylococcus aureus	847 (11.6)	602 (11.5)	249 (9.6)
Methicillin R	99 (11.9)	65 (10.9)	28 (11.3)
Vancomycin R	2 (0.3)	1 (0.2)	0
Enterococcus faecium	94 (1.3)	71 (1.4)	27 (1.0)
Ampicillin R	79 (86.8)	58 (84.1)	21 (77.8)
Vancomycin R	3 (3.3)	2 (2.9)	2 (7.4)
Enterococcus faecalis	219 (3.0)	181 (3.5)	144 (5.6)
Ampicillin R	11 (5.4)	3 (1.7)	5 (3.5)
Vancomycin R	2 (1.0)	0	1 (0.7)
Enterobacterales	2783 (38.1)	2084 (39.8)	1023 (39.6)
3GC R	713 (26.4)	557 (27.3)	312 (30.8)
ESBL	368 (13.7)	271 (13.3)	166 (16.5)
Carbapenem R	37 (1.4)	31 (1.5)	15 (1.5)
Gram - non enterobacterales	1581 (21.6)	1190 (22.7)	658 (25.5)
Acinetobacter sp.	124 (1.7)	61 (1.2)	30 (1.2)
Ceftazidime R	41 (45.6)	8 (28.6)	3 (17.6)
Carbapenem R	30 (33.0)	3 (8.8)	2 (11.8)
Colistin R	6 (9.0)	1 (4.5)	0
Pseudomonas aeruginosa	1022 (14.0)	821 (15.7)	479 (18.5)
Tazobactam R	294 (29.3)	243 (29.9)	133 (28.1)
Ceftazidime R	230 (23.0)	195 (24.1)	86 (18.1)
Carbapenem R	193 (19.3)	185 (22.8)	97 (20.5)
Colistin R	42 (6.0)	22 (3.8)	13 (4.4)
Yeast / parasites	361 (4.9)	224 (4.3)	122 (4.7)
Virus	20 (0.3)	5 (0.1)	16 (0.6)
Other microorganismsMO	172 (2.4)	92 (1.8)	46 (1.4)

3GC R: resistant to third generation cephalosporin, ESBL: extended spectrum betalactamase. Data are expressed as the number n (%) of isolated strains.

Table S5: Detailed distribution of microorganisms isolated in pneumonia (PNE) and bloodstream infections (BSI).

Micro-organisms	2019Control			2020NonCov			2020Cov		
	PNE	BSI	Total	PNE	BSI	Total	PNE	BSI	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Gram + cocci	932 (21.3)	641 (39.4)	2392 (32.7)	710 (21.2)	459 (39.3)	1618 (30.9)	339 (18.6)	233 (44.4)	724 (28.0)
Staphylococcus aureus	606 (13.8)	142 (8.7)	847 (11.6)	451 (13.5)	100 (8.6)	602 (11.5)	193 (10.6)	44 (8.4)	249 (9.6)
Staphylococcus coag. neg	79 (1.8)	285 (17.5)	1010 (13.8)	54 (1.6)	195 (16.7)	606 (11.6)	22 (1.2)	95 (18.1)	240 (9.3)
Streptococcus pneumoniae	85 (1.9)	7 (0.4)	92 (1.3)	58 (1.7)	0 (0.0)	58 (1.1)	13 (0.7)	3 (0.6)	16 (0.6)
Streptococcus others	55 (1.3)	44 (2.7)	114 (1.6)	50 (1.5)	29 (2.5)	82 (1.6)	31 (1.7)	11 (2.1)	44 (1.7)
Enterococcus faecium	31 (0.7)	51 (3.1)	94 (1.3)	25 (0.7)	39 (3.3)	71 (1.4)	11 (0.6)	16 (3)	27 (1)
Enterococcus faecalis	71 (1.6)	103 (6.3)	219 (3.0)	66 (2)	87 (7.4)	181 (3.5)	67 (3.7)	62 (11.8)	144 (5.6)
Other Gram + cocci	5 (0.1)	9 (0.6)	16 (0.2)	6 (0.2)	9 (0.8)	18 (0.3)	2 (0.1)	2 (0.4)	4 (0.2)
Enterobacterales	1827 (41.7)	545 (33.5)	2783 (38.1)	1432 (42.8)	416 (35.6)	2084 (39.8)	823 (45.3)	141 (26.9)	1023 (39.5)
Escherichia coli	375 (8.6)	153 (9.4)	590 (8.1)	258 (7.7)	81 (6.9)	371 (7.1)	133 (7.3)	22 (4.2)	164 (6.3)
Proteus	126 (2.9)	33 (2.0)	218 (3.0)	94 (2.8)	10 (0.9)	134 (2.6)	52 (2.9)	4 (0.8)	62 (2.4)
Klebsiella	469 (10.7)	151 (9.3)	718 (9.8)	352 (10.5)	117 (10)	527 (10.1)	208 (11.4)	44 (8.4)	266 (10.3)
Citrobacter	126 (2.9)	11 (0.7)	159 (2.2)	113 (3.4)	24 (2.1)	145 (2.8)	62 (3.4)	7 (1.3)	72 (2.8)
Enterobacter	438 (10.0)	128 (7.9)	677 (9.3)	383 (11.4)	124 (10.6)	567 (10.8)	234 (12.9)	44 (8.4)	296 (11.4)
Hafnia	59 (1.3)	5 (0.3)	68 (0.9)	52 (1.6)	8 (0.7)	65 (1.2)	45 (2.5)	2 (0.4)	49 (1.9)
Morganella	49 (1.1)	15 (0.9)	83 (1.1)	43 (1.3)	14 (1.2)	81 (1.5)	19 (1)	3 (0.6)	23 (0.9)
Serratia	175 (4.0)	47 (2.9)	255 (3.5)	122 (3.6)	35 (3)	173 (3.3)	67 (3.7)	12 (2.3)	85 (3.3)
Other enterobacterales	10 (0.2)	2 (0.1)	15 (0.2)	15 (0.4)	3 (0.3	21 (0.4)	3 (0.2)	3 (0.6)	6 (0.2)
Gram negative bacilli non enterobacterales	1218 (27.8)	194 (11.9)	1581 (21.6)	923 (27.6)	159 (13.6)	1190 (22.7)	514 (28.3)	96 (18.3)	658 (25.4)
Acinetobacter	92 (2.1)	21 (1.3)	124 (1.7)	53 (1.6)	7 (0.6)	61 (1.2)	23 (1.3)	4 (0.8)	30 (1.2)
Haemophilus	208 (4.7)	2 (0.1)	210 (2.9)	126 (3.8)	1 (0.1)	128 (2.4)	57 (3.1)	1 (0.2)	59 (2.3)
Pseudomonas aeruginosa	734 (16.8)	139 (8.5)	1022(14.0)	589 (17.6)	130 (11.1)	821 (15.7)	357 (19.6)	83 (15.8)	479 (18.5)
Stenotrophomonas maltophilia	155 (3.5)	19 (1.2)	180 (2.5	126 (3.8)	8 (0.7)	136 (2.6)	60 (3.3)	3 (0.6)	65 (2.5)
Other bacilli	29 (0.7)	13 (0.8)	45 (0.6)	29 (0.9)	13 (1.1)	44 (0.8)	17 (0.9)	5 (1)	25 (1.0)
Yeast / parasites	100 (2.3)	171 (10.5)	361 (4.9)	72 (2.2)	102 (8.7)	224 (4.3)	62 (3.4)	43 (8.2)	122 (4.7)
Candida albicans	56 (1.3)	87 (5.3)	197 (2.7)	36 (1.1)	63 (5.4)	127 (2.4)	35 (1.9)	29 (5.5)	77 (3)
Candida other	25 (0.6)	79 (4.9)	137 (1.9)	17 (0.5)	38 (3.3)	76 (1.5)	7 (0.4)	14 (2.7)	25 (1)
Aspergillus	15 (0.3)	1 (0.1)	16 (0.2)	15 (0.4)		15 (0.3)	19 (1)	0 (0.0)	19 (0.7)
Other	4 (0.1)	4 (0.2)	11 (0.2)	4 (0.1)	1 (0.1)	6 (0.1)	1 (0.1)	0 (0.0)	1 (0)
Virus	17 (0.4)	2 (0.1)	20 (0.3)	5 (0.1)	0 (0)	5 (0.1)	16 (0.9)	0 (0)	16 (0.6)
Herpes simplex Virus	12 (0.3)		12 (0.2)	2 (0.1)		2 (0)	12 (0.7)		12 (0.5)
Other Virus	5 (0.1)	2 (0.1)	8 (0.1)	3 (0.1)		3 (0.1)	4 (0.2)		4 (0.2)
Other microorganism	65 (1.5)	71 (4.4)	172 (2.4)	44 (1.3)	32 (1.0)	92 (1.8)	25 (0.7)	12 (0.4)	46 (1.4)
Total	4379 (100)	1627 (100)	7309 (100)	3347 (100)	1168 (100)	5234 (100)	1818 (100)	525 (100)	2589 (100)