



CONVEGNO INTERNAZIONALE
**GIORNATE
INFETTIVOLOGICHE
“LUIGI SACCO”**



**HYBRID
EDITION**



UNIVERSITÀ DEGLI STUDI
DI MILANO

Sistema Socio Sanitario



Regione
Lombardia

ASST Fatebenefratelli Sacco

18–19 Ottobre 2021

Batteriemie in corso di infezione da SARS-CoV-2

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Outline

❖ Burden

❖ Etiology

❖ Risk factors

❖ Diagnostic issues



Acute Bacterial Co-Infection in COVID-19

A Rapid Living Review and Meta-analysis



24 Studies
included



3338 COVID-19
Patients



December 2019
to March 2020

3.5%
Co-Infection

On presentation

14.3%
**Secondary
Infection**

After presentation

71.8% Antibiotic
Prescribing

Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, Soucy JPR, Daneman N.
Clinical Microbiology and Infection. 2020.



TARRN
www.tarrn.org/covid

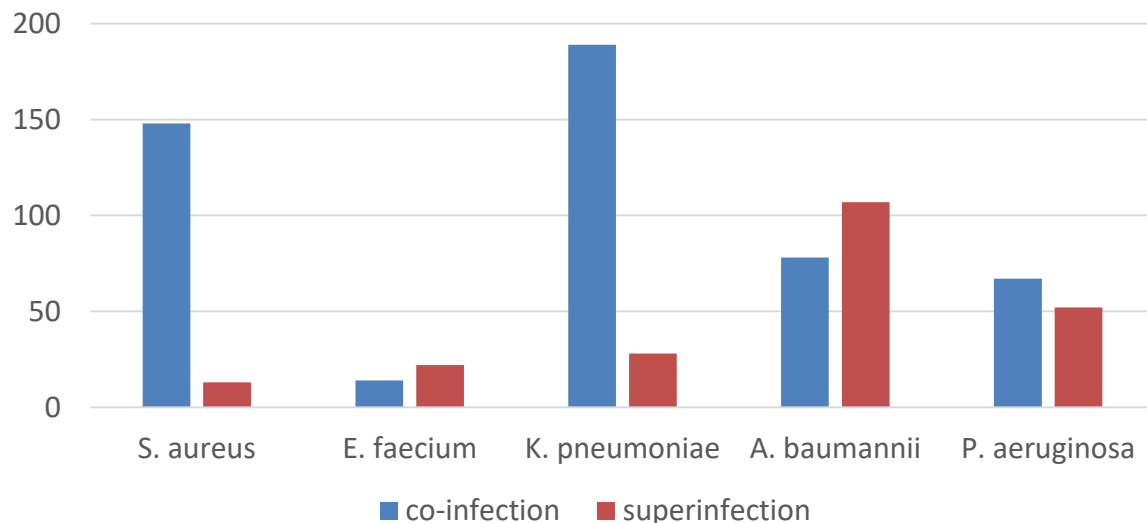


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Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis

Musuuza J et al. PLOS ONE May 6 2021

- 118 studies (42% China, 15% US), hospitalized patients 92%, mixed setting (ICU and non-ICU) 72%
- Pooled prevalence of co-infection 19% (95%CI 14-25%)
- Pooled prevalence of superinfection 24% (19-30%), **among ICU patients 41% (24-58%)**



- Patients with co- or super-infection had a higher odds of dying than other SARS-CoV2 patients (OR 3.31)



Bacteremia

Ref	Country	Period	Setting	N COVID-19	BSI	Prevalence
Abelenda-Alonso CMI 2021	Spain	Feb-April 2020	Hospitalized	2005	142 in 100 pts	4.98%
Engsbro ID 2020	Denmark	March-May 2020	Hospitalized	227	12	5.2%
Pasquini IJID 2021	Italy	Jan-June 2020	Hospitalized	1182	107	8.2%
Bhatt CID 2021	US	March-May 2020	Hospitalized with BCs	375	128	34%
Kokkoris JHI 2021	Greece	March-May 2020	ICU	50	20	40%
Giacobbe EJCI2020	Italy	Feb-Apr 2020	ICU	78	45 in 31 pts	40%
Cataldo JGAR 2020	Italy	March-Apr 2020	ICU	57	28	49%
Bonazzetti CCM 2021	Italy	Feb-Apr 2020	ICU	89	93 in 60 pts	67.4%

Bloodstream infections in the COVID-19 era: results from an Italian multi-centre study

Pasquini Z et al. Intern Journal Infect Dis 2021; 111:31-36

	BSIs in first half of 2019, <i>n</i> per 1000 patient-years	BSIs in first half of 2020, <i>n</i> per 1000 patient-years		
		All patients	Patients without COVID-19	Patients with COVID-19
BSIs – overall	751 (2.76)	665 (3.05)	558 (2.72)	107 (8.19) ^{a,b}
BSIs – normal ward	675 (2.52)	555 (2.60)	492 (2.44)	63 (5.46) ^{a,b}
BSIs – ICU	76 (18.17)	110 (23.56)	66 (21.01)	44 (28.82) ^c

1. Immune system dysregulation
2. Longer hospitalization and higher rate of ICU admission
3. High use of immunosuppressive drugs
4. Gut-lung dysfunction



Bloodstream infections in the COVID-19 era: results from an Italian multi-centre study

Pasquini Z et al. Intern Journal Infect Dis 2021; 111:31-36

Without COVID-19

CoNS
4.5

CPE
0.5

CR-Ab
2.2

With COVID-19

CoNS
15.2

CPE
14.4

CR-Ab
16.1

N per 1000 hospitalizations in 2020

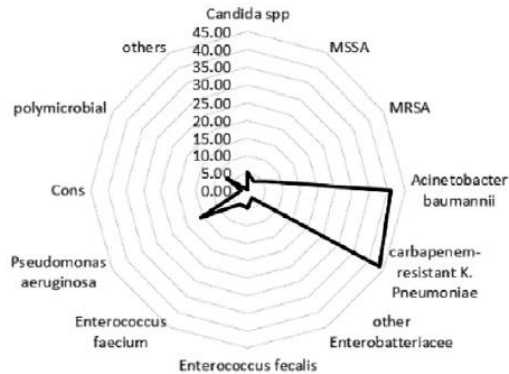


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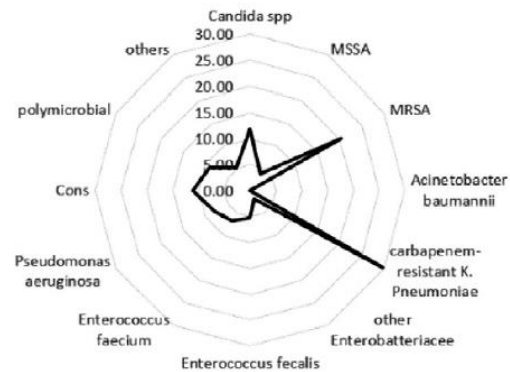
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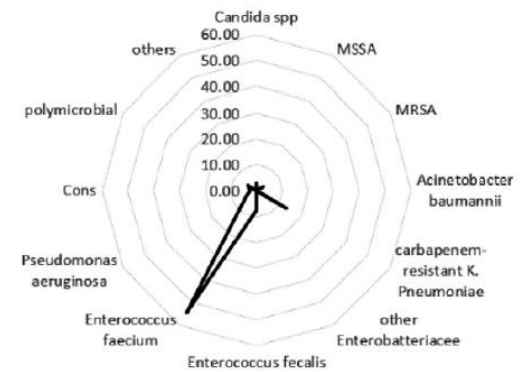
Marche Nord hospitals



Ancona hospital

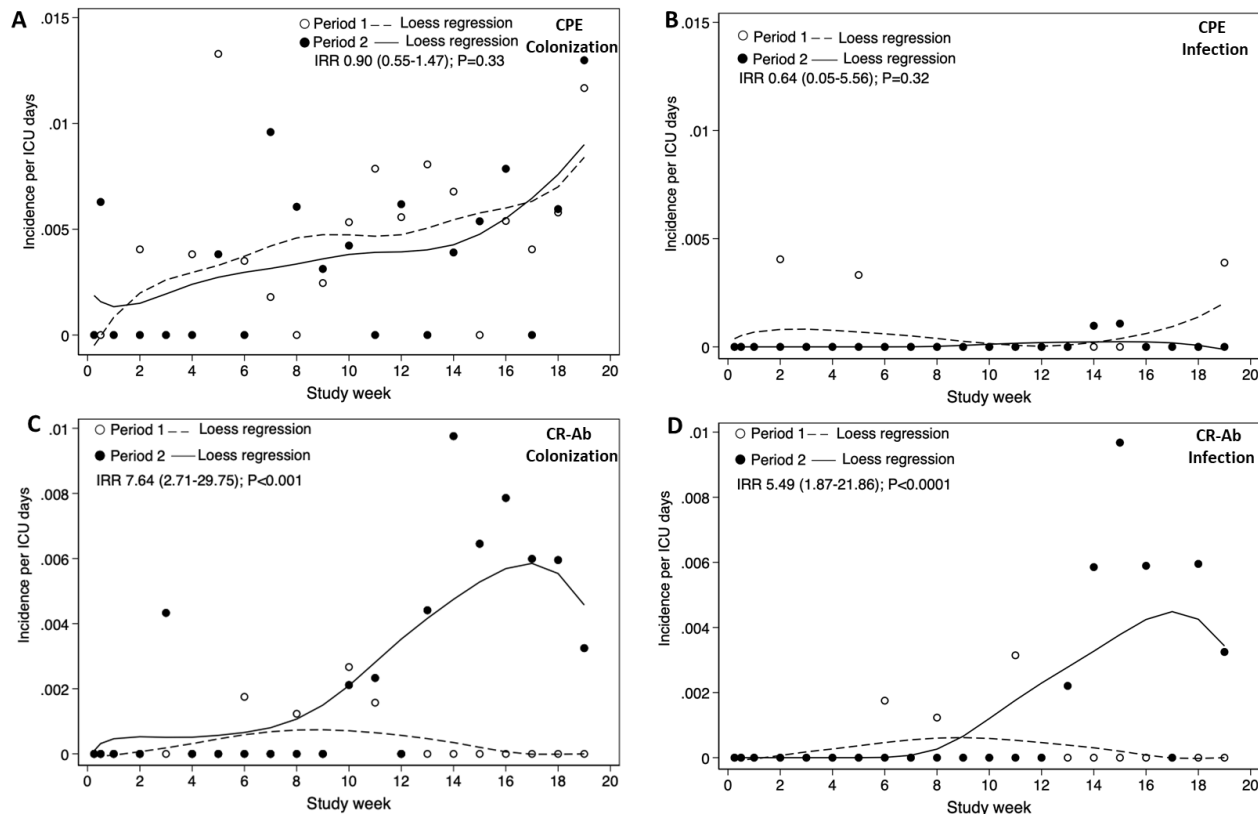


Fermo hospital



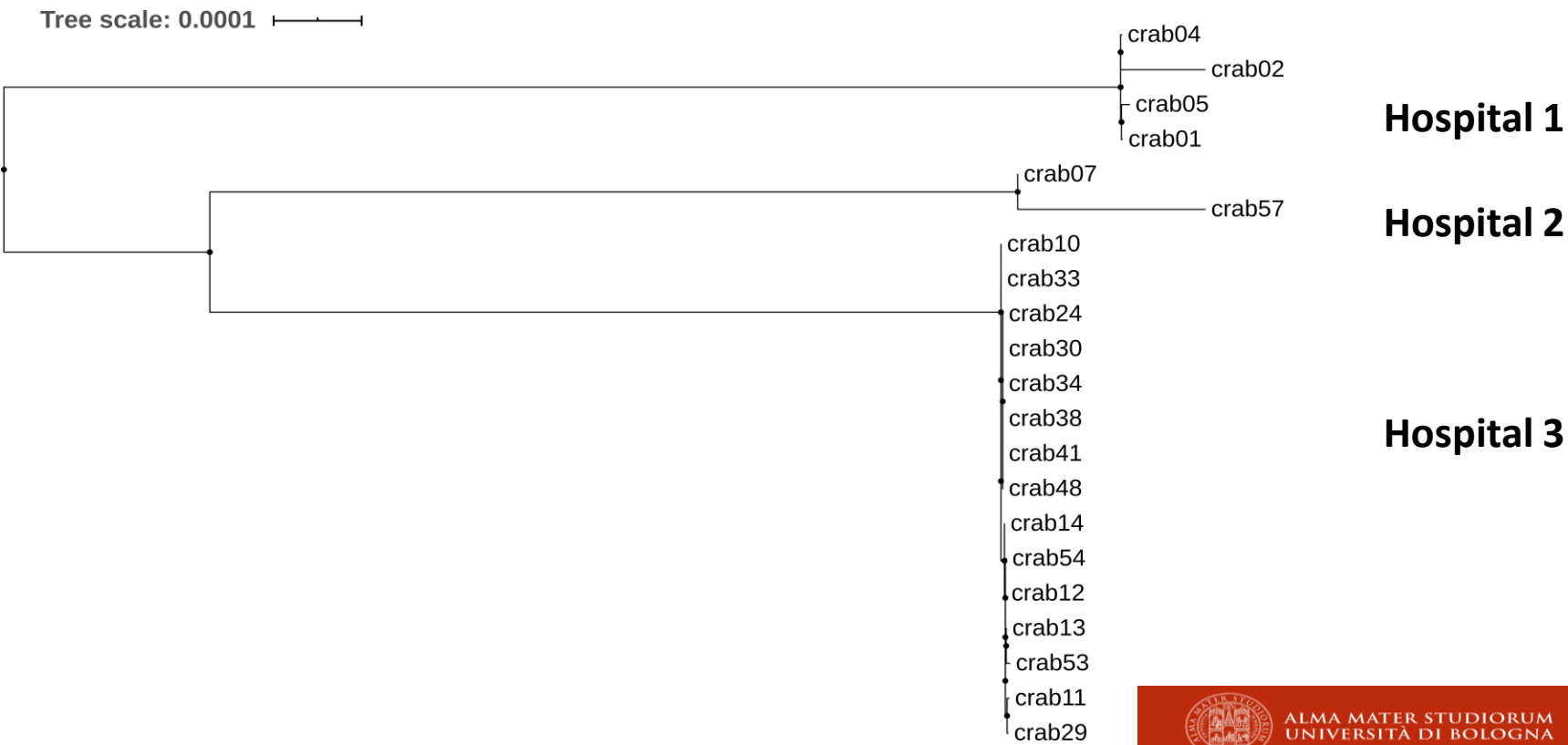
Carbapenem resistant bacteria in Intensive Care Unit during COVID-19 pandemic: multicenter before-after cross sectional study

Pascale R et al. Infect Control Hosp Epidemiol 2021 Apr 16;1-25



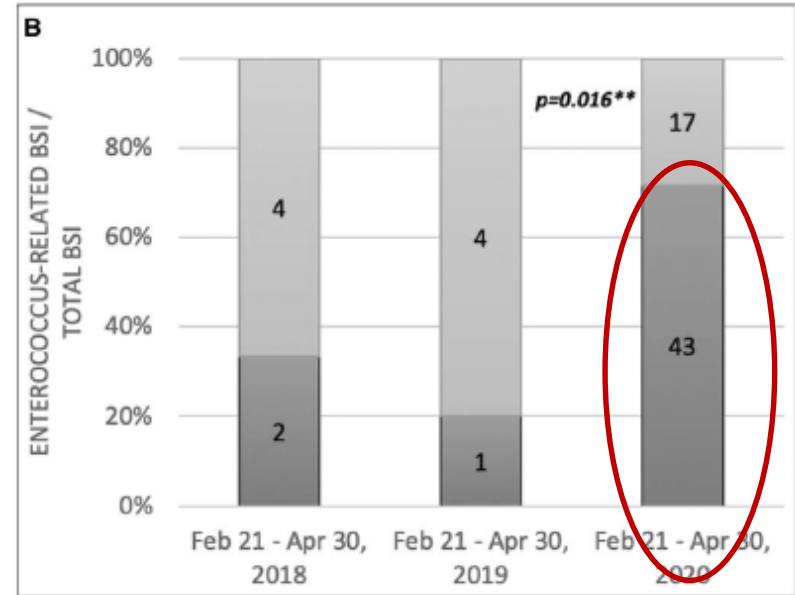
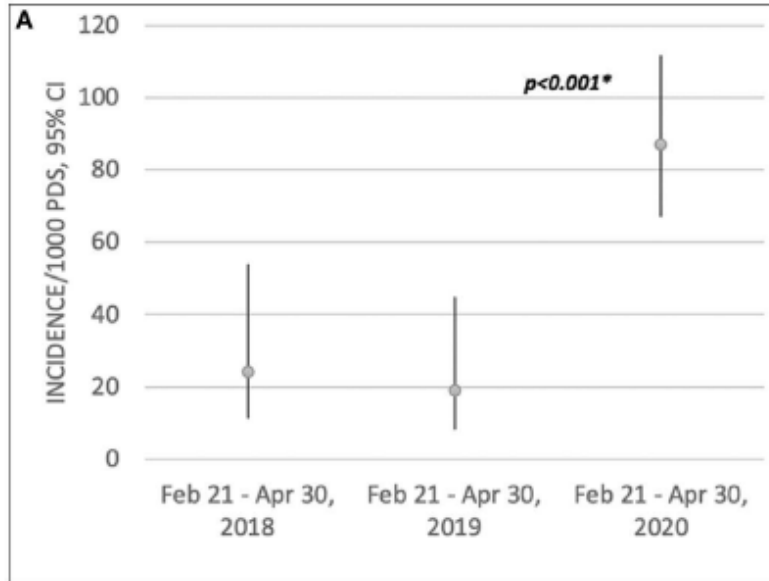
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Unexpectedly High Frequency of Enterococcal Bloodstream Infections in Coronavirus Disease 2019 Patients Admitted to an Italian ICU: An Observational Study

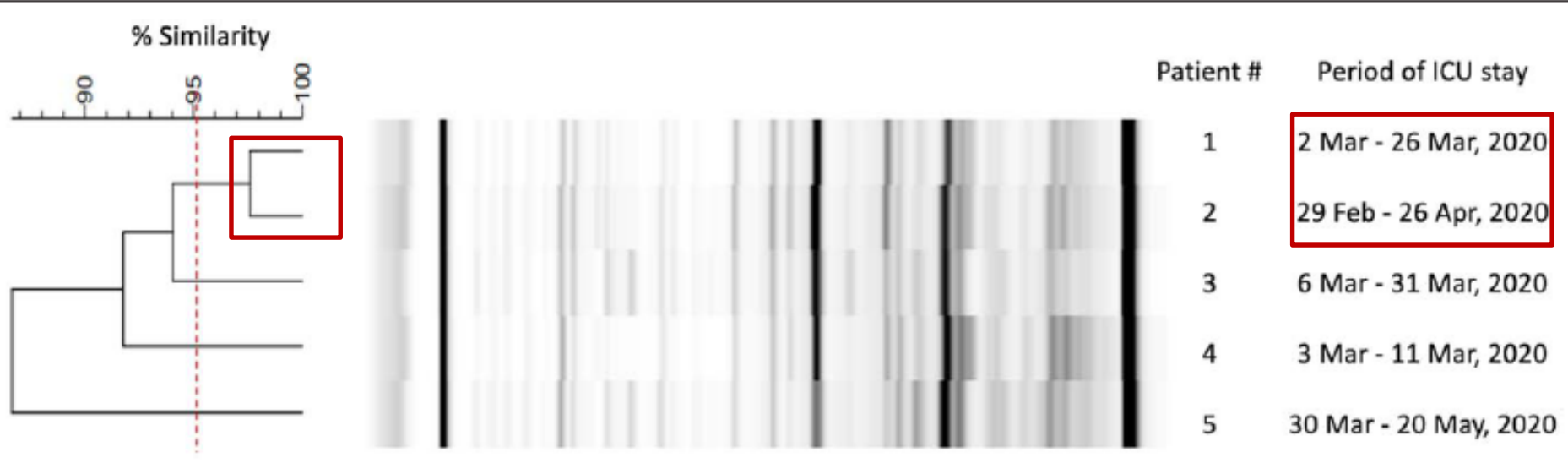
Bonazzetti C et al. Crit Care Med 2021; 49:1



Unexpectedly High Frequency of Enterococcal Bloodstream Infections in Coronavirus Disease 2019 Patients Admitted to an Italian ICU: An Observational Study

Bonazzetti C et al. Crit Care Med 2021; 49:1

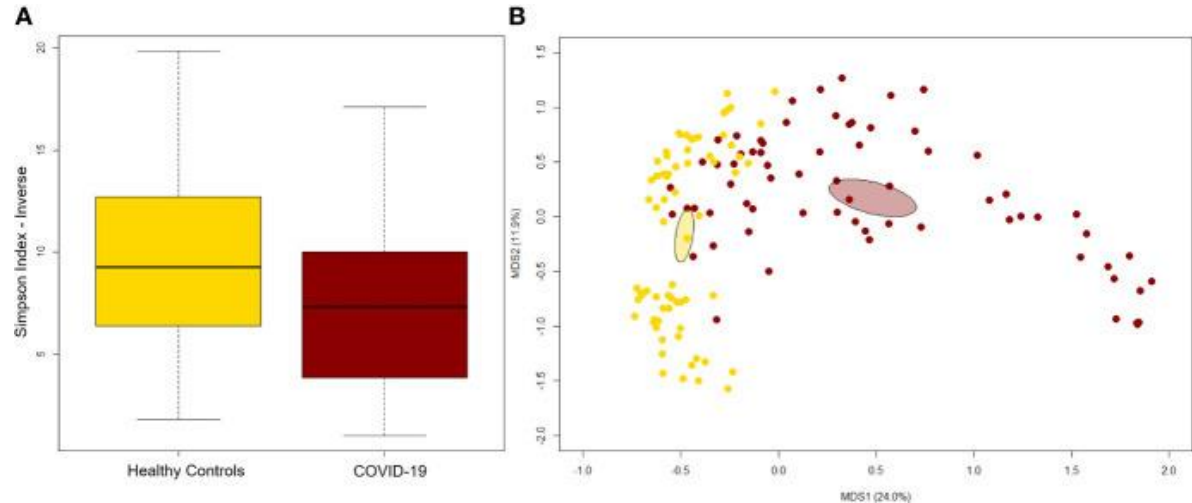
- 5 VRE isolates



The Gut Microbiota of Critically Ill Patients With COVID-19

Gaibani P et al. Front Cell Infect Microbiol 2021;11:670424

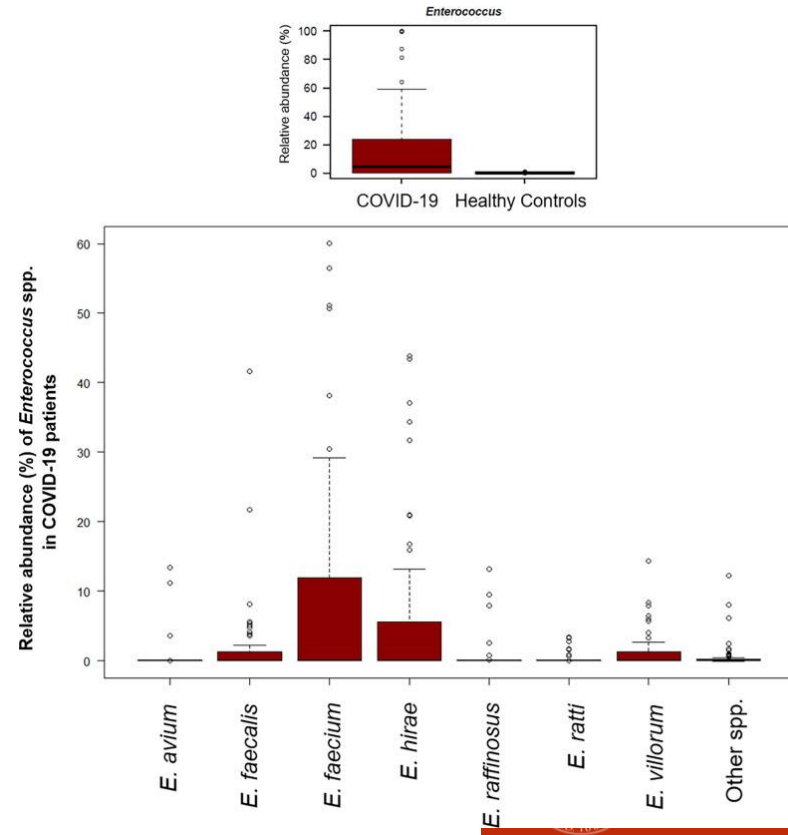
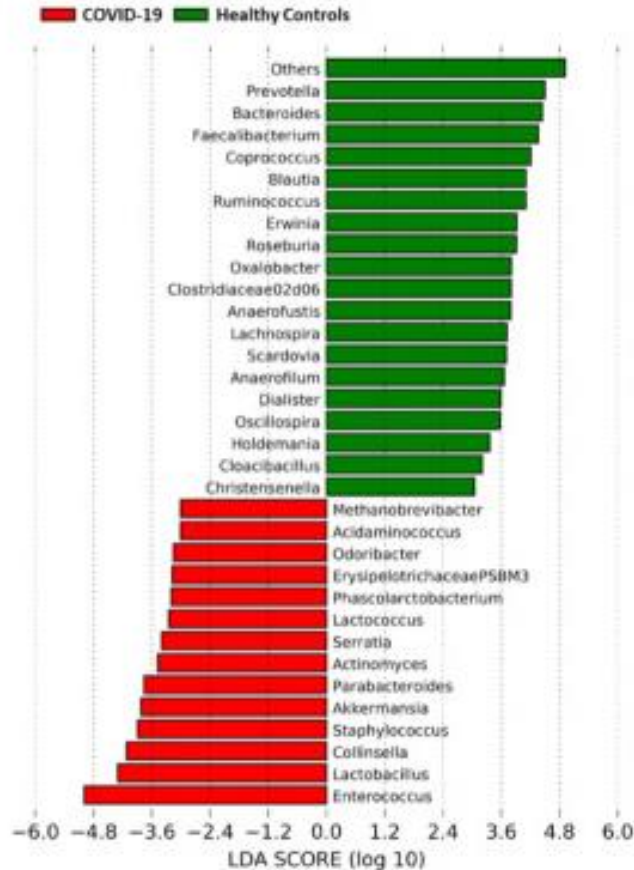
	N=69
Age	73, 59-85
Male	38 (55.1)
Charlson	5, 2-7
Days symptoms onset-hospitalization	3, 1-7
SOFA	2, 1-3
ICU admission	16 (23.2)
Days hospitalization-fecal sample collection	14, 6-23
Exposure to antibiotics	61 (88)
In-hospital mortality	9 (13)
Length of stay	25, 13-33



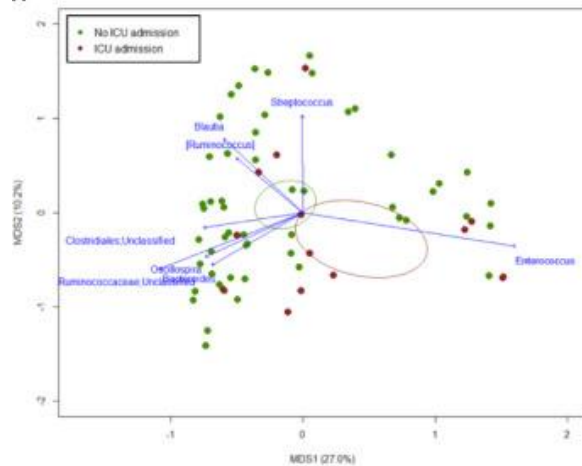
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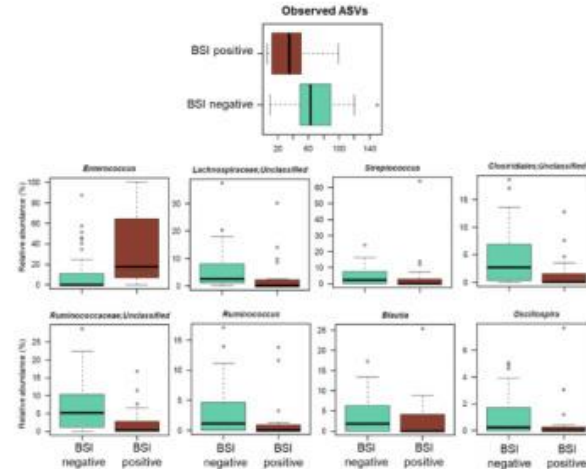
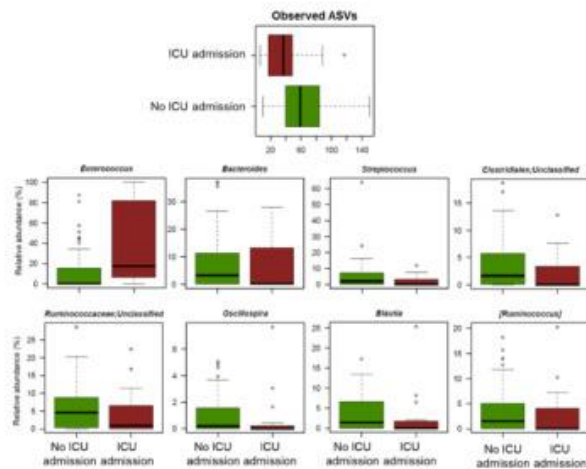
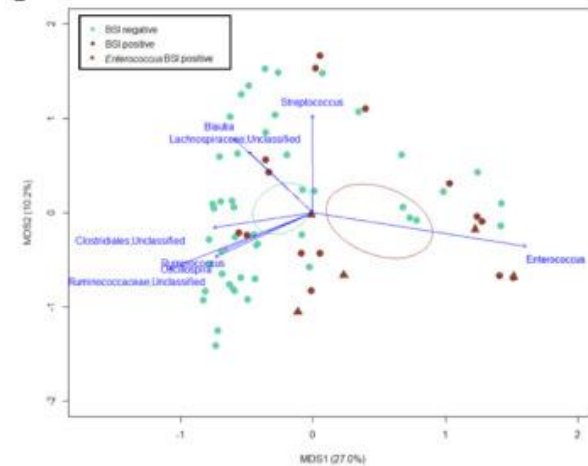
B

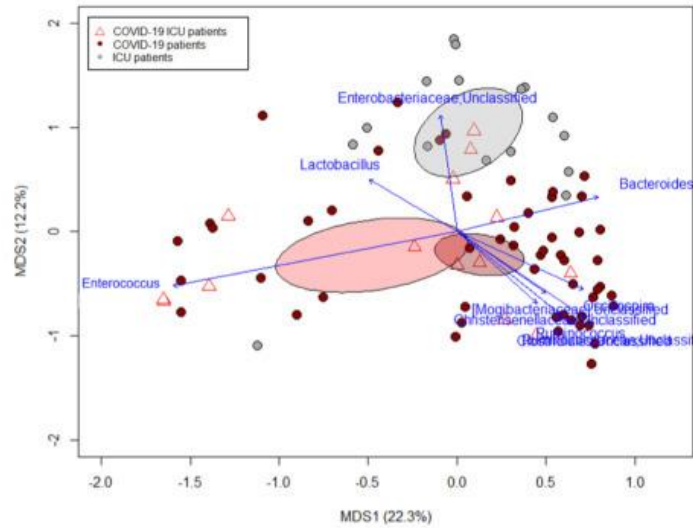
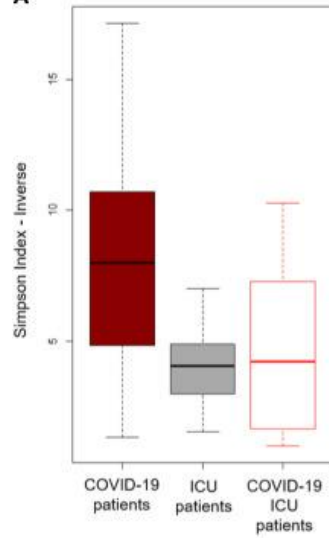
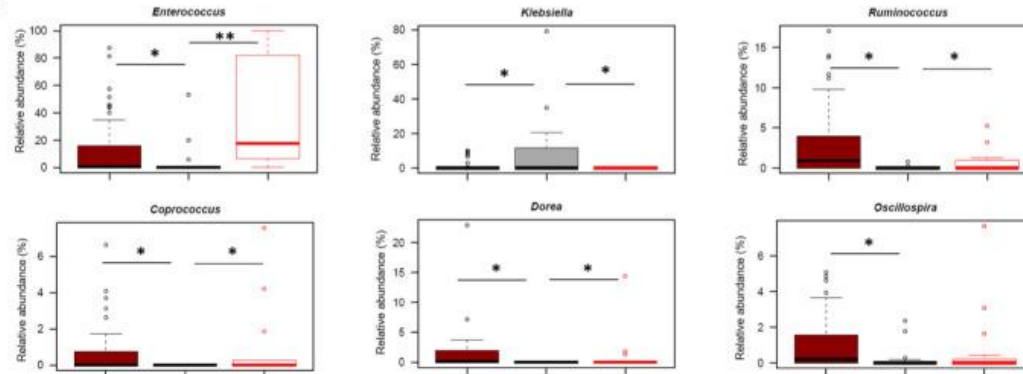


A



B



A**B**

Bloodstream infections in critically ill patients with COVID-19

Giacobbe D et al. Eur J Clin Invest 2020; 50:e13319

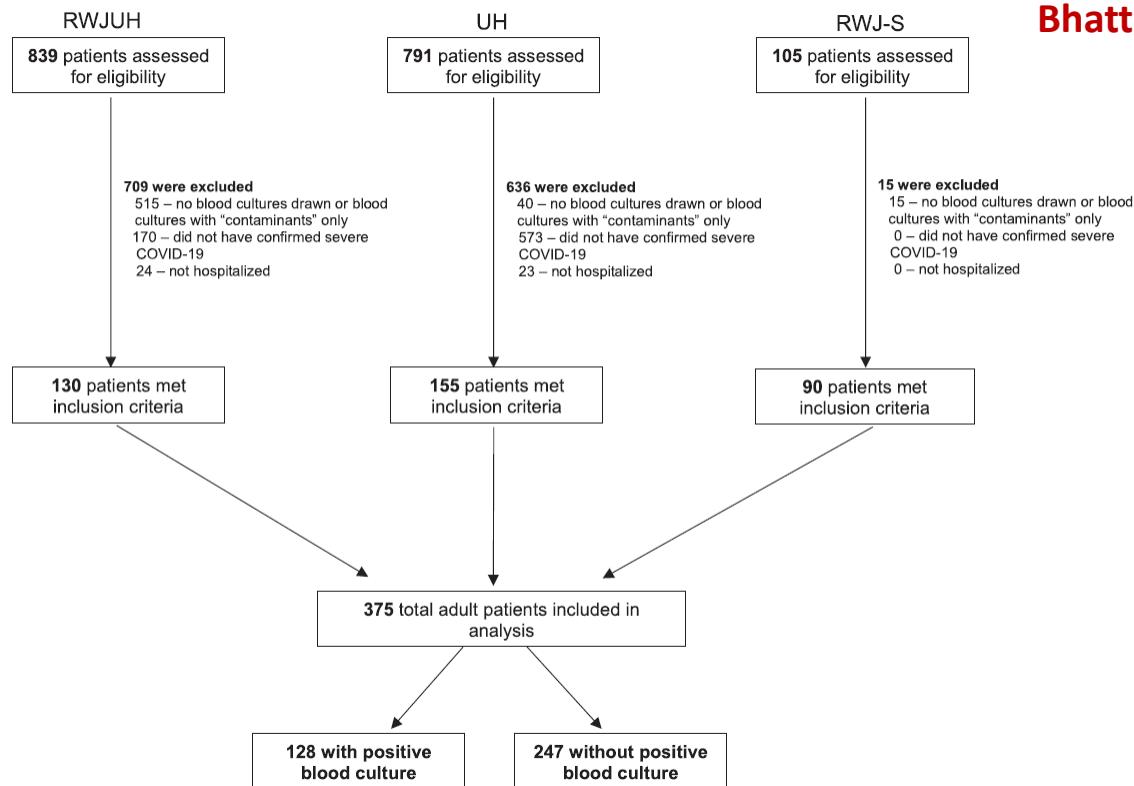
Variable	Unadjusted cause-specific HR (95% CI)	P	Adjusted cause-specific HR (95% CI)	P
Age in years	1.00 (0.96-1.04)	.970		
Male gender	1.60 (0.65-3.94)	.304		
Diabetes mellitus	2.76 (1.09-6.98)	.032	2.22 (0.80-6.20)	.127
Hypertension	0.89 (0.43-1.85)	.755		
Respiratory disease	1.87 (0.54-6.43)	.323		
Moderate/severe liver failure	6.71 (0.77-58.29)	.084	6.36 (0.59-68.39)	.127
Solid cancer	2.71 (0.35-20.99)	.340		
Haematological malignancy	^b	-		
Hospital stay before ICU admission in days	1.02 (0.98-1.08)	.339		
SOFA score	1.00 (0.80-1.25)	.996		
Antibiotic therapy	^b	-		
Anti-inflammatory treatment				
Methylprednisolone	4.48 (1.38-14.56)	.002	3.95 (1.20-13.03)	.003
Tocilizumab	1.21 (0.44-3.30)		1.07 (0.38-3.04)	
Both of them	10.84 (2.79-42.08)		10.69 (2.71-42.17)	
None of them	(ref)		(ref)	

- 78 critically ill covid-19 patients
- 45 BSI in 31 patients
 - ✓ tocilizumab (n = 16)
 - ✓ steroid (n = 12)
 - ✓ tocilizumab and steroid (n = 7)
 - ✓ neither tocilizumab nor steroid (n = 10)



Risk Factors and Outcomes of Hospitalized Patients With Severe Coronavirus Disease 2019 (COVID-19) and Secondary Bloodstream Infections: A Multicenter Case-Control Study

Bhatt PJ et al CID 2021;72(12):e995–e1003



Risk Factors and Outcomes of Hospitalized Patients With Severe Coronavirus Disease 2019 (COVID-19) and Secondary Bloodstream Infections: A Multicenter Case-Control Study

Bhatt PJ et al CID 2021;72(12):e995–e1003

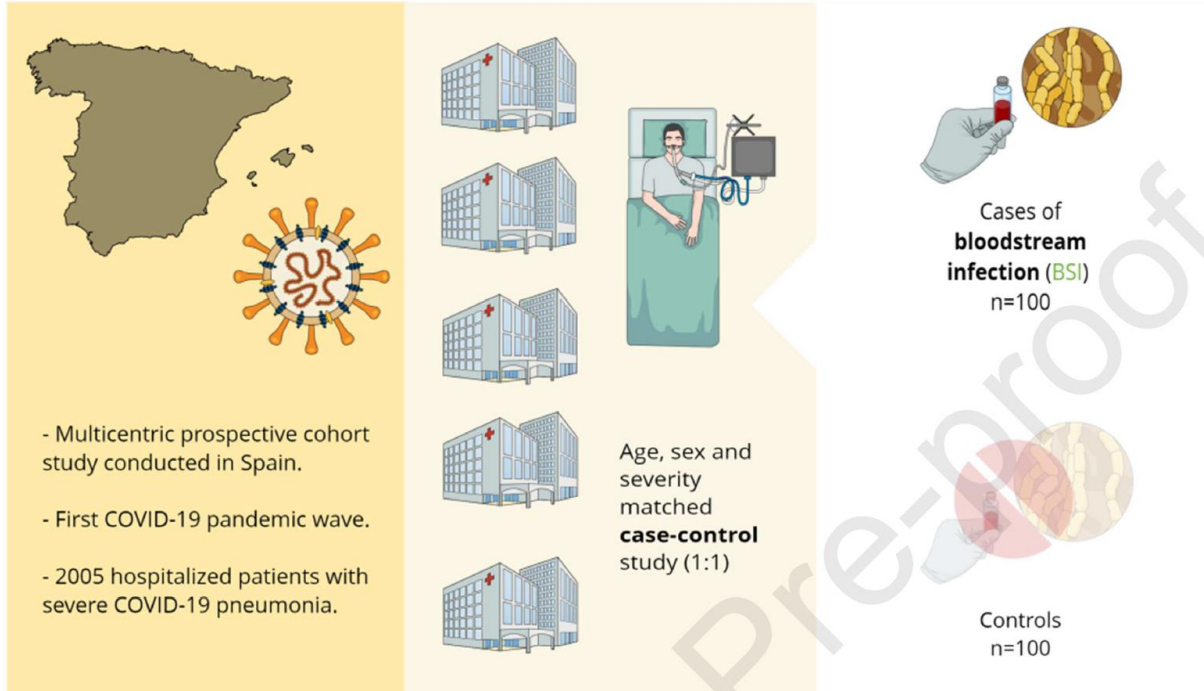
Propensity score matching by age, sex, and race/ethnicity

	No sBSI (n=128)	sBSI (n=128)	p value
Ever received intravenous antimicrobial therapy, N (%)	94 (73.4)	127 (99.2)	<0.001
Ever received systemic glucocorticoids, N (%)	25 (19.5)	41 (32.0)	0.02
Ever received tocilizumab, N (%)	27 (21.1)	34 (26.6)	0.305
Admission to ICU, N (%)	44 (34.4)	91 (71.1)	<0.001
Septic shock requiring vasopressors, N (%)	16 (12.5)	71 (55.5)	<0.001
In-hospital death, N (%)	81 (32.8)	68 (53.1)	0.0006
Of those who died, died <7 days (admission to death)	51 (63.0)	22 (32.3)	<0.001
Of those who died, died 8-14 days (admission to death)	17 (21.0)	11 (16.2)	
Of those who died, died >15 days (admission to death)	13 (16.1)	35 (51.5)	
Alive as of 6/3/20, N (%)	166 (67.2)	60 (46.9)	0.0001
Of those alive, discharged	164 (98.8)	38 (63.3)	<0.0001
Of those alive, still hospitalized as of 6/3/20	2 (1.2)	22 (36.7)	
Readmission with bacteremia, N (%)	1 (1.2)	1 (2.7)	0.337



Immunomodulatory therapy, risk factors and outcomes of hospital-acquired bloodstream infection in patients with severe COVID-19 pneumonia: a Spanish case-control matched multicenter study (BACTCOVID)

Abelenda-Alonso G et al. CMI in press



Main isolates:

- ✓ CoNS 27%
- ✓ E. faecalis 19%
- ✓ P. aeruginosa 9%



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Immunomodulatory therapy, risk factors and outcomes of hospital-acquired bloodstream infection in patients with severe COVID-19 pneumonia: a Spanish case-control matched multicenter study (BACTCOVID)

Abelenda-Alonso G et al. CMI in press

	Patients with BSI n=100	Controls n=100	p-value	OR; CI 95%	p-value
Age† (median; IQR)	64.50 (57 – 71.75)	64 (57 – 72)	1.000	1.05 (0.96 – 1.16)	0.256
Gender: Male	66; 66%	66; 66%	1.000	1.12 (0.71 – 1.75)	0.631
D-dimer [> 700 ug/L]	42; 42%	9; 9%	<0.001	2.68 (1.61 – 4.44)	<0.001
Tocilizumab	45; 45%	45; 45%	1.000	1.23 (0.73 – 2.07)	0.447
Corticosteroids [> 10 days]	39; 39%	36; 36%	0.770	1.22 (0.68 – 2.20)	0.509
Tocilizumab and corticosteroids [>10 days]	21; 21%	22; 22%	0.880	0.74 (0.44 – 1.78)	0.500
Previous Broad-spectrum antibiotic therapy	61 (61%)	33 (33%)	<0.001	1.23 (0.80 – 1.88)	0.347
ICU admission	91; 91%	91; 91%	1.000	1.15 (0.43 – 3.08)	0.779



Bacteremia in critically ill COVID-19 patients from Milan and Bologna

	Total N= 537 (%)	Milano N= 236 (%)	Bologna N= 301 (%)	p
Age (years) (median, IQR)	65 (57-72)	63.3 (55.6-70)	67 (58.5-73.5)	<0.001
Sex, male	402 (74.9)	181 (76.7)	221 (73.4)	0.4
Charlson Index	3 (2-4)	2 (1-3)	3 (2-5)	<0.001
Days admission-ICU	2 (0-5)	2 (0-5)	2 (1-5)	0.09
BSI	265 (49.3)	153 (64.8)	112 (37.2)	<0.001
SOFA score at BSI onset	9 (7-11)	9 (7-11)	9 (8-11)	0.05
Days from ICU admission to BSI onset (median, IQR)	7 (4-13)	6 (4-9)	11 (4-23)	<0.001
Treatments				
Tocilizumab	228 (42.5)	39 (16.5)	189 (62.8)	<0.001
Remdesivir	102 (19)	70 (29.7)	32 (10.6)	<0.001
Heparin	426 (79.3)	164 (69.5)	262 (87)	<0.001
Steroids	366 (68.2)	149 (63.1)	217 (72.1)	0.03
Antibiotic treatment before BSI	487 (90.7)	205 (86.9)	282 (93.7)	0.01
Outcome				
Length of ICU stay	13 (7.5-22)	12 (6-20)	14 (8-23)	0.007
All cause 30-day mortality	258 (48)	123 (52.1)	135 (44.9)	0.1

Diagnostic issues

MILANO (campione del 10% del totale di pazienti: 24 pazienti)	
Mediana emocolture eseguite per paziente	6 (IQR 4- 10)
Totale emocolture eseguite	189
Totale giorni degenza ICU	414
Emocolture/giorni degenza ICU	0,456

BOLOGNA (campione del 10% del totale di pazienti: 30 pazienti)	
Mediana emocolture eseguite per paziente	2 (IQR 1-3)
Totale emocolture eseguite	95
Totale giorni degenza ICU	610
Emocolture/giorni degenza ICU	0,155



	1 st wave	2 nd wave	Total
Total	165 (100)	140 (100)	305 (100%)
Gram +	107 (64.8)	101 (72.1)	208 (68.2%)
Enterococcus spp.	50 (30.3)	47 (33.6)	97 (31.8)
VRE	2 (1.2)	2 (1.4)	4 (1.3)
S. aureus	12 (7.3)	18 (12.9)	30 (9.8)
MRSA	10 (6.1)	6 (4.3)	16 (5.2)
CoNS	41 (24.8)	2 (1.4)	43 (14.1)
Viridans Streptococci	1(0.6)	6 (4.3)	7 (2.3)
Other	3 (1.8)	3 (2.1)	6 (2)
Gram -	52 (31.5)	36 (25.7)	88 (28.9)
Enterobacteriaceae	25 (15.2)	19 (13.6)	44 (14.4)
ESBL +	9 (5.5)	1 (0.7)	10 (3.3)
CPE	6 (3.6)	0 (0)	6 (2)
Enterobacter spp	4 (2.4)	11 (7.9)	15 (4.9)
Pseudomonas aeruginosa	14 (8.5)	5 (3.6)	19 (6.2)
MDR	7 (4.2)	2 (1.4)	9 (3)
S. maltophilia	0 (0)	0 (0)	0 (0)
A. baumannii	9 (5.5)	1 (0.7)	10 (3.3)
CRAB	9 (5.5)	1 (0.7)	10 (3.3)
Yeasts	6 (3.6)	3 (2.1)	9 (3)
Candida albicans	4 (2.4)	2 (1.4)	6 (2)
Candida parapsilosis	2 (1.2)	1 (0.7)	3 (1)
0_Primary	48 (32.2)	58 (50)	106 (40)
1_CLABSI	56 (37.6)	31 (26.7)	87 (32.9)
2_LUNG	29 (19.5)	12 (10.3)	41 (15.5)
3_UTI	15 (10.1)	12 (10.3)	27 (10.2)
4_IAI	1 (0.7)	3 (2.6)	4 (1.5)

FATTORI DI RISCHIO ASSOCIATI ALLO SVILUPPO DI BATTERIEMIA NEI PAZIENTI CON INFEZIONE DA SARS-COV-2 RICOVERATI IN TERAPIA INTENSIVA: STUDIO MULTICENTRICO RETROSPETTIVO

Parameter	p-value	Unadjusted cause-specific HR (95% CI)		
Wave: 2 vs. 1	<.0001	1,780	1,382	2,292
Hospital: BO vs. MI	<.0001	0,216	0,165	0,283
Sex: Female vs. Male	0,394	0,883	0,663	1,176
Age (x 1 year more)	0,295	0,994	0,982	1,005
Obesity: Yes vs. No	0,448	0,905	0,699	1,172
Days from symptoms to RIA (x 1 day more)	0,446	1,007	0,989	1,026
Charlson Score Unadjusted for age (x 1 unit more)	0,209	1,053	0,972	1,141
Remdesivir: Yes vs. No	0,055	1,335	0,994	1,793
Steroids: Yes vs. No	0,640	1,065	0,819	1,385
Sofa Score (x 1 unit more)	0,002	1,073	1,027	1,120
IOT: Yes vs. No	0,041	1,656	1,021	2,687

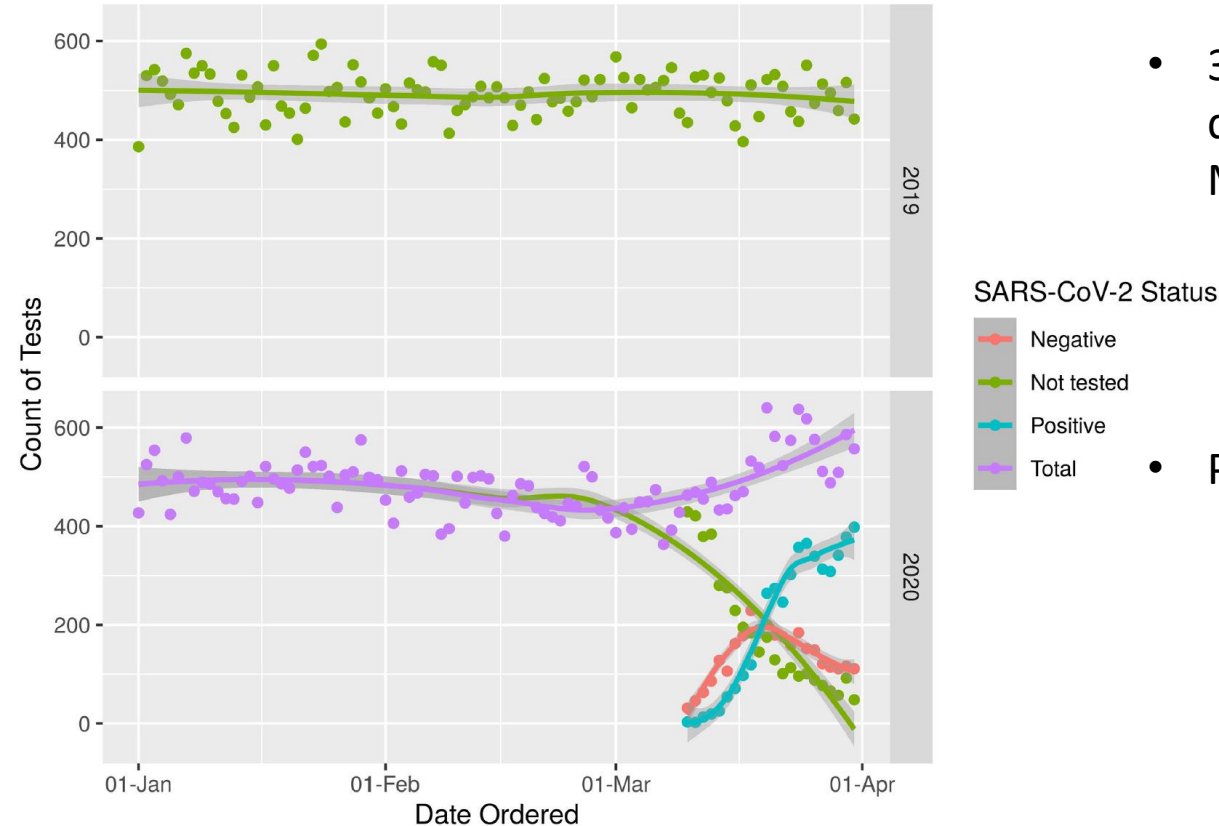
Parameter	p-value	Adjusted cause-specific HR (95% CI)		
Wave: 2 vs. 1	0,723	1,064	0,754	1,502
Hospital: BO vs. MI	<.0001	0,196	0,142	0,270
Sex: Female vs. Male	0,715	0,947	0,706	1,270
Age (x 1 year more)	0,365	0,994	0,982	1,007
Obesity: Yes vs. No	0,947	1,009	0,773	1,318
Days from symptoms to RIA (x 1 day more)	0,553	0,994	0,975	1,014
Charlson Score Unadjusted for age (x 1 unit more)	0,001	1,146	1,055	1,246
Remdesivir: Yes vs. No	0,878	1,025	0,745	1,411
Steroids: Yes vs. No	0,225	1,240	0,876	1,756
Sofa Score (x 1 unit more)	0,001	1,076	1,029	1,125
IOT: Yes vs. No	0,081	1,573	0,946	2,615

Table 4. Univariable and multivariable analysis with Cox regression models for estimating the cause-specific hazard ratio



Bacteremia and Blood Culture Utilization during COVID-19 Surge in New York City

Sepulveda J et al. JCM 2020;58:8



- 34.8% increase in BCs drawing during second half of March 2020

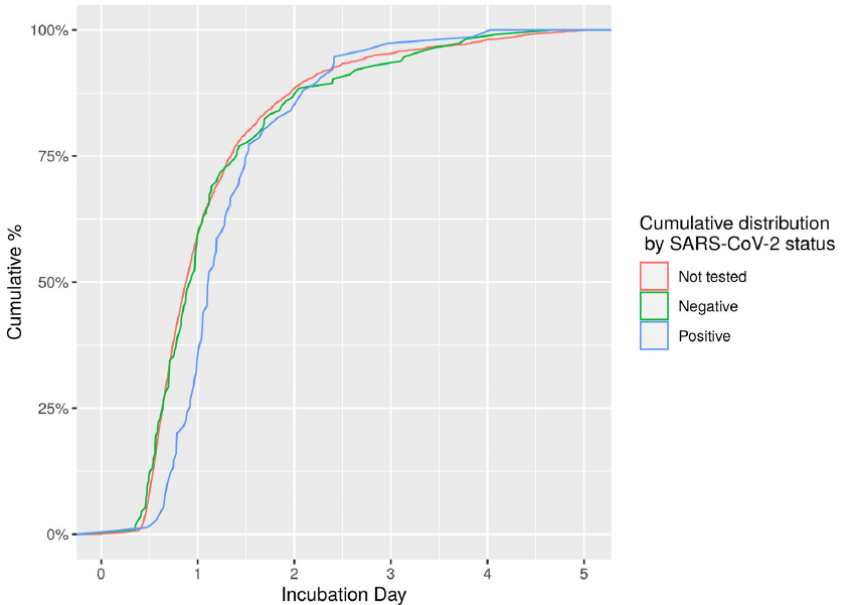
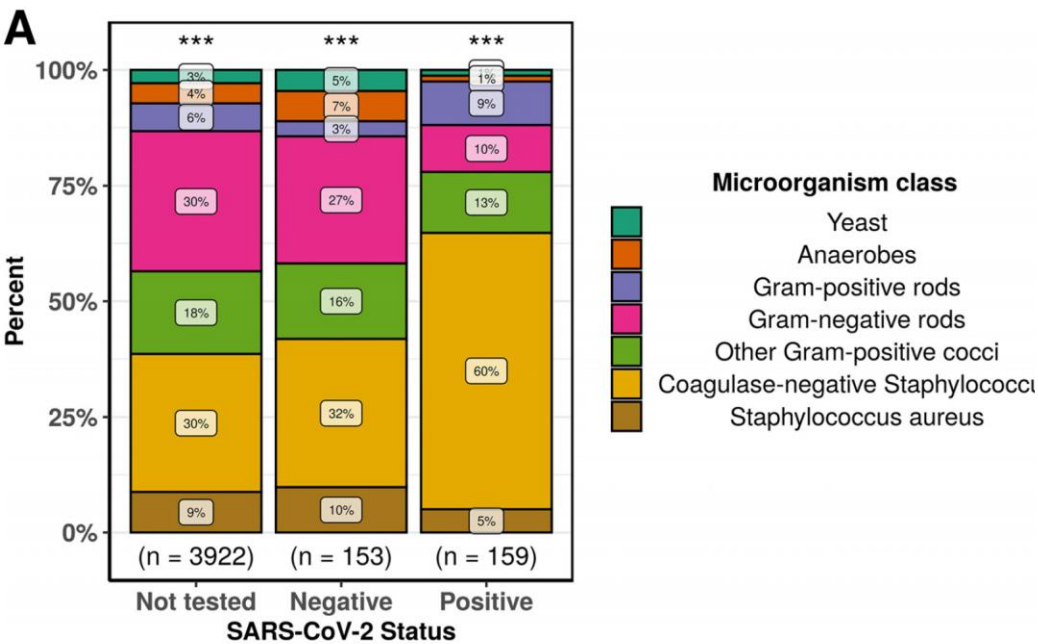
- Positivity rate:
 - ✓ 3.8% COVID-19 pos
 - ✓ 8% COVID-19 neg
 - ✓ 7.1% COVID-19 no tested



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Bacteremia and Blood Culture Utilization during COVID-19 Surge in New York City

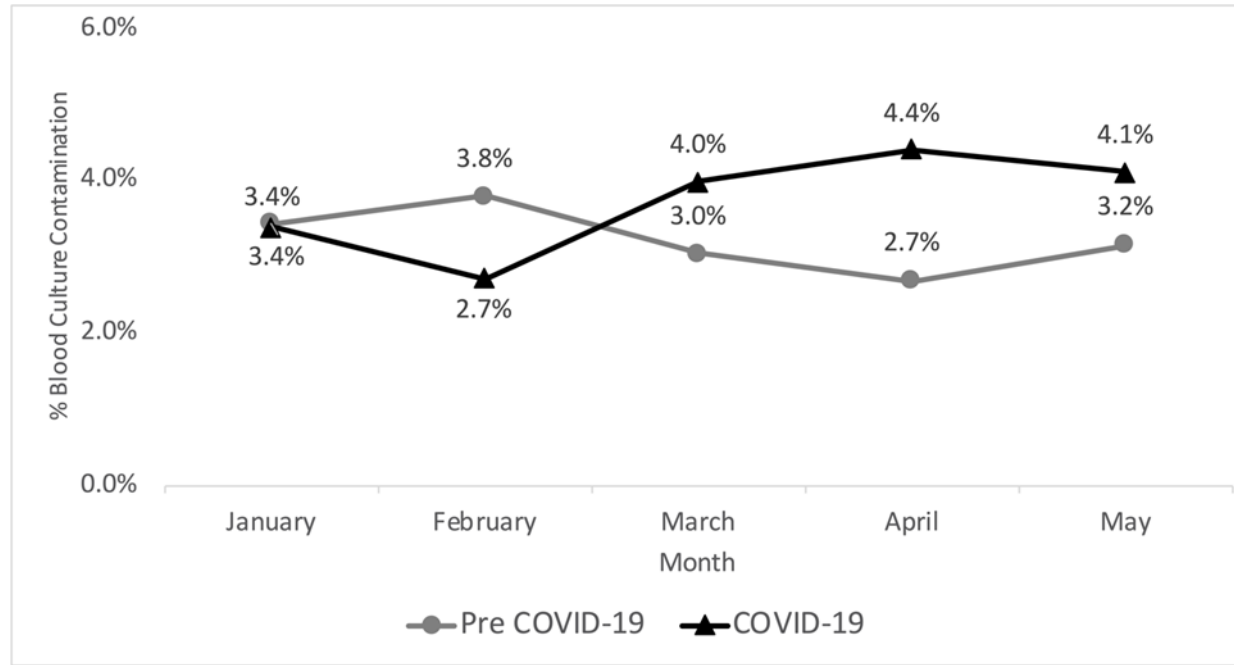
Sepulveda J et al. JCM 2020;58:8



The impact of coronavirus disease 2019 (COVID-19) response on central-line–associated bloodstream infections and blood culture contamination rates at a tertiary-care center in the Greater Detroit area

Sepulveda et al. ICHE 2021; 42: 997-1000

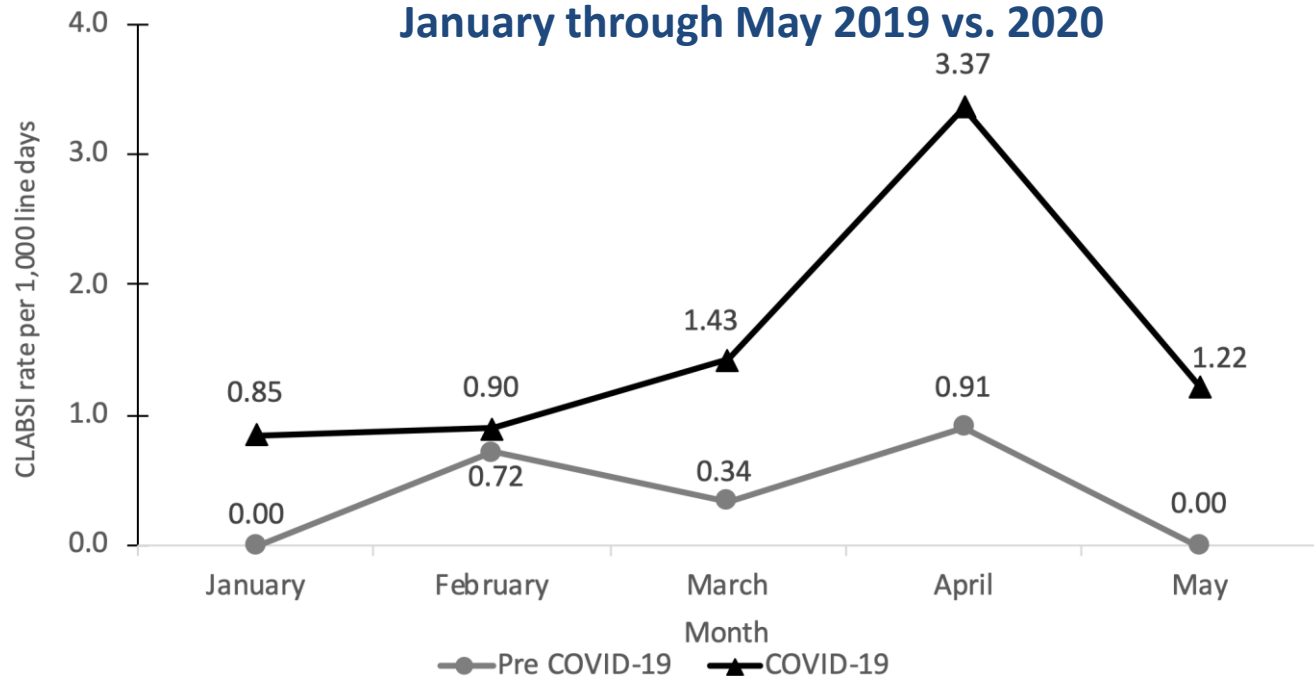
Blood culture contamination rates between January through May 2019 vs. 2020



The impact of coronavirus disease 2019 (COVID-19) response on central-line–associated bloodstream infections and blood culture contamination rates at a tertiary-care center in the Greater Detroit area

Sepulveda et al. ICHE 2021; 42: 997-1000

Central-line–associated bloodstream infections per 1,000 central-line days between January through May 2019 vs. 2020



Conclusions

- Significant increase in rate/incidence of BSI during COVID-19 pandemic confirmed in several studies/settings
- Mostly hospital acquired episodes, high prevalence of nosocomial (MDR) pathogens as well as *Enterococcus* spp.
- Contributing factors: higher use of BCs, lower attention to infection control procedures, severity of patients, gut dysbiosis
- Role of IS drugs not confirmed, data about the impact of immune dysregulation due to the COVID-19 on BSI epidemiology are currently missing

