Predisposition of COVID-19 patients to secondary infections: set in stone or subject to change?

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Parkland

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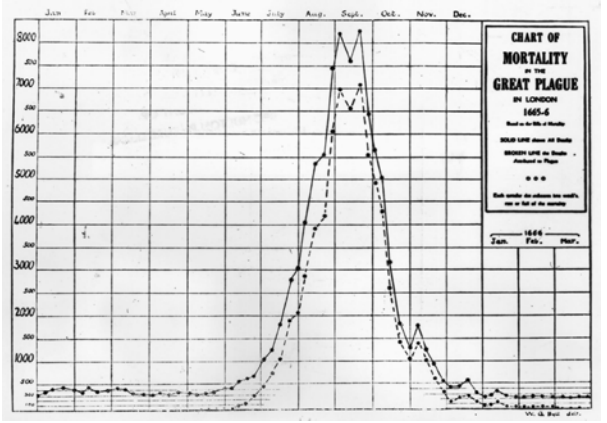
Medical Center

Conflicts of Interest

- None except:
  - I live COVID-19 24/7 these days
  - I have had COVID-19 (Once, I think)
  - I have had all of my indicated COVID-19 shots

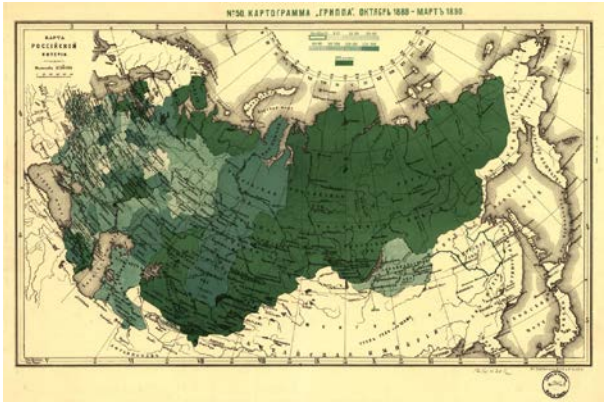
Leprosy 11th Century

Black Death 1350

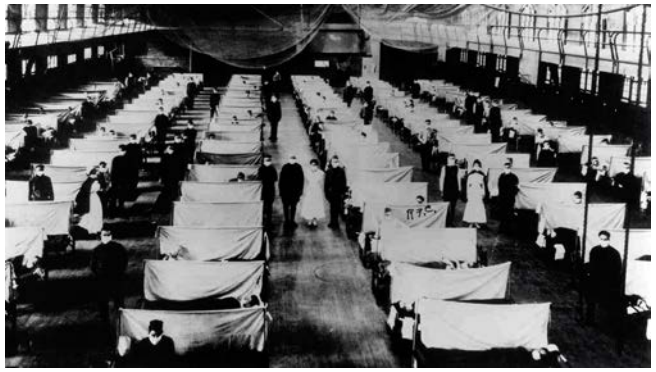


The Great Plague of London 1665

Cholera 1817



Russian Flu 1889



Spanish Flu 1918

Asian Flu 1957

AIDS 1981

SARS 2003

Pandemics of the World

COVID-19 2019 - now

1918 SPANISH FLU

The most notorious pandemic before COVID-19

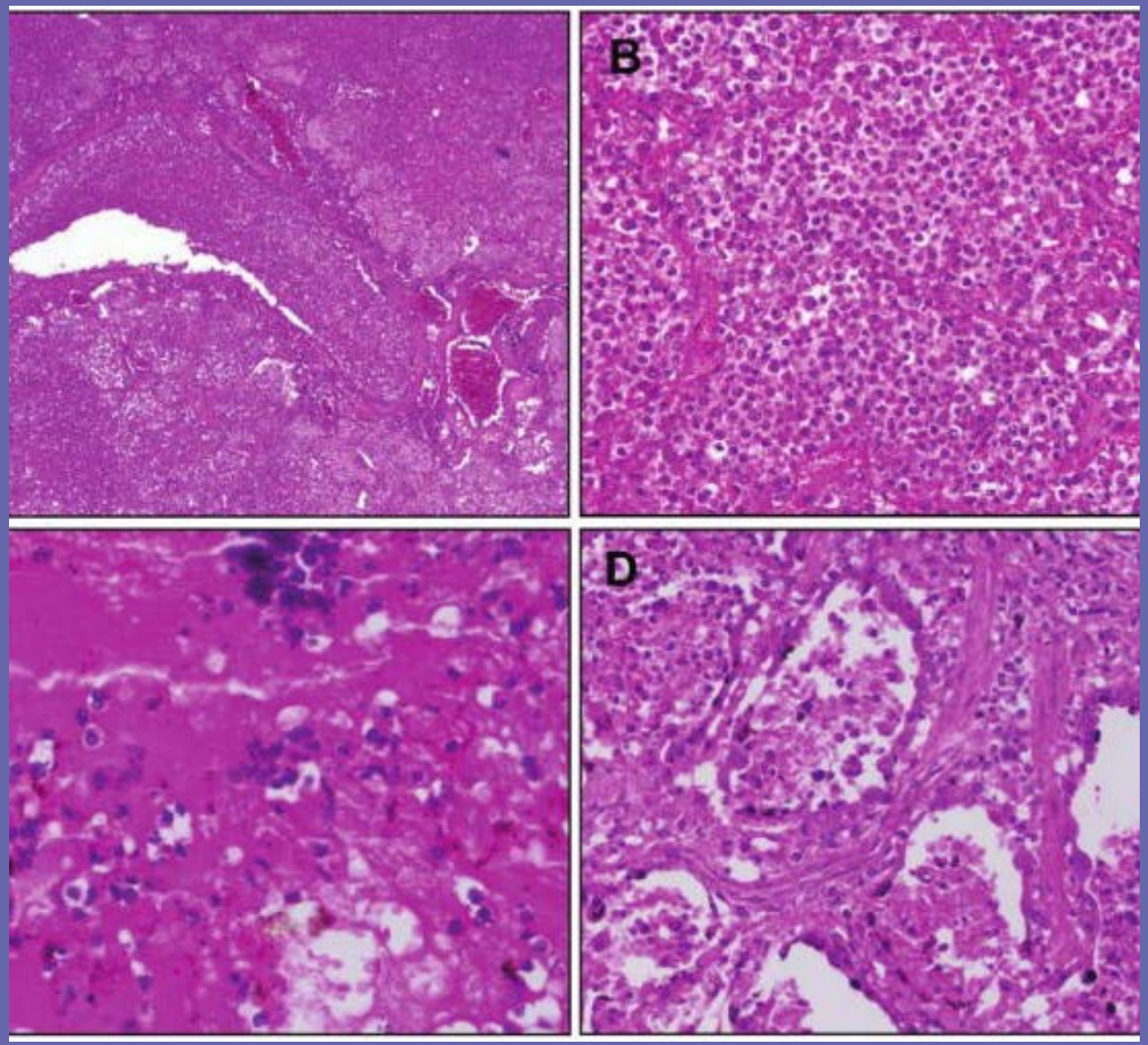
How America Struggled to Bury the Dead During 1918 Flu Pandemic

Undertakers, gravediggers and casket makers couldn't keep up with history's deadliest p

CHRISTOPHER KLEIN • FEB 12, 2020

"IF GRIPPE CONDEMNS, THE SECONDARY INFECTIONS EXECUTE"

- Louis Cruveilhier 1919



Morens DM et al. J Infect Dis. 2008 Oct 1; 198(7): 962–970.

Volume 198, Issue 7
1 October 2008

Predominant Role of Bacterial Pneumonia as a Cause of Death in Pandemic Influenza: Implications for Pandemic Influenza Preparedness FREE

David M.. Morens ✉, Jeffery K. Taubenberger, Anthony S. Fauci

The Journal of Infectious Diseases, Volume 198, Issue 7, 1 October 2008, Pages 962–970, https://doi-org.foyer.swmed.edu/10.1086/591708

Table 1. Bacterial culture results in autopsy series involving 96 postmortem cultures of lung tissue from victims of the 1918–1919 influenza pandemic.

Type of autopsy series	No. of results	No. (%) of cultures from which organism was recovered, by organism							
		Streptococcus pneumoniae	*Streptococcus hemolyticus*	*Staphylococcus aureus*	*Diplococcus intracellularis meningitidis*	Mixed pneumopathogens	*Bacillus influenzae*	Other bacteria	No growth
All military ($n = 60$)	3515	**855 (24.3)**	615 (17.5)	263 (7.5)	40 (1.1)	707 (20.1)	387 (11.0)	494 (13.8)	164 (4.7)
All civilian ($n = 36$)	1751	380 (21.7)	281 (16.0)	164 (9.4)	1 (<0.1)	**398 (22.7)**	132 (7.5)	339 (19.4)	56 (3.2)
All military and civilian ($n = 96$)	5266	**1235 (23.5)**	896 (17.0)	427 (8.1)	41 (0.8)	1105 (21.0)	519 (9.9)	823 (15.6)	220 (4.2)
All higher- quality military and civilian[a] ($n = 68$)	3074	712 (23.2)	553 (18.0)	238 (7.7)	21 (0.7)	**828 (26.9)**	144 (4.7)	353 (11.5)	225 (7.3)
Predominance of pneumopathogens not confirmed ($n = 14$)	1115	209 (18.7)	132 (11.8)	52 (4.7)	0 (0.0)	24 (2.2)	210 (18.9)	**402 (36.1)**	86 (7.7)

Table 2. Bacterial culture results in autopsy series involving culture of blood and pleural fluid or empyema fluid from victims of the 1918–1919 influenza epidemic.

Type of autopsy series	No. of results	No. (%) of cultures from which organism was recovered, by organism							
		Streptococcus pneumoniae	*Streptococcus hemolyticus*	*Staphylococcus aureus*	*Diplococcus intracellulare meningitidis*	Mixed pneumopathogens	*Bacillus influenzae*	Other bacteria	No growth
Blood culture ($n = 42$)									
All military and civilian	1887	509 (27.0)	377 (20.0)	68 (3.6)	5 (0.3)	28 (1.5)	61 (3.2)	278 (14.7)	**561 (29.7)**
Pleural fluid or empyema fluid culture ($n = 35$)									
All military and civilian	1245	263 (21.1)	**539 (43.3)**	59 (4.7)	0 (0.0)	74 (5.9)	21 (1.7)	45 (3.6)	244 (19.6)

Table 3. Summary of evidence from the 1918–1919 influenza pandemic consistent with the conclusion that bacterial pneumonia, rather than primary viral pneumonia, was the cause of most deaths.

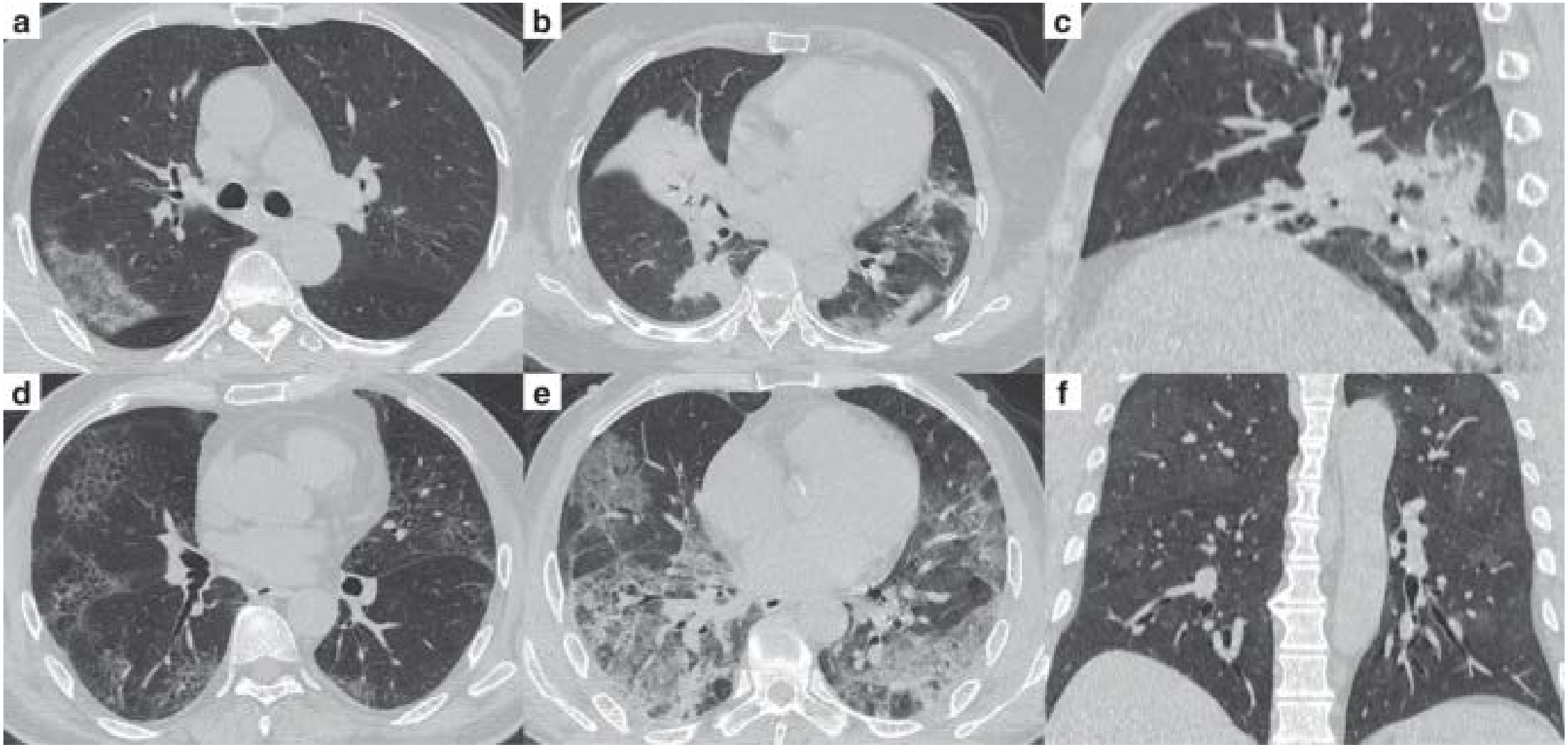
Evidence, by type	Relevant reference(s)
Pathologic Evidence	
Most autopsies revealed severe bacterial pneumonia caused by common upper respiratory organisms	{20, 27–33}
In type, pattern, and case-fatality rate, influenza-associated bacterial pneumonia, including chronic lobar pneumonia, was typical of pneumonia during periods when influenza was not prevalent; bronchopneumonia, associated with diffuse "panbronchitis," predominated	[25, 28, 33, 34]
At autopsy, early and/or extensive repair of what are now thought to be primary viral changes was evident; severe sequelae in pneumonia survivors were minimal	[20, 30, 32]
Pathologic picture of bacterial bronchopneumonia associated with influenza in 1918–1919 was strongly similar to the more highly fatal measles–bacterial bronchopneumonia epidemics of 1917–1918	[20, 27, 63]
Mixed pneumopathogen–associated pneumonia was more fatal than single-pneumopathogen pneumonia	[29]
Pneumonia cases exhibited uniformly diffuse and extensive tracheobronchitis and/or bronchiolitis, the severity of which correlated with pneumonia severity in degree and anatomical location	[29]
Demographic and/or epidemiologic evidence	
Most influenza cases were typical of cases seen today: mild, uncomplicated, and associated with full recovery	[13–17]
Mortality at all ages was associated with bacterial pneumonia rates, not with influenza attack rates or pneumonia case-fatality rates	[19, 21]
Children 5–15 years old in 1918–1919 had the highest attack rates but the lowest mortality rates, similar to low rates seen in 1889–1893 and immediately before and after the 1918–1919 pandemic—rates seemingly inconsistent with viral virulence alone	[14, 21]
Influenza-associated pneumonia incidence rates and influenza death rates were significantly higher in US military camps, which experienced bacterial "colonization epidemics"	[63]
Average time from influenza onset to pneumonia onset in ultimately fatal cases (~10 days) may be more consistent with bacterial than viral pneumonia	[29]
Treatment response evidence	
The near universal observation that strict bed rest early in the course of uncomplicated influenza prevented pneumonia and death is consistent with an effect of isolation from carriers of bacterial pathogens	[13, 14]

1957

1968

pandemics

likely primed clinicians to expect bacterial superinfections to play a significant role during the current pandemic



Feng Z et al. Nat Commun 11, 4968 (2020)

Perspective

Preparing for the Next Pandemic

Michael T. Osterholm, Ph.D., M.P.H.

N Engl J

"…in 1968, when the most recent influenza pand
had a human population of 790 million, a
12.3 million; today, these populati
Similar changes have occu
creating an incredi

"Gi
ing the past 50 years, we
be caused by H5N1 or by

ere could be 1.7 million deaths in the United States and 180
bally…

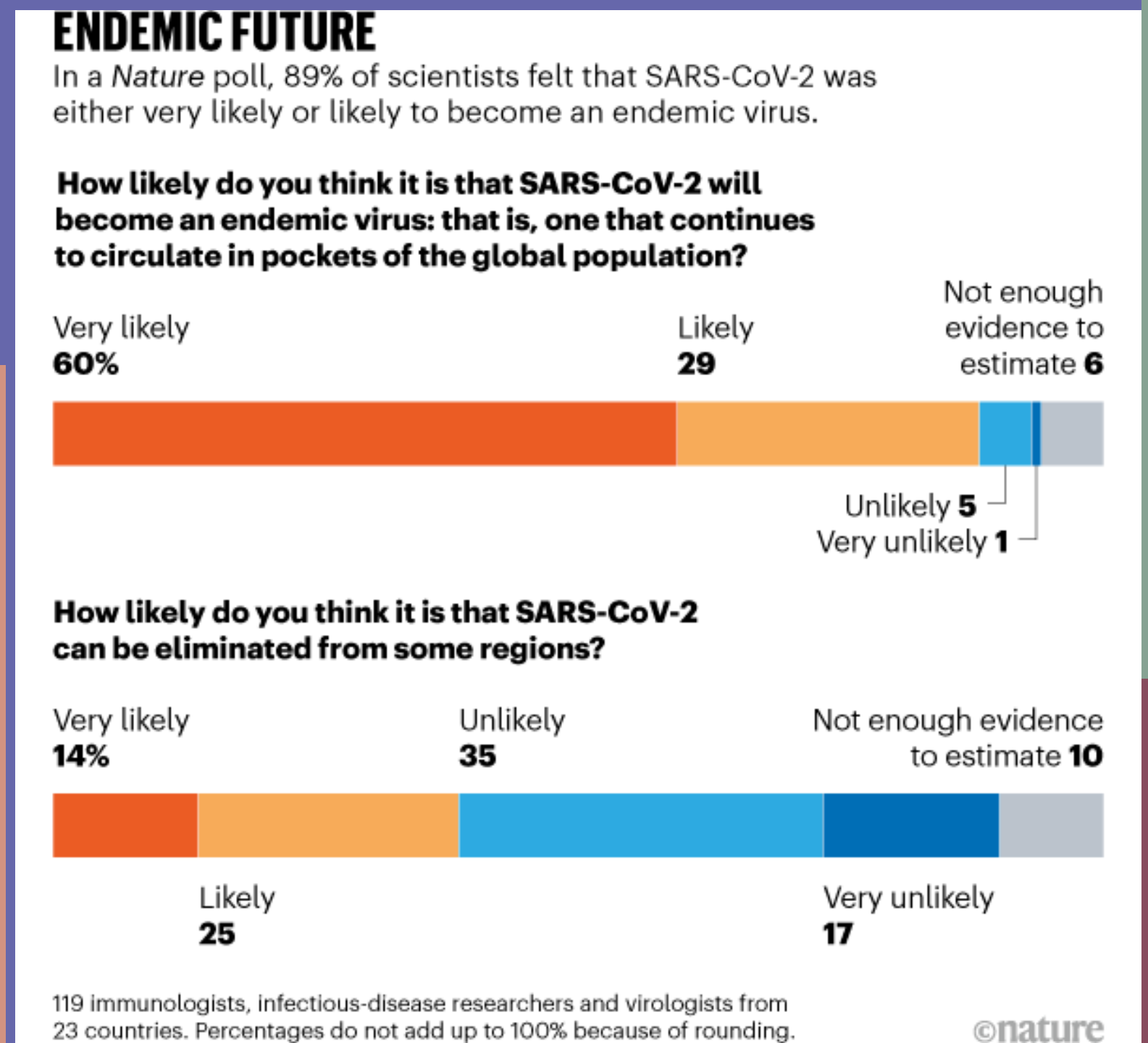
ely limited armamentarium with which to handle millions of cases of ARDS —
different from that available to the front-line medical corps in 1918."

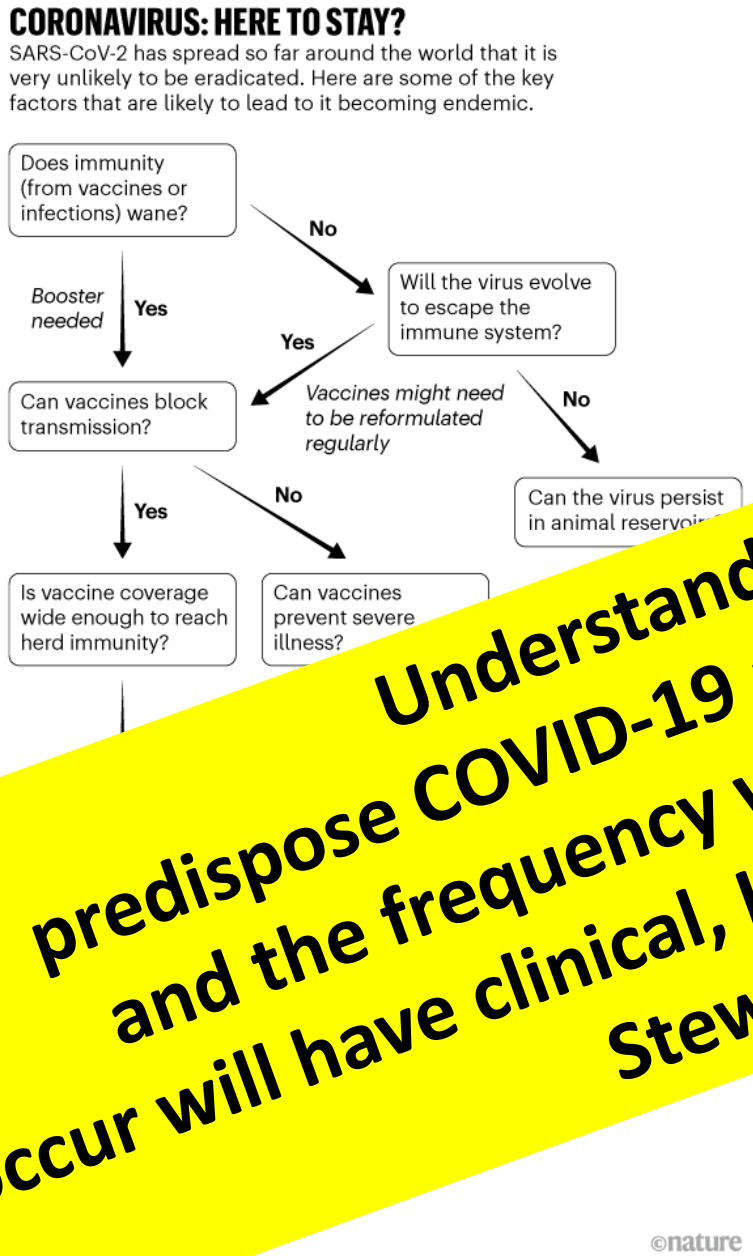
The world was stunned by the arrival of COVID-19 and was caught in a resource-limited state…

…changes in standard of care including adjustments to evidence-based infection control safeguards

COVID-19 IS HERE TO STAY

Phillips N. The coronavirus is here to stay: here's what that means. Nature 2021; 590:382–384.



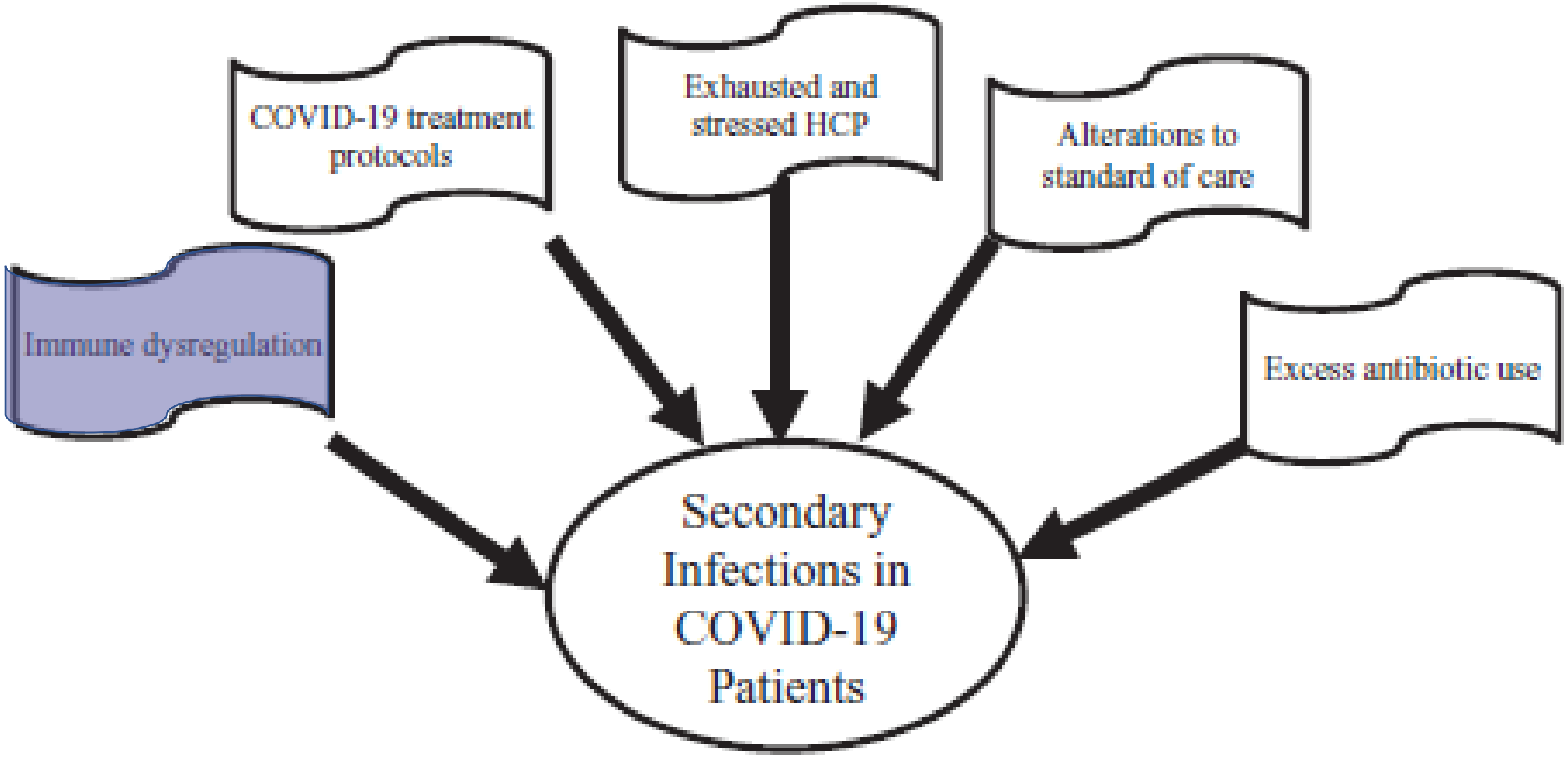


"…clinicians will be caring for … the foreseeable future"

Understanding the factors that predispose COVID-19 patients to secondary infections and the frequency with which secondary infections occur will have clinical, Infection Prevention and Antimicrobial Stewardship implications

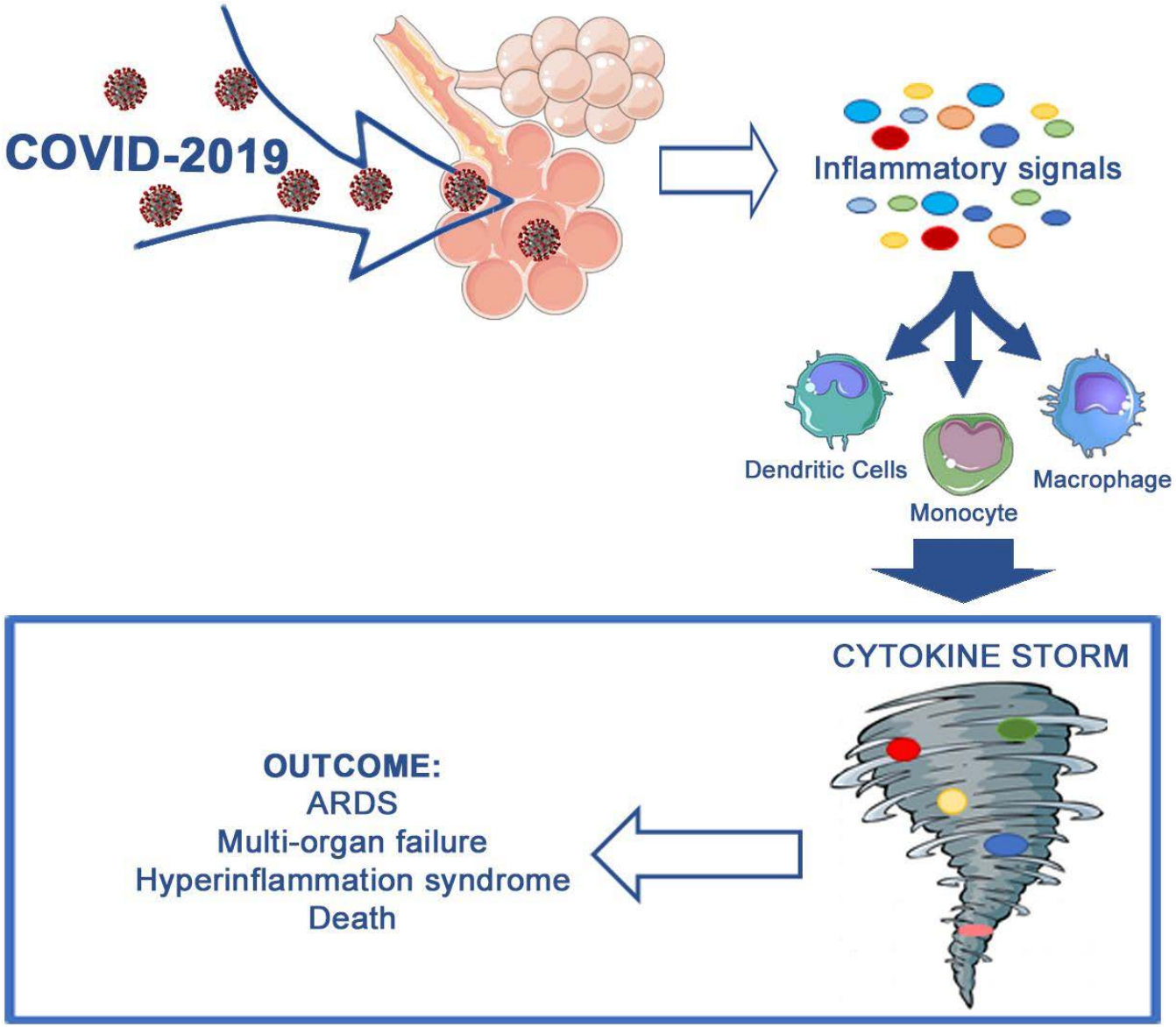
…navirus is here to stay: here's what that means. Nature 2… 382–384.

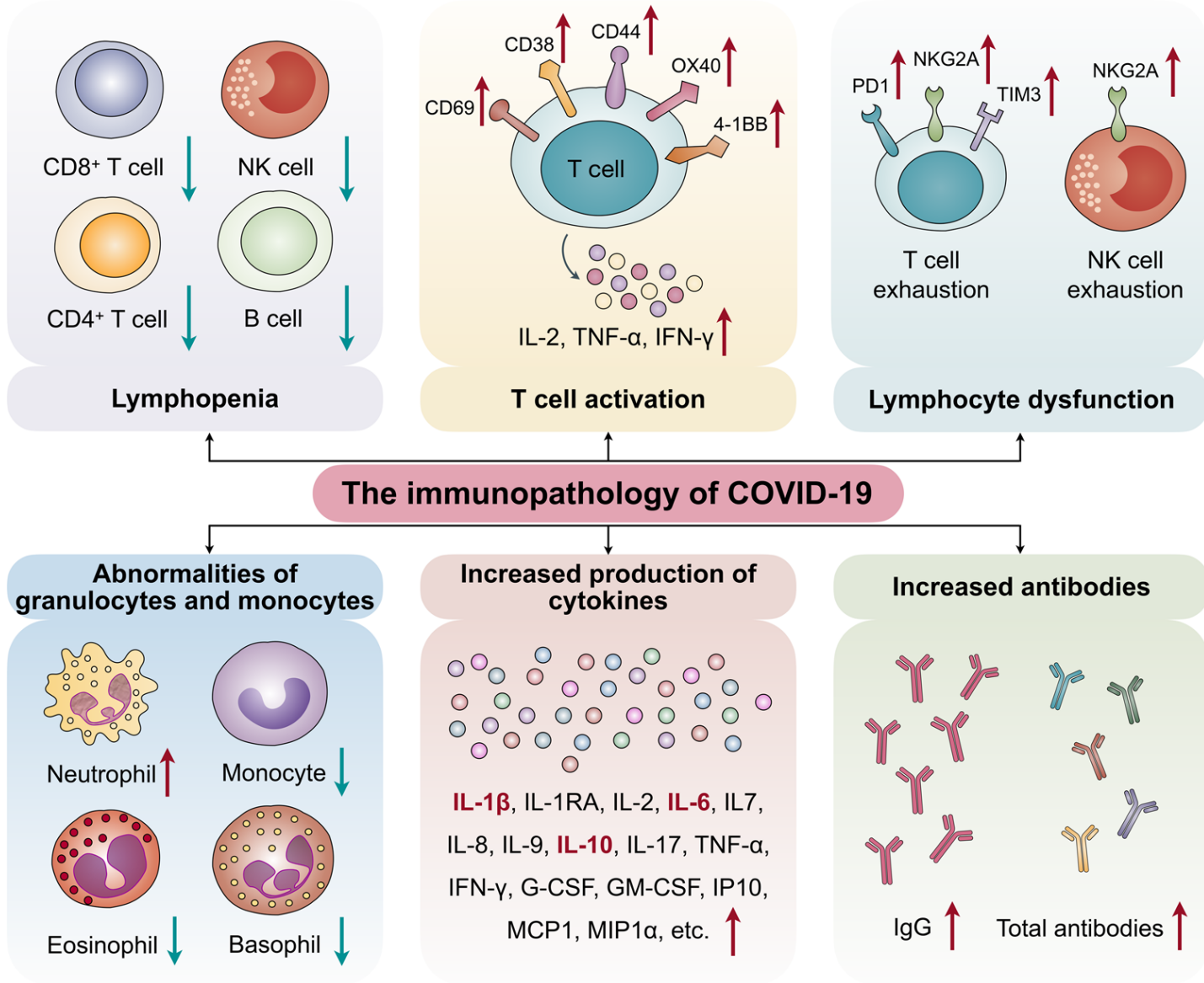
Sopirala MM. Curr Opin Infect Dis. 2021 Aug 1;34(4):357-364.



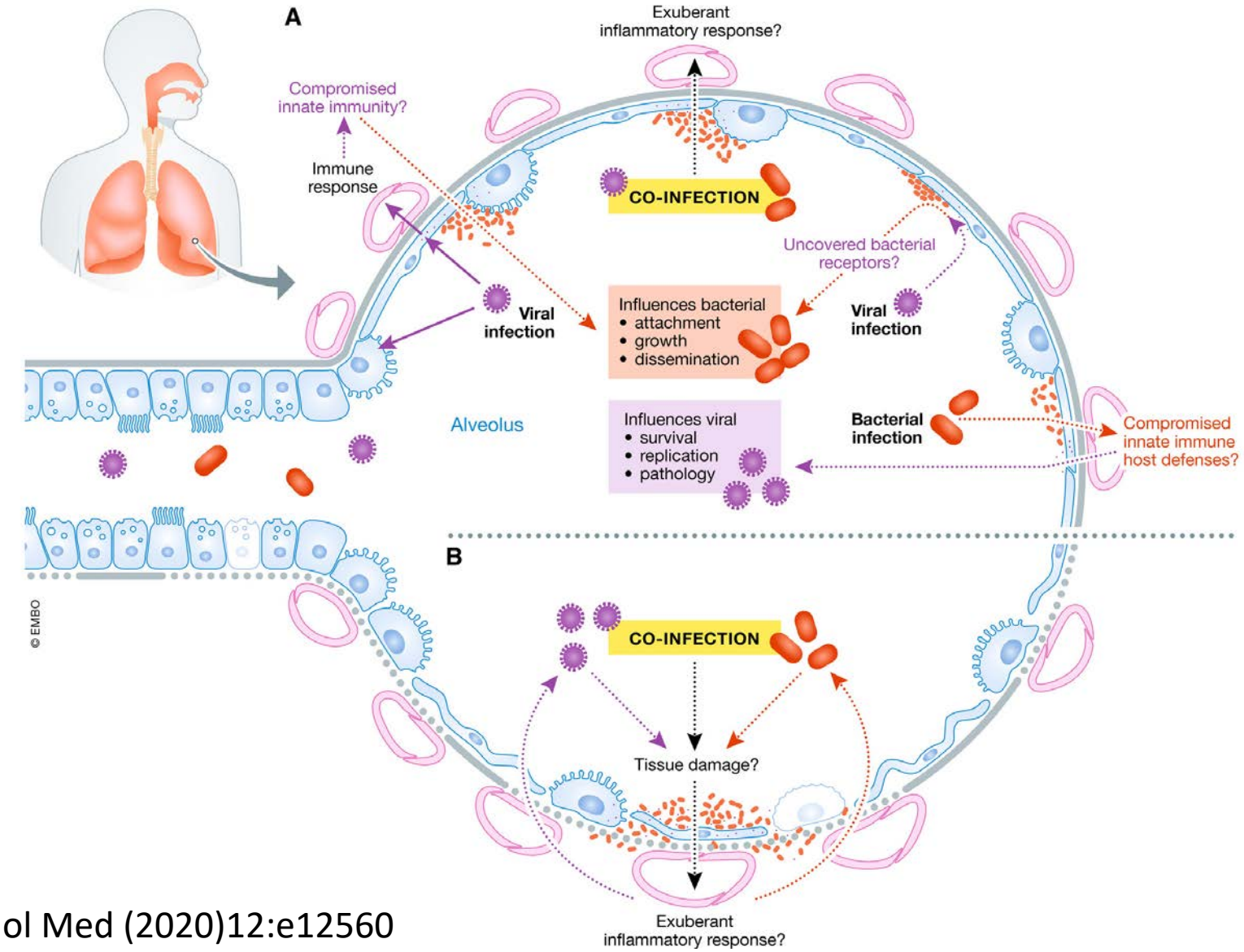
Sopirala MM. Curr Opin Infect Dis 2021, 33:000–000

Immune Dysregulation

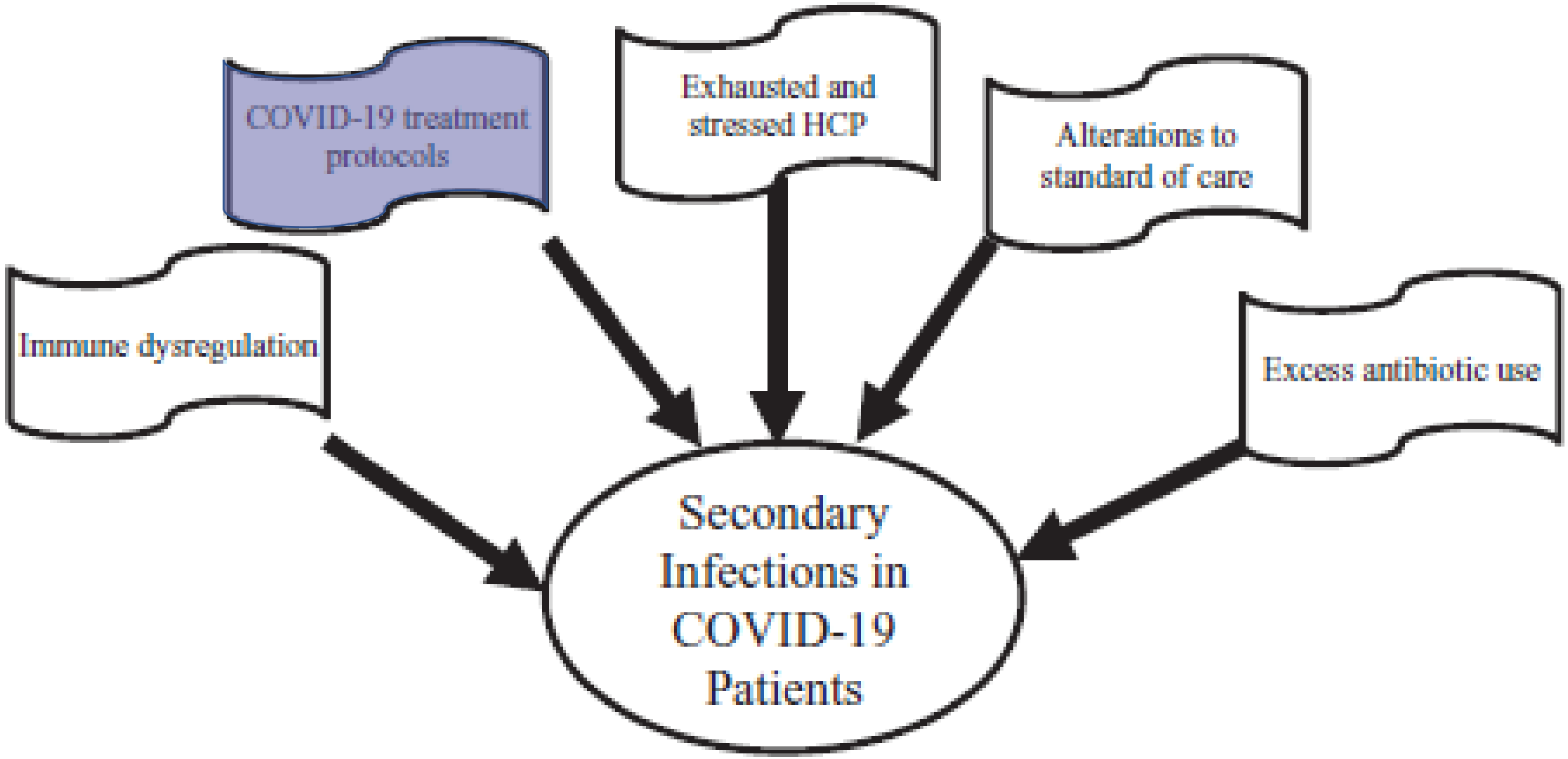



CD8⁺ T cell
NK cell
CD4⁺ T cell
B cell
Lymphopenia
CD38
CD44
OX40
CD69
4-1BB
T cell
IL-2, TNF-α, IFN-γ
T cell activation
PD1
NKG2A
TIM3
NKG2A
T cell exhaustion
NK cell exhaustion
Lymphocyte dysfunction
The immunopathology of COVID-19
Abnormalities of granulocytes and monocytes
Neutrophil
Monocyte
Eosinophil
Basophil
Increased production of cytokines
IL-1β, IL-1RA, IL-2, IL-6, IL7,
IL-8, IL-9, IL-10, IL-17, TNF-α,
IFN-γ, G-CSF, GM-CSF, IP10,
MCP1, MIP1α, etc.
Increased antibodies
IgG
Total antibodies

Predisposition to Secondary Infections due to Immune Dysregulation

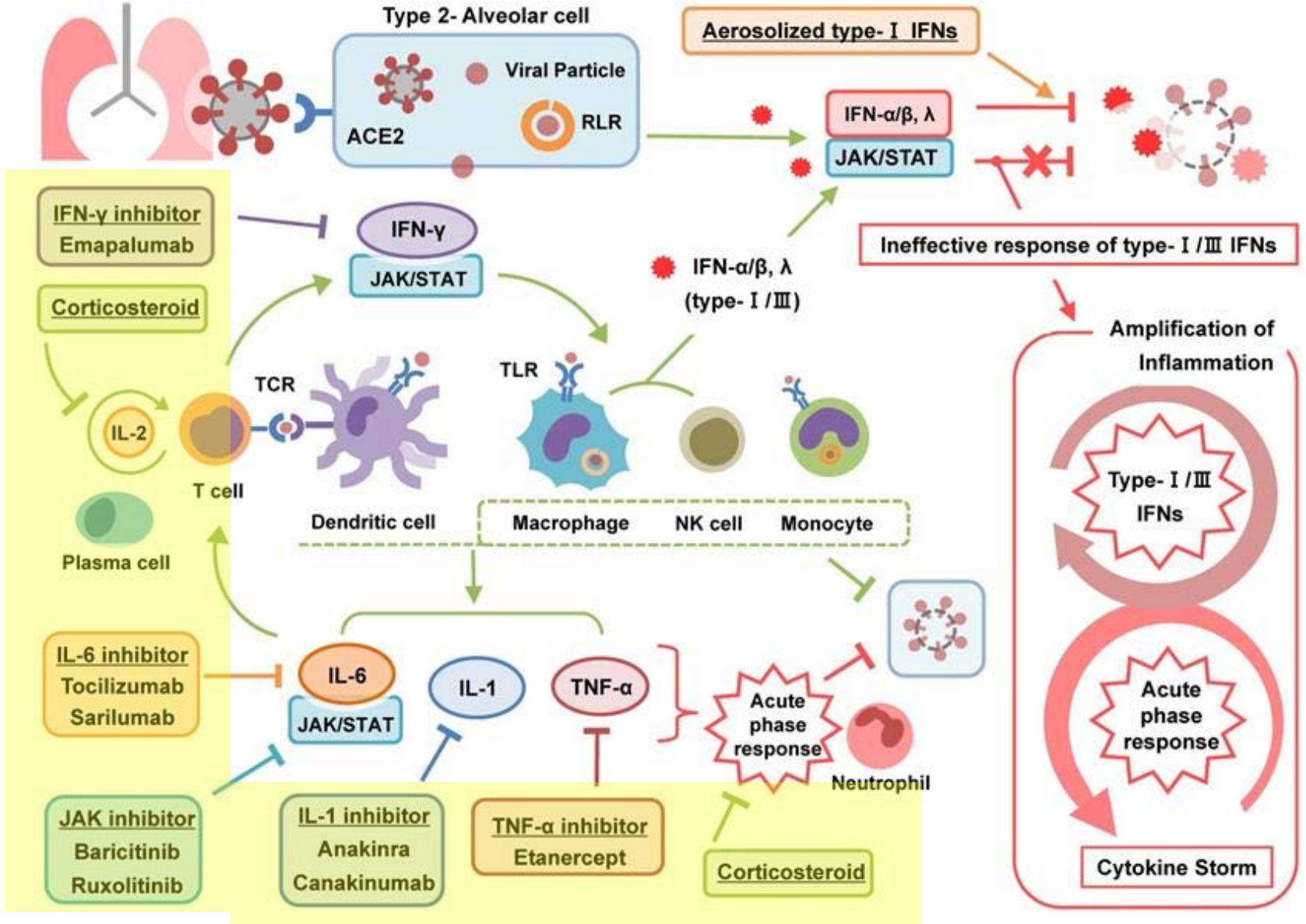


Bengoechea JA. EMBO Mol Med (2020)12:e12560



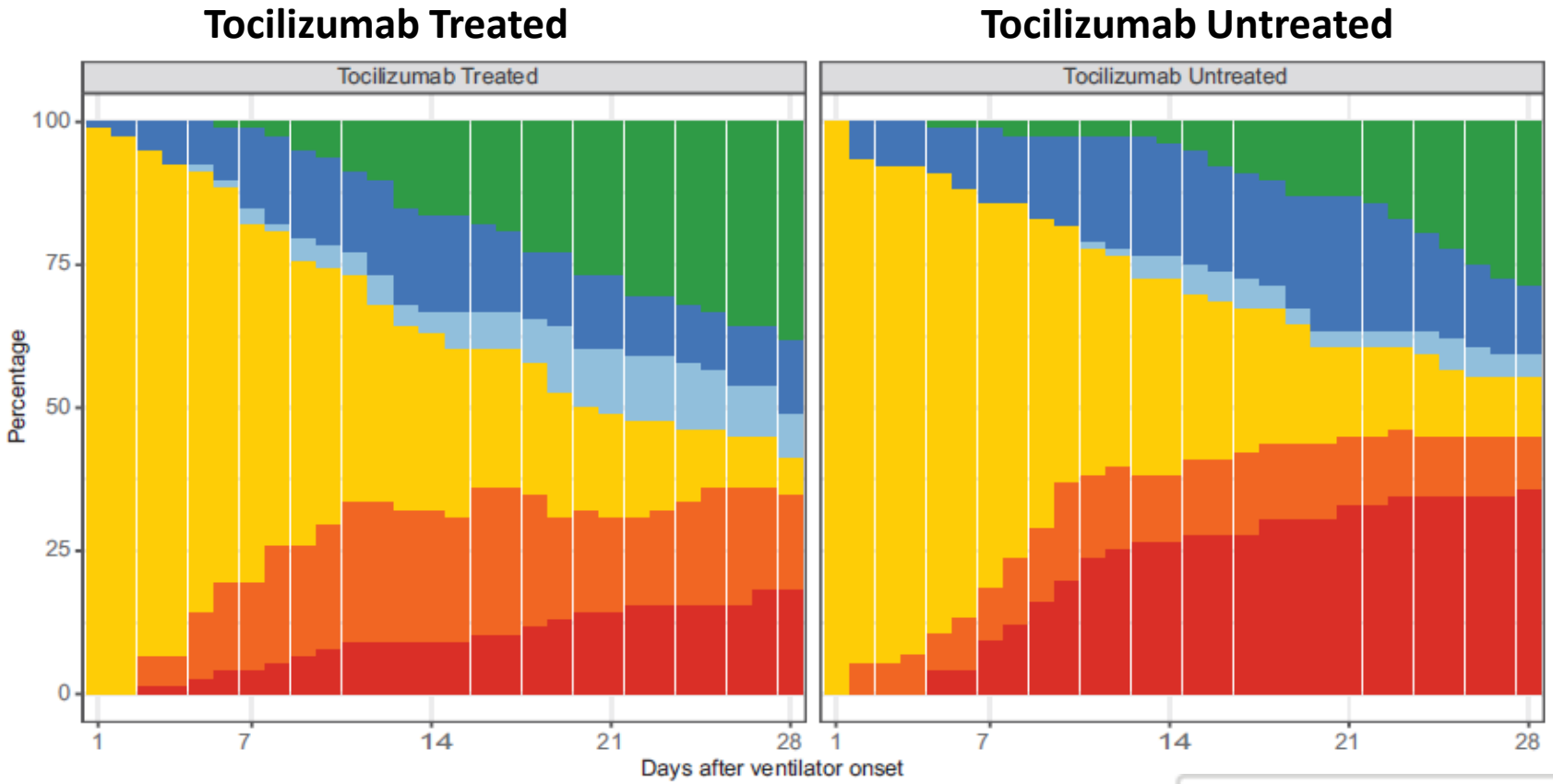
Sopirala MM. Curr Opin Infect Dis 2021, 33:000–000

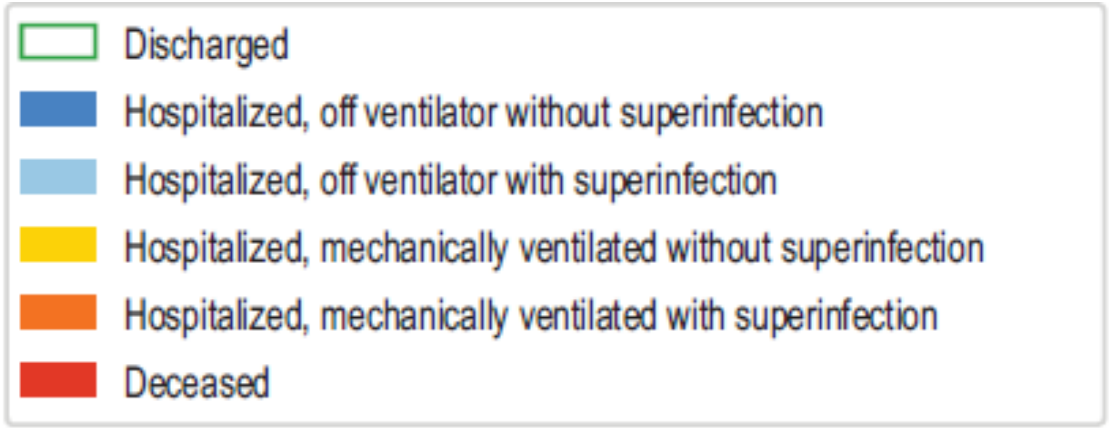
Predisposition to Secondary Infections due to COVID-19 Treatment



Kim JS. Theranostics 2021; 11(1):316-329.

Tocilizumab & Secondary Infections in COVID-19 Patients





Somers EC et al. Clin Infect Dis. 2021 Jul 15; 73(2): e445–e454.

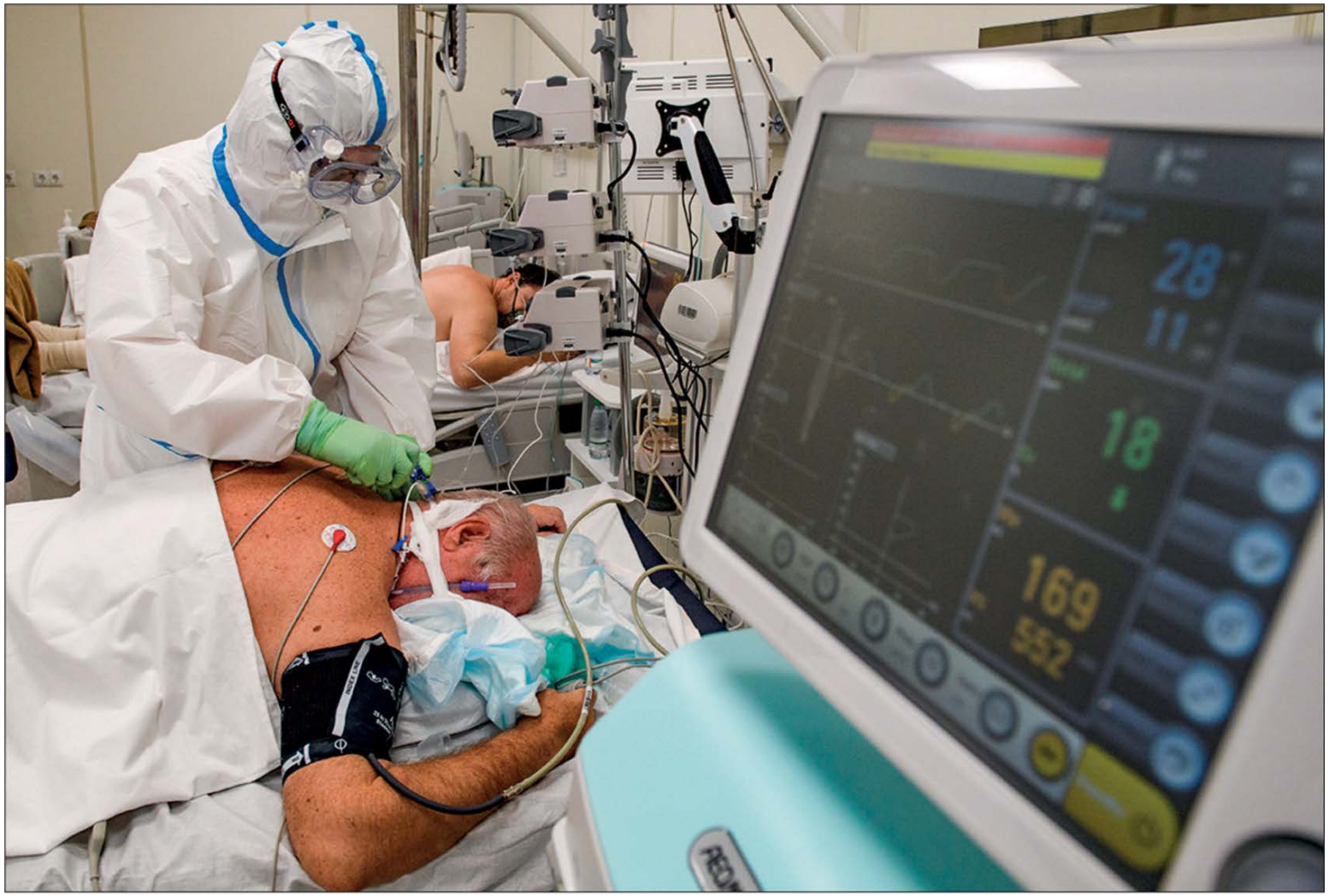
Steroids – Independent Risk Factor for Secondary Infections in COVID-19

Factors associated with development of healthcare-associated infections.

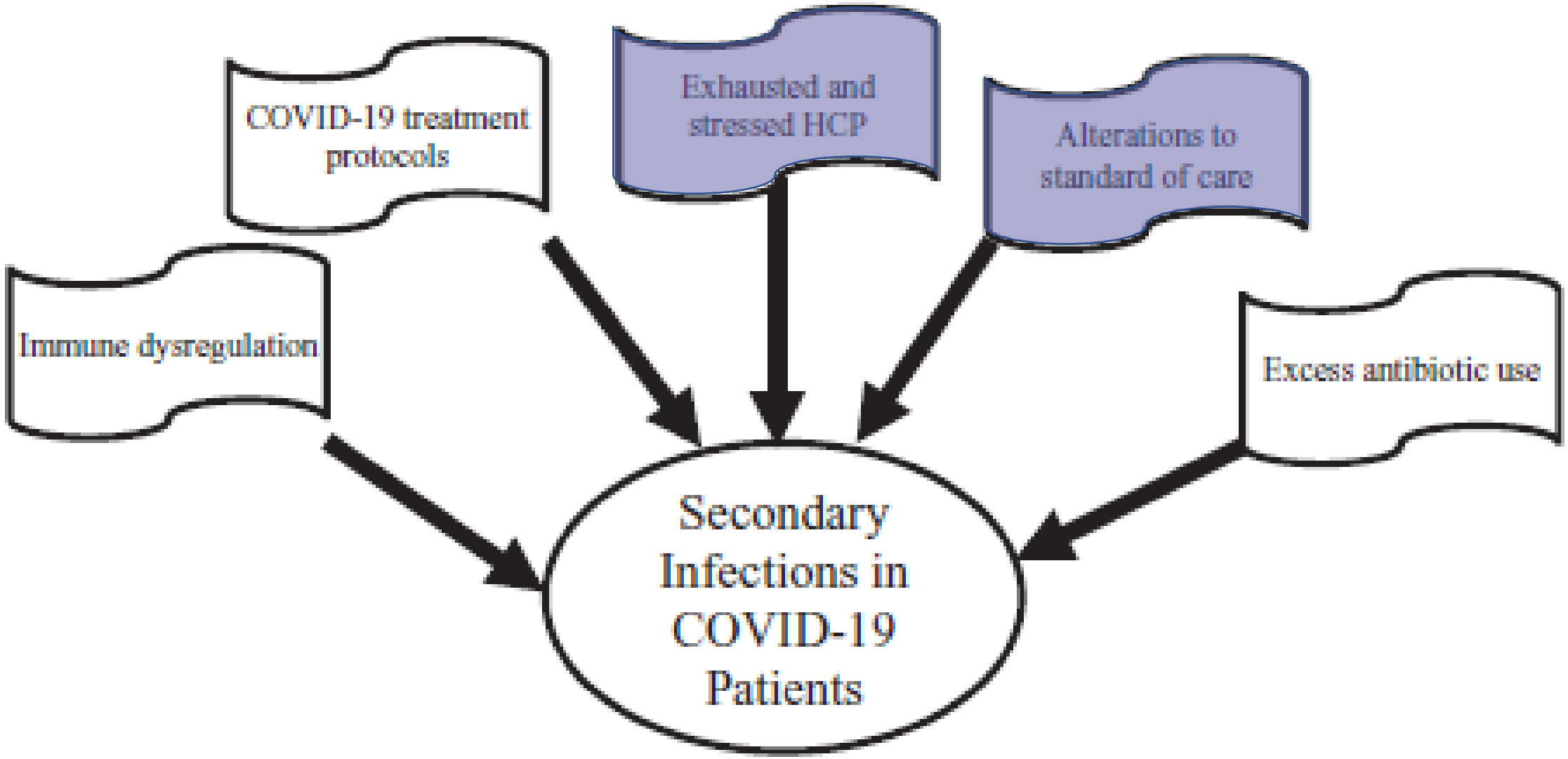
	Odds ratio	95% CI	*p*
Age	0.99	0.96–1.01	0.58
Male gender	0.76	0.37–1.53	0.45
DM	1.29	0.62–2.69	0.48
ESRD	1.05	0.24–4.55	0.94
COPD	0.82	0.38–1.77	0.62
Cancer	1.36	0.37–4.98	0.63
Hydroxychloroquine*	2.96	1.00–8.86	0.05
Steroids*	3.79	1.44–10.01	0.007
Tocilizumab*	5.04	2.39–10.65	< 0.001
Convalescent plasma	1.86	0.88–3.92	0.10
Central venous catheter	2.47	0.87–6.97	0.088
Mechanical ventilation	1.11	0.34–3.54	0.86
AKI requiring hemodialysis*	3.67	1.05–12.80	0.04
Antibiotics on admission	1.02	0.31–3.32	0.96
SOFA score >2 on admission	1.21	0.52–2.76	0.65

Kumar G. Int J Infect Dis. 2021 Mar; 104: 287–292.

Non-pharmacologic Treatment Methods



McGuire WC, et al. Lancet Respir Med. 2021



Sopirala MM. Curr Opin Infect Dis 2021, 33:000–000

Predisposition to Secondary Infections due to Alterations to Standard of Care

Editorial

March 20, 2020

Conserving Supply of Personal Protective Equipment—A Call for Ideas

Howard Bauchner, MD[1]; Phil B. Fontanarosa, MD, MBA[1]; Edward H. Livingston, MD[1]

≫ Author Affiliations | Article Information

JAMA. 2020;323(19):1911. doi:10.1001/jama.2020.4770

"We seek creative immediate solutions for how to maximize the use of PPE, to conserve the supply of PPE, and to identify new sources of PPE."

Proposed Solutions

Gowns: plastic ponchos or poly bags, bedbug sheet material

Adhesive bandage as nasal PPE

Box. Summary of Recommendations for PPE Conservation and Management

Import
Purchase from international suppliers: China proposed as a primary market given manufacturing capacity, experience with and decline in COVID-19 incidence

Reclaim
Dentists, farmers, construction, high schools, universities, veterinarians, salons, manufacturing, aerospace, industrial "clean labs"
- Individual HCW procurement in towns and communities
- Charitable movements
- Public or private buybacks
- Public or private bounties

Reuse
Rotate through 72-h cycles given current understanding of surface viability

Reusable elastomeric respirators (have exchangeable filter cartridges)

Disinfectants
- Heat (eg, autoclave), UV, ozone, ethylene oxide, hydrogen peroxide, bleach, isopropyl alcohol, gamma or e-beam radiation, microwave, copper sulfate, methylene blue with light, sodium chlorine, iodine, zinc oxide impregnation (gowns), hypochlorous acid, commercial laundering (for cloth)

Repurpose
Prefabricated masks: snorkel and scuba, 3D printed, welder's, civilian military grade gas masks, ski buffs

Eye and face shields: sports eye protectors, motorcycle helmets with visors, balaclavas

Gowns: plastic ponchos or poly bags, bedbug sheet material

Adhesive bandage as nasal PPE

Create supply
Sewn fabric masks and gowns, coffee filter masks, home HVAC filter masks

Extend supply
Plastic face shields (water bottle cutouts, thermoplastic sheets, A4 acetate sheets, Ziploc bags) to preserve face masks and eyewear

Reduce nonessential services
Cancel elective and ambulatory procedures; reduce questionable contact and isolation precautions (eg, MRSA/VRE, influenza, cellulitis)

Reduce patient contact
Utilize mobile and out-of-room monitoring and device controls, e-consults, extended dwell IVs, batching medications or self-administration, barrier visits

Alter staffing
Reduce student and trainee patient contacts

Use nonhuman services
Nonhuman services (drones and robots) for delivery of test kits for self-testing, robots for equipment movement within hospitals, decontamination protocols

Stratify use by patient risk
Cohort patients and reduce PPE use for those at low risk (ideally requires testing to accurately stratify low and high risk)

Employ immune workers
HCWs recovered from clinical illness or with demonstrated immunity care preferentially for COVID-19 patients without PPE

Use government solutions
Regionalize care and supply, import international supply, ration supply, loosen import regulations, commandeer business to accelerate supply

Manage supply
Reduce bulk packaging, Pyxis-like controlled distribution, nongovernment regional coordination of PPE distribution

Miscellaneous
Convert RV trailers to negative pressure spaces; phase change material to improve comfort and reduce reuse of gowns

Abbreviations: COVID-19, coronavirus disease 2019; HCW, health care worker; HVAC, heating, ventilating, and air-conditioning; MRSA, methicillin-resistant *Staphylococcus aureus*; PPE, personal protective equipment; VRE, vancomycin-resistant Enterococcus.

Livingston E. JAMA. 2020;323(19):1912-1914.

Predisposition to Secondary Infections due to Exhaustion and Stress of HCP

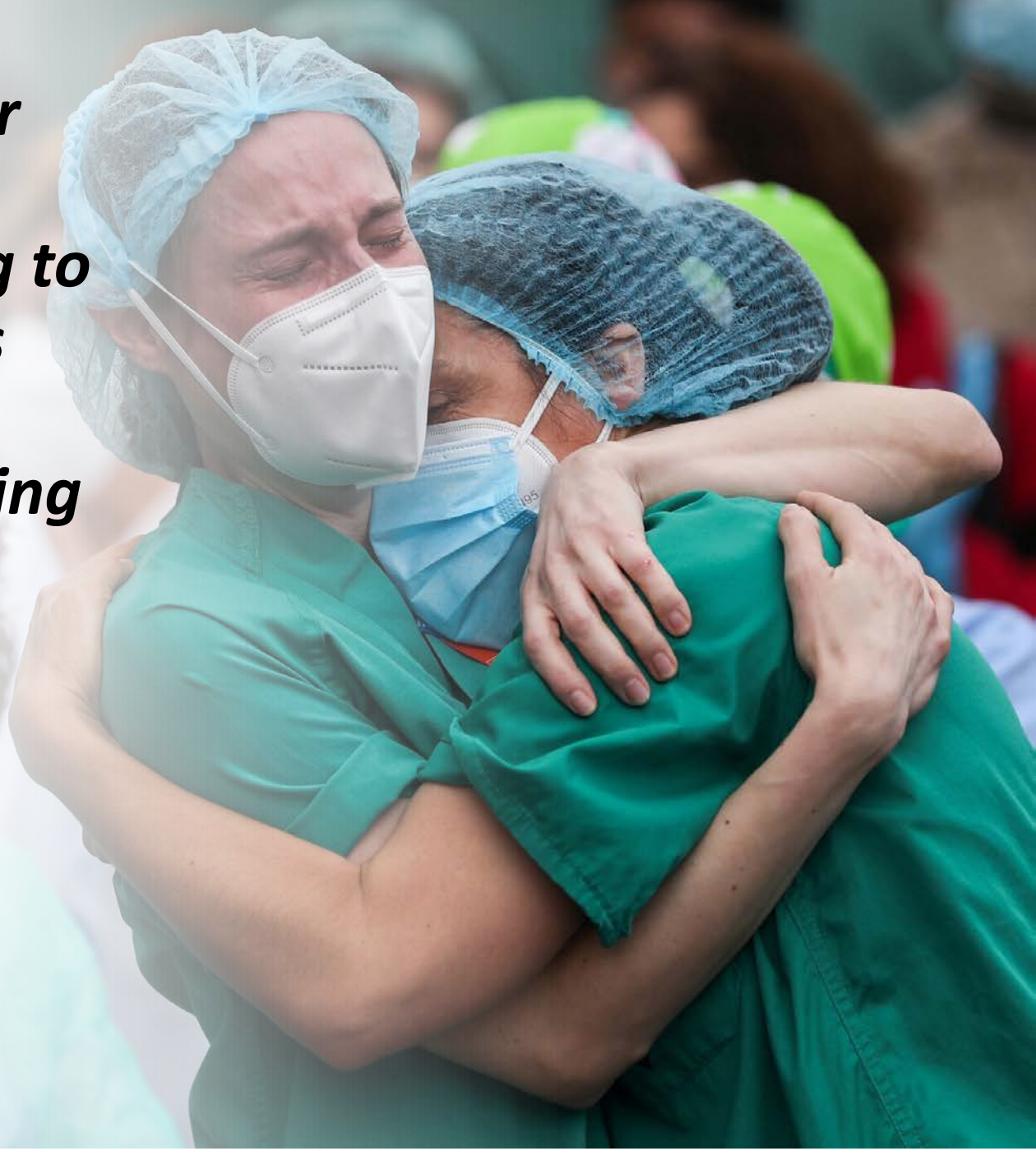
NEW YORK POST

Worker at NYC hospital where nurses wear trash bags as protection dies from coronavirus

By Ebony Bowden, Carl Campanile and Bruce Golding

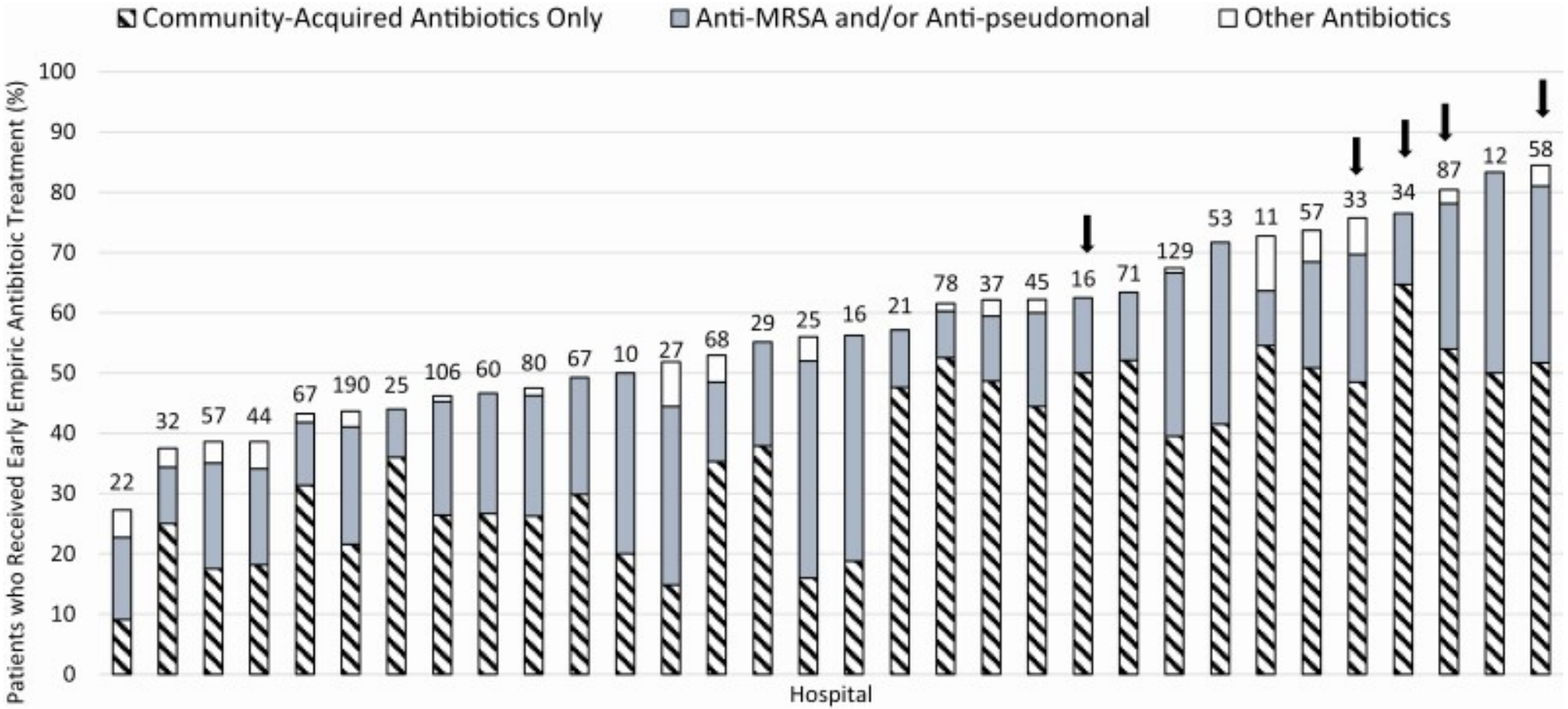
March 25, 2020 | 4:32pm | Updated

"Among the many valid reasons for fear in this pandemic are fear of developing infection, fear of failing to provide adequate care for patients given limited resources, fear of carrying the virus home and infecting family and friends, fear of stigmatization, and many others."



Cawcutt et al. Fighting fear in healthcare workers during the COVID-19 pandemic. Infect Control Hosp Epidemiol. 2020 Oct;41(10):1192-1193.

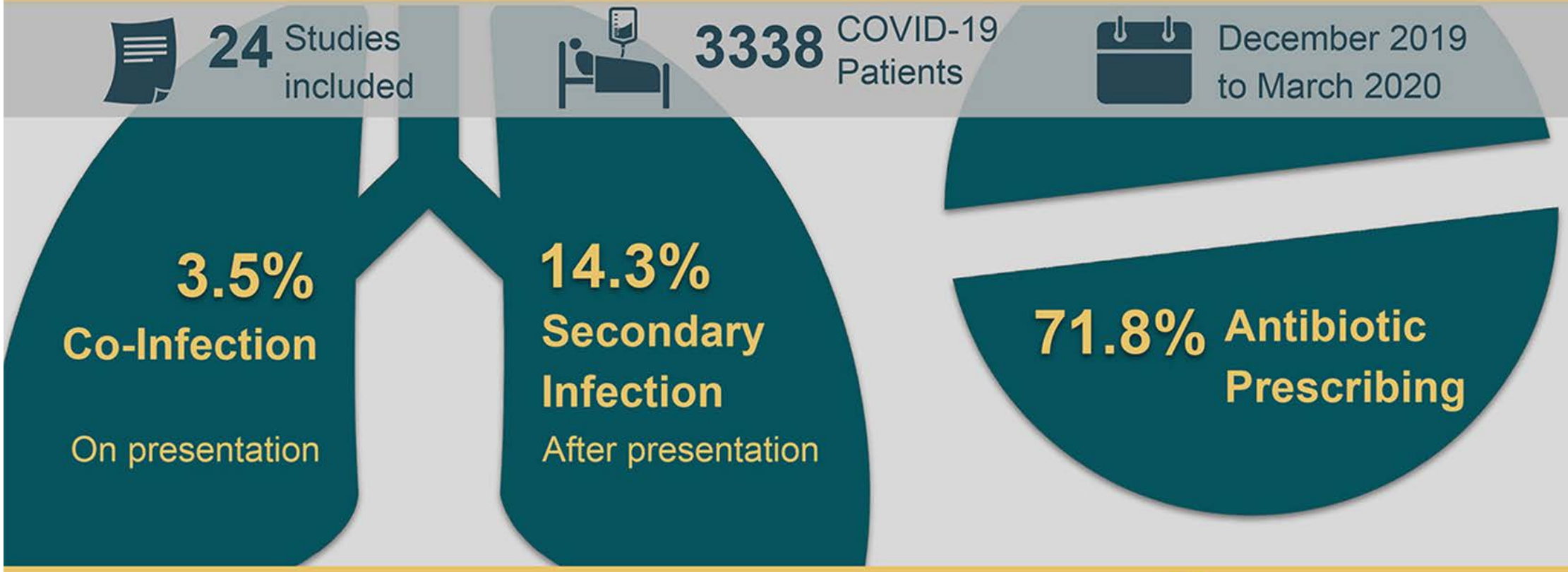
Predisposition to Secondary Infections due to Antibiotic Use



Clin Infect Dis. 2021 May 18;72(10):e533-e541.

Acute Bacterial Co-Infection in COVID-19

A Rapid Living Review and Meta-analysis



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

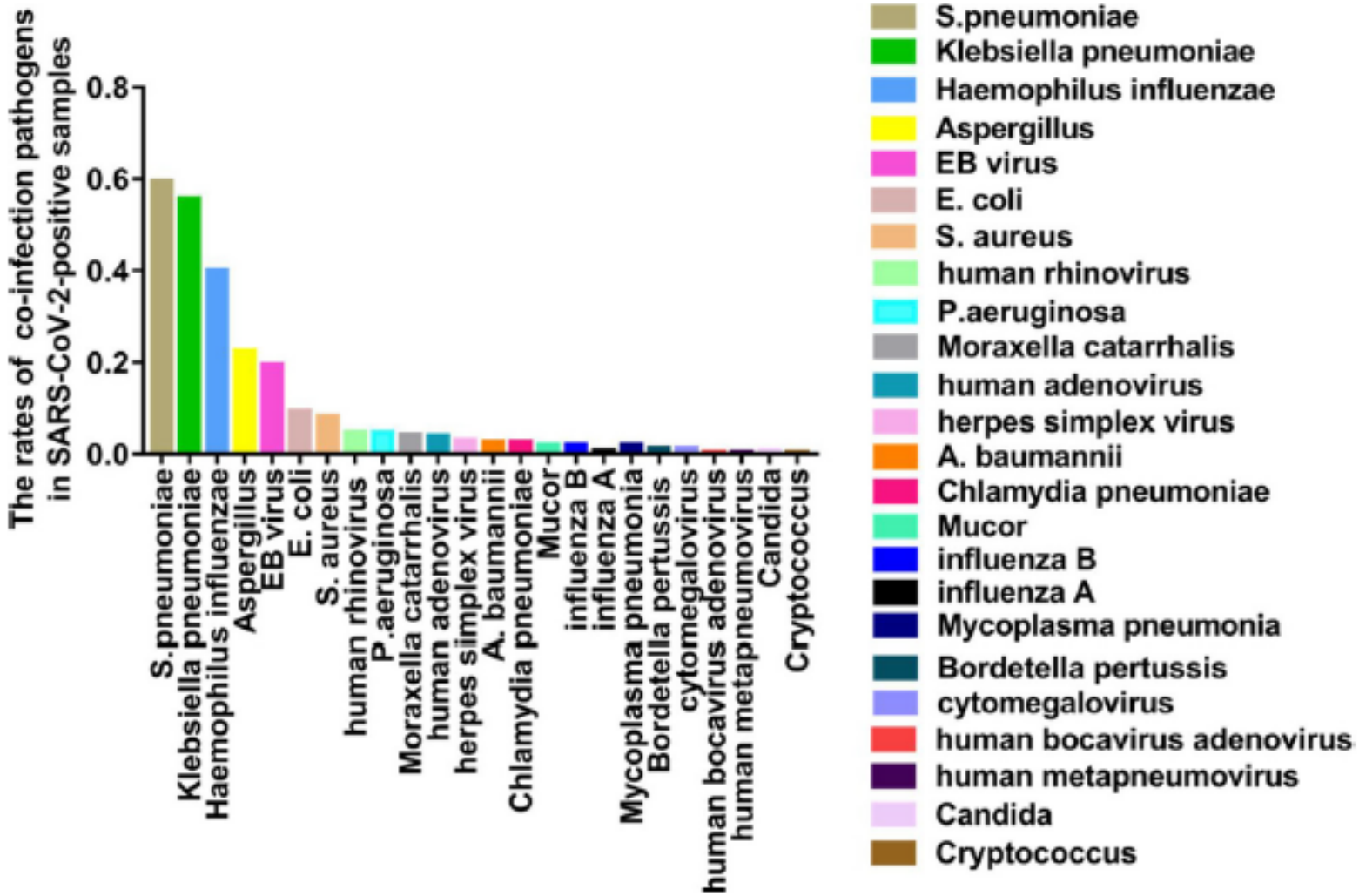
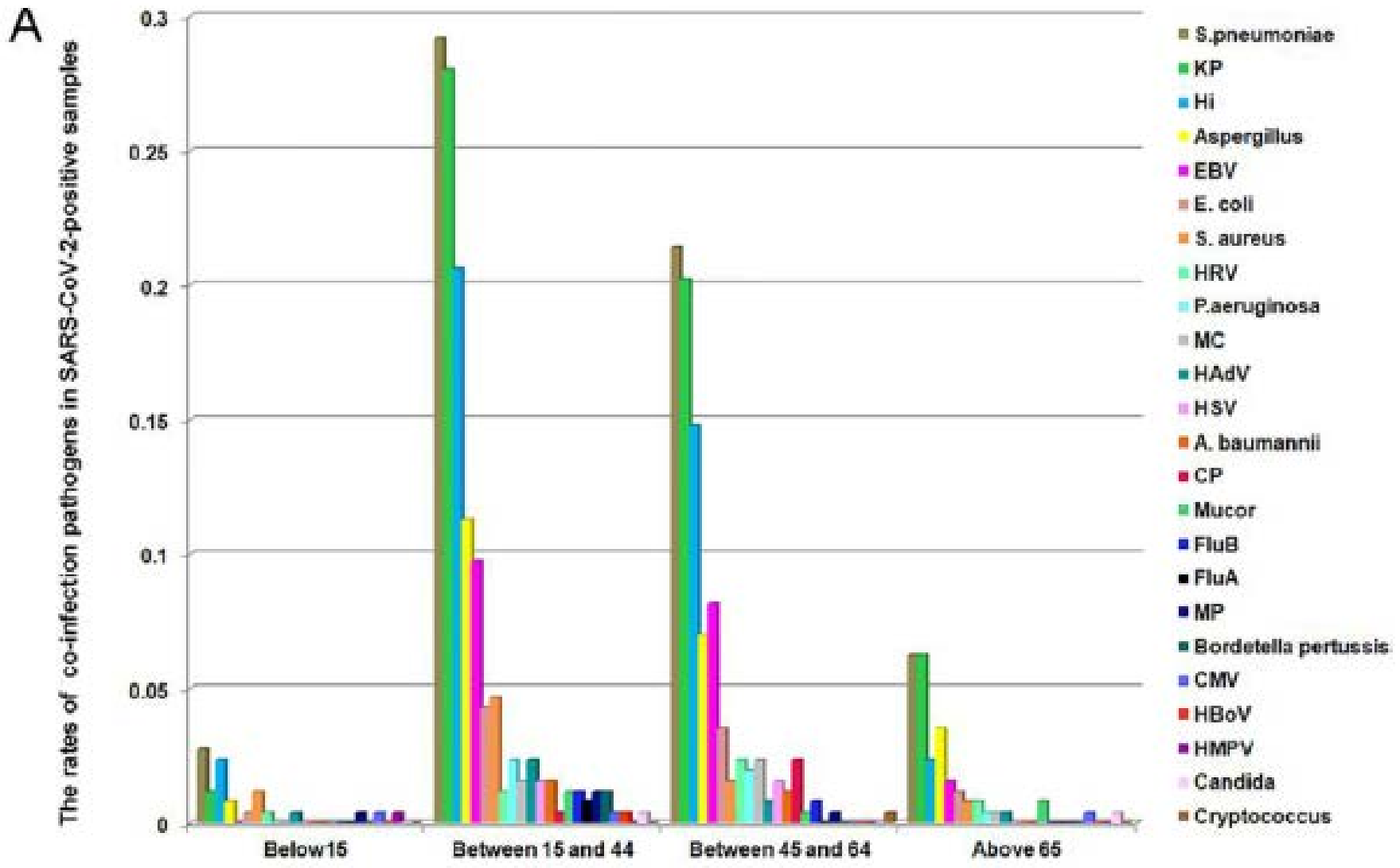


Fig. 1. Distribution of respiratory pathogens with the SARS-CoV-2 co-infection.

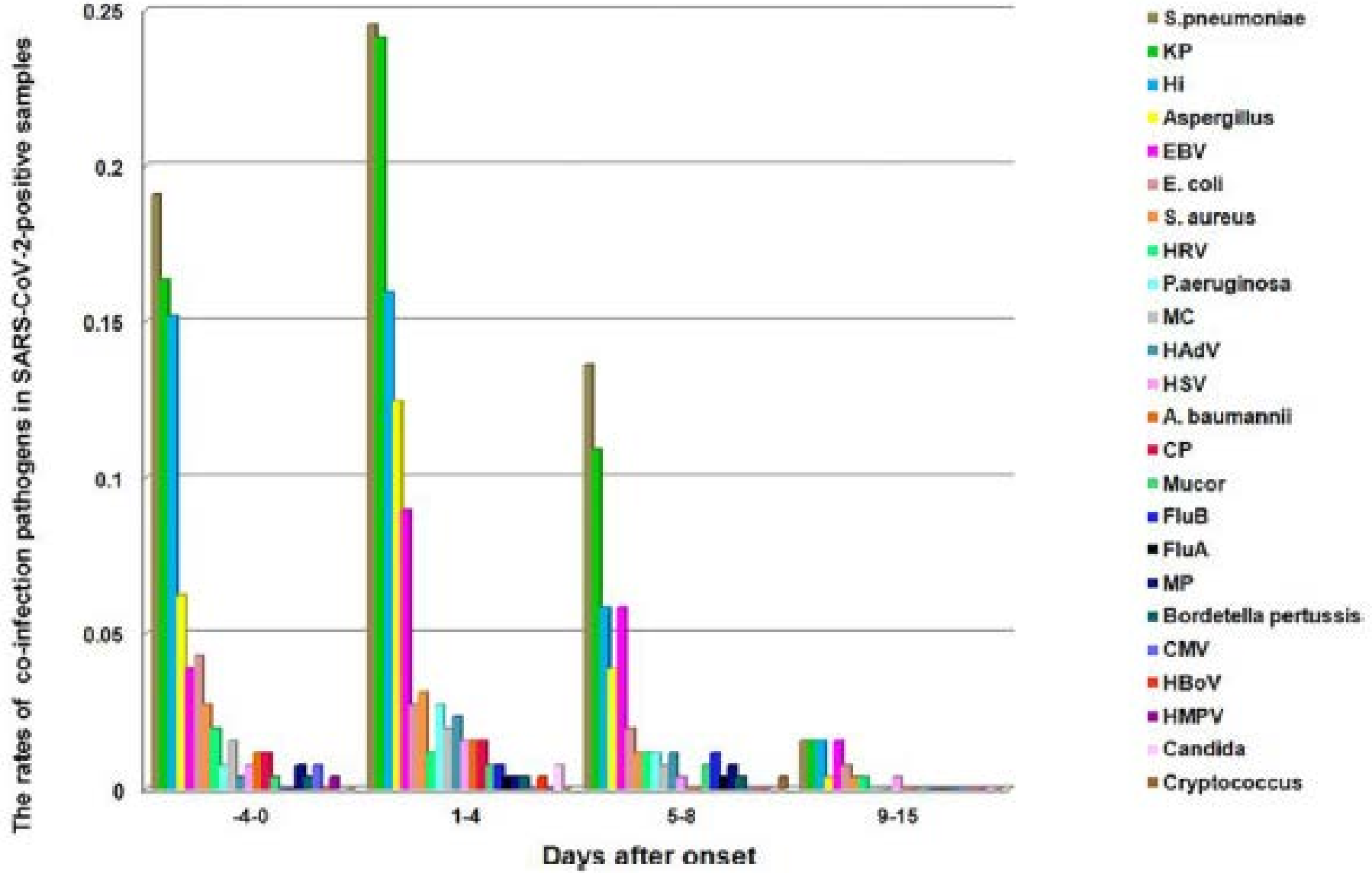
X. Zhu, et al. Virus Research 285 (2020) 198005

Distribution pathogens in different ages



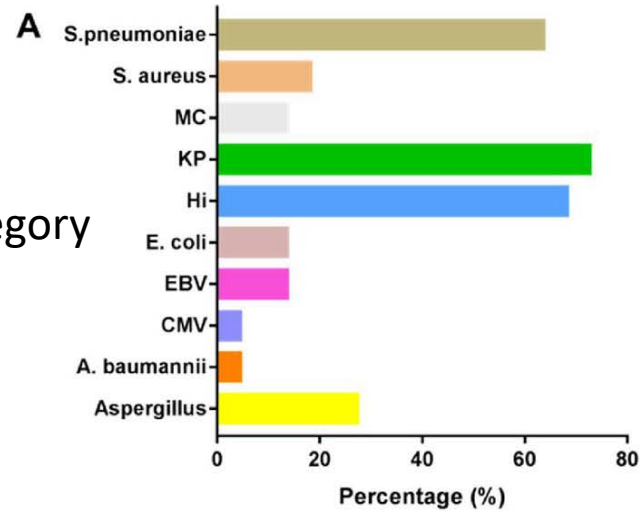
X. Zhu, et al. Virus Research 285 (2020) 198005

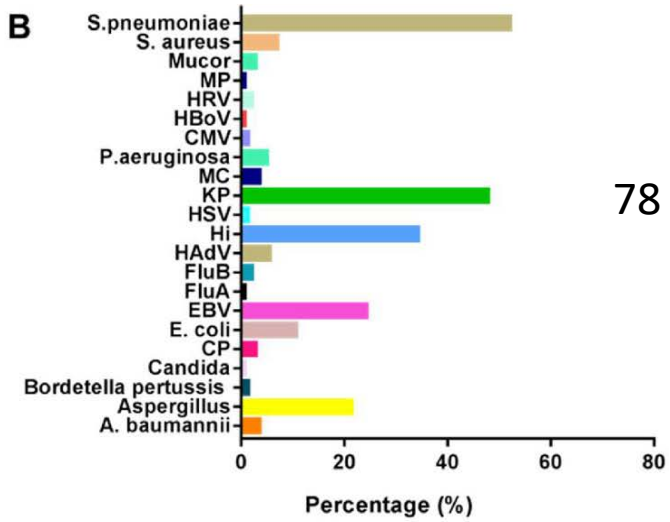
Distribution of pathogens in different time of onset.



X. Zhu, et al. Virus Research 285 (2020) 198005

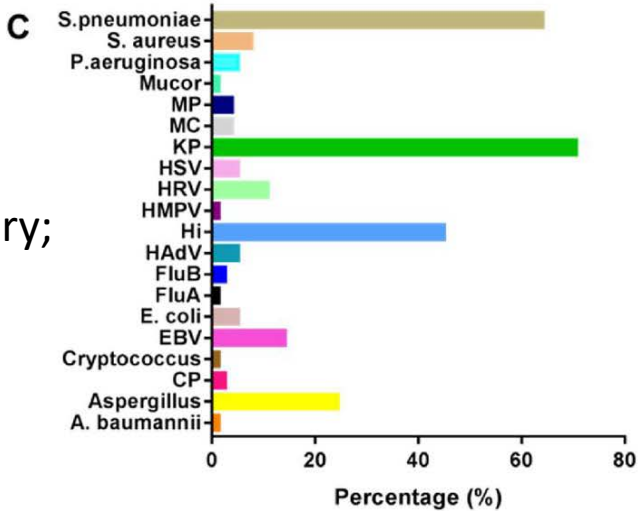
22 symptomatic category

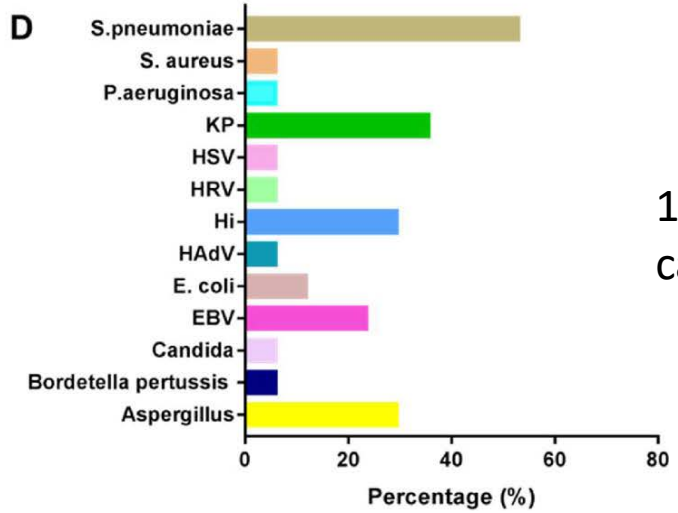




78 mild category

140
moderate category;





17 severe/critical
category

Table 1. Multidrug-resistant organism outbreaks in COVID-19 patients

Author	Geographic location	Outbreak time period	Organism/s	Changes to infection control standard of care
Patel *et al.* [40]	Maryland, USA	May–June 2020	MDR *Escherichia coli* *Pseudomonas aeruginosa* *Acinetobacter baumannii*	Possible contamination: two layers of gown and gloves Remove outer layers before moving to another patient. Inner layer stays Team nursing model Tight spaces and close proximity in double occupancy
Perez *et al.* [35▪]	New Jersey, USA	February–July 2020	Carbapenem-resistant *Acinetobacter baumannii*	Extended use of ventilator circuits and suctioning catheters only replacing when visibly soiled or malfunctioning
Tiri *et al.* [41]	Terni, Italy	March–June 2020	Carbapenem-resistant *Klebsiella pneumoniae*	Four to five healthcare workers turning the patient to prone position None other reported
Nori *et al.* [42]	Bronx, NY, USA	March–April 2020	New Delhi Metallo-betalactamase (NDM) producing carbaenem-resistant *Enterobacterales*	Reuse of PPE Lapses of standard of care for device maintenance Patient cohorting in surge ICU
Porretta *et al.* [43]	Tuscany, Italy	March–May 2020	NDM producing carbapenem-resistant *Enterobacterales*	NR
Kampmeier *et al.* [44]	Münster, Germany	March–April, 2020	Vancomycin-resistant enterococci	Hand hygiene Environmental hygiene
Prestel *et al.* [36▪]	Florida, USA	July-August 2020-	*Candida auris*	Contamination due to multiple layers of gown and gloves. One inner gown and one pair of gloves are worn the entire shift
Chaudhary *et al.* [39]	New Delhi, India	April–July 2020	*Candida auris (67%)* *Other Candida spp.*	NR

Incidence, mortality and antibiotic use in COVID-19 patients with BSI, CLABSI, CAUTI and VAP

Before and after comparisons that do not control for the multiple changes in practices

Table 2. Incidence, mortality and antibiotic use in COVID-19 patients with BSI, CLABSI, CAUTI and VAP

Type of infection	Author	Study Design	Incidence	Predominant organisms	Mortality	Antibiotic Use
BSI	Buetti *et al.* [49]	Matched case-cohort	15%	CoNS Enterococci	NR	79%
	Bhatt *et al.* [50]	Multicentre case–control (BSI vs. no BSI)	34%	*Staphylococcus epidermidis*, Methicillin susceptible *Staphylococcus aureus*, *Enterococcus fecalis*	53%	80%
	Bonazzetti *et al.*[48]	Retrospective observational	67%	*Enterococcus* species, CoNS, *S. aureus*	NR	NR
CLABSI	Knepper *et al.* [51]	Retrospective cohort	65% higher in COVID-19 areas	NR	NR	NR
	Fakih *et al.* [52]	Retrospective observational	Five times greater in COVID-19 patients	CoNS, *Candida* spp.	53.8%	NR
CAUTI	Knepper *et al.* [51]	Retrospective cohort	83% higher in COVID-19 areas	NR	NR	NR
	Fakih *et al.* [52]	Retrospective observational	No significant change from prepandemic timeframe	NR	NR	NR
VAP	Maes[a] *et al.* [53]	Retrospective observational	48%	Enterobacteriaceae, *Hemophilus influenza*, *P. aeruginosa*	38%	94%
	Rouze *et al.* [54]	Multicentre retrospective cohort	51%	*P. aeruginosa*, *Enterobacter spp.*, *Klebsiella spp.*	29%	95%
	COVID-ICU Group [55]	Multicentre prospective cohort	58%	NR	31%	NR
	Luyt *et al.* [56]	Retrospective cohort	86%	Enterobacteriaceae (40% Amp-C cephalosporinase producers) *P. aeruginosa*	34%	100%
	Zhou *et al.* [57]	Retrospective multicentre cohort	31%	NR	NR	95%
	Giacobbe *et al.* [58]	Multicentre retrospective observational	29%	*P. aeruginosa*	46%	95%

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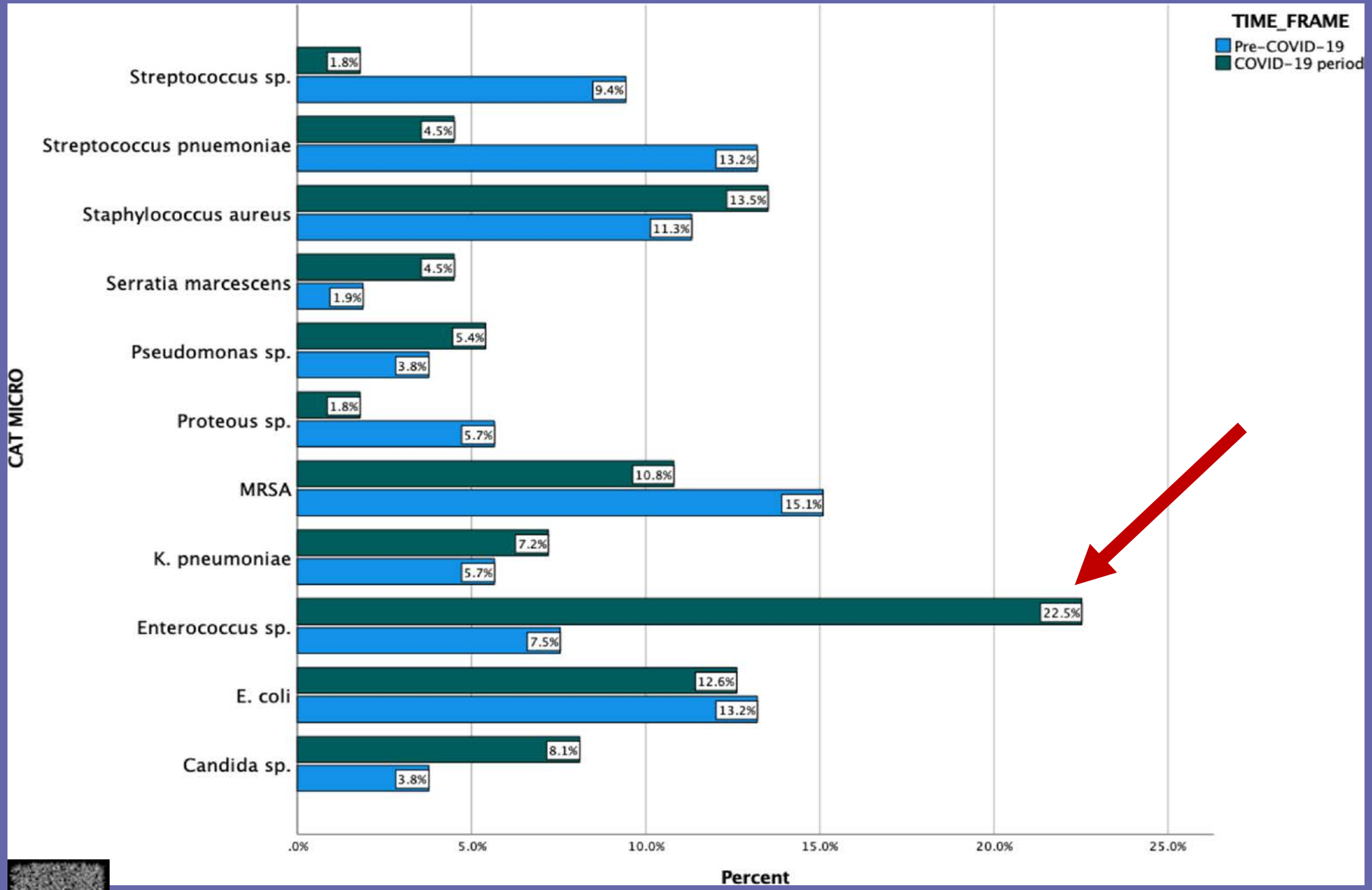
56% isolates from BSI are *Enterococcus* species

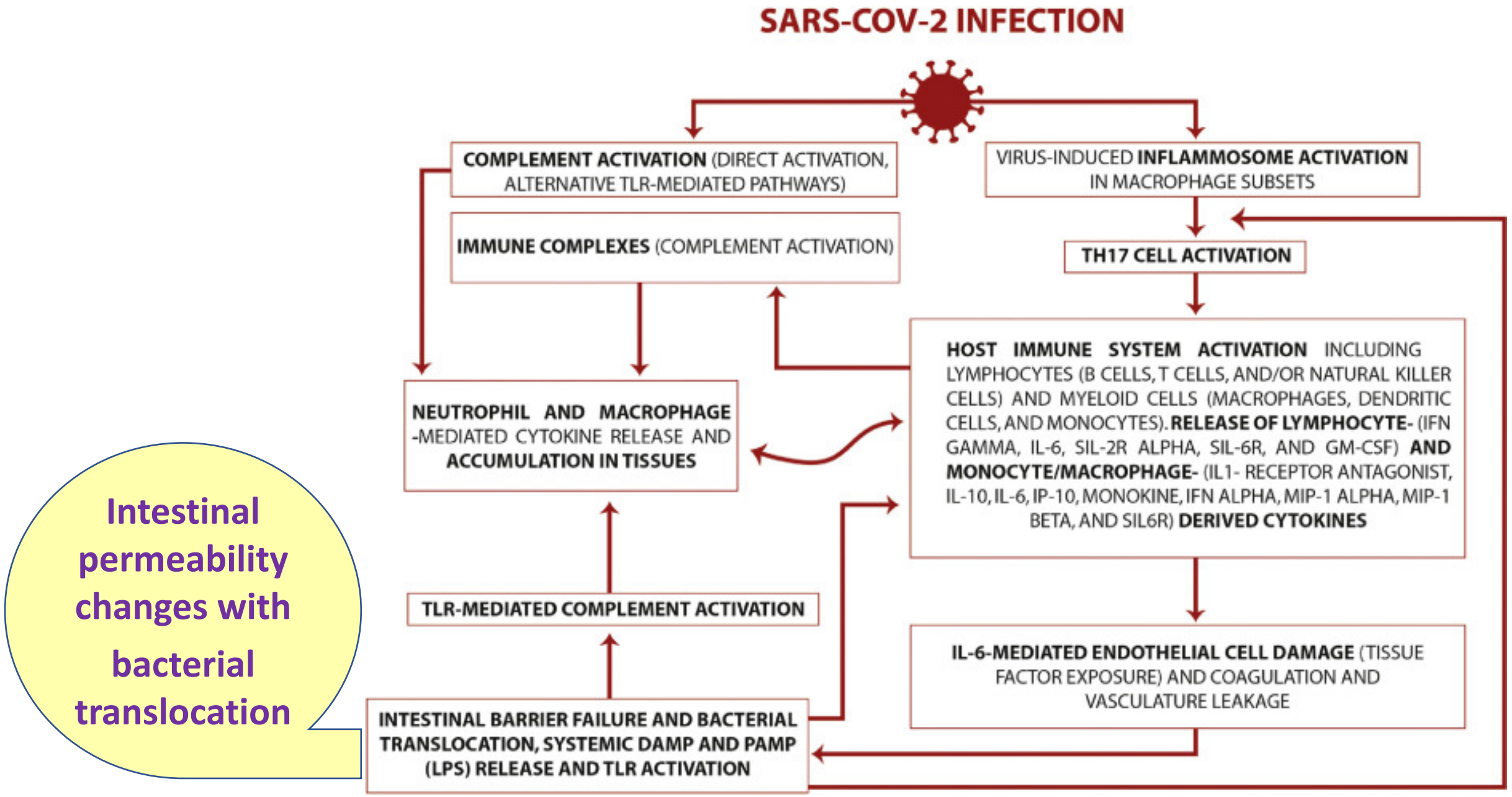
Characteristics of the Isolates and Types of Bloodstream Infection

Microorganisms	Isolates ($n = 117$)	Bloodstream Infection Episodes ($n = 93$)	Monomicrobial, $n = 71$ (76.3%)	Polymicrobial, $n = 22$ (23.7%)	Recurrent, $n = 19$ (20.4%)
Gram-positive, *n* (%)	85 (72.6)	74 (79.6)	52 (73.2)	22 (100)	14 (73.7)
Enterococcus species[b]	53 (45.3)	53 (55.8)	32 (45.1)	22 (100)	11 (57.9)
Vancomycin-resistant *Enterococcus faecium*	5 (4.3)	5 (5.4)	3 (4.2)	2 (9.1)	1 (5.3)
Staphylococcus aureus	7 (6)	7 (7.5)	3 (4.2)	4 (18.2)	2 (10.5)
Methicillin-resistant *S. aureus*	5 (4.3)	5 (5.4)	2 (2.8)	3 (13.6)	1 (5.3)
Coagulase-negative *Staphylococci*	24 (20.5)	24 (25.8)	16 (22.5)	8 (36.4)	5 (26.3)
Gemella sanguinis	1 (0.8)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)
Gram-negative, *n* (%)	29 (24.8)	27 (29.0)	16 (22.5)	12 (54.5)	10 (52.6)
Enterobacterales[a]	19 (16.2)	19 (20.4)	10 (14.1)	9 (40.9)	5 (26.3)
Extended spectrum beta lactamase-positive Enterobacterales	6 (5.1)	6 (6.5)	3 (4.2)	3 (13.6)	2 (10.5)
Carbapenemase-producing Enterobacterales	10 (8.5)	10 (10.8)	6 (8.5)	4 (18.2)	2 (10.5)
Enterobacter species	6 (5.1)	6 (6.5)	4 (5.6)	2 (9.1)	3 (15.8)
Cephalosporin-resistant *Enterobacter*	4 (3.4)	4 (4.3)	3 (4.2)	1 (4.5)	1 (3.6)
Pseudomonas aeruginosa	2 (1.7)	2 (2.2)	1 (1.4)	1 (4.5)	1 (5.3)
MDR *P. aeruginosa*	1 (0.8)	1 (1.1)	1 (1.4)	0 (0.0)	1 (5.3)
Stenotrophomonas maltophilia	1 (0.8)	1 (1.1)	1 (1.4)	0 (0.0)	1 (5.3)
MDR *S. maltophilia*	1 (0.8)	1 (1.1)	1 (1.4)	0 (0.0)	1 (5.3)
Acinetobacter baumannii	1 (0.8)	1 (1.1)	0 (0.0)	1 (4.5)	0 (0.0)
Yeasts, *n* (%)	3 (2.6)	3 (3.2)	3 (4.2)	0 (0.0)	0 (0.0)
Candida albicans	3 (2.6)	3 (3.2)	4 (4.2)	0 (0.0)	0 (0.0)

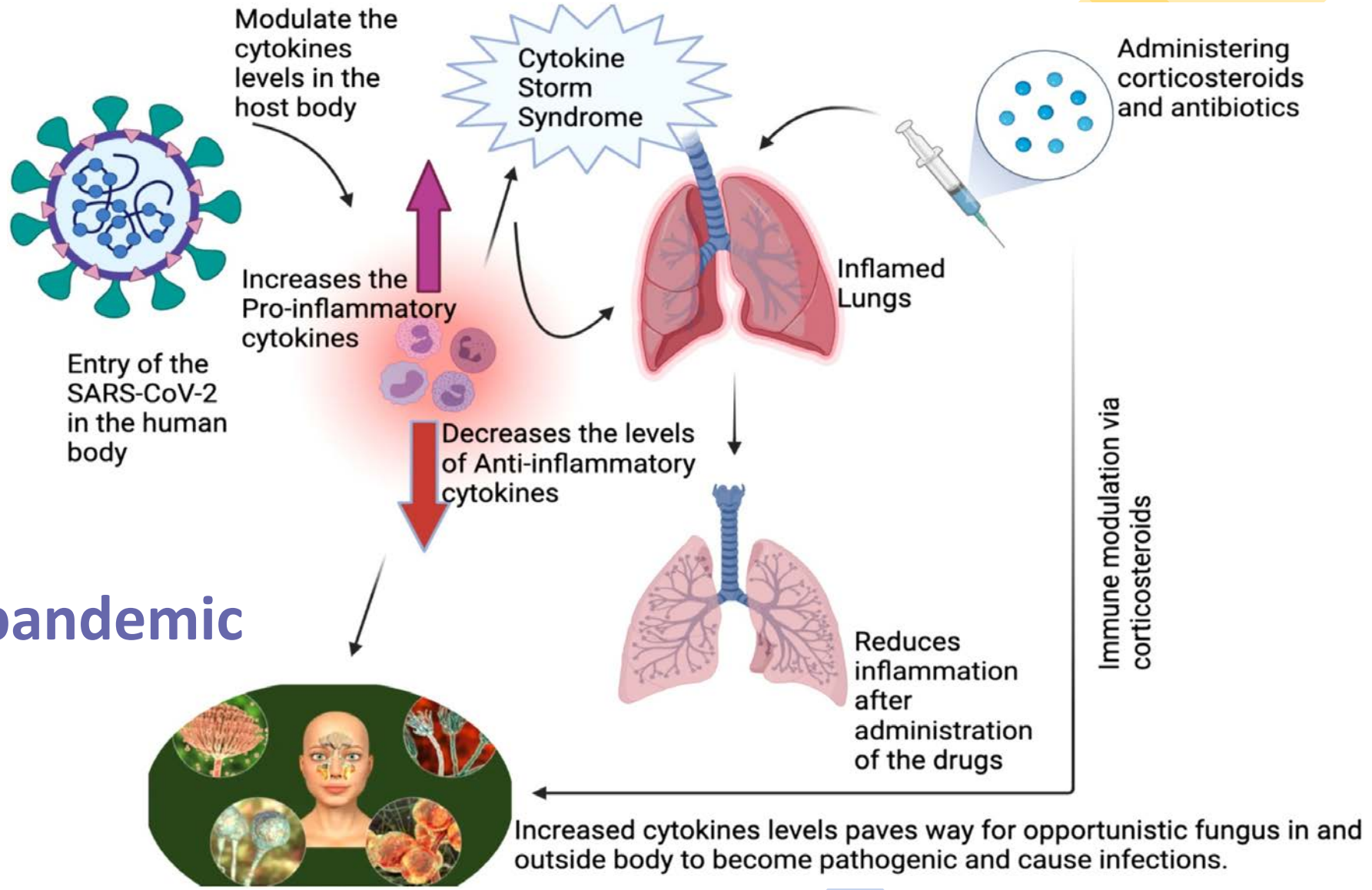
Crit Care Med. 2021 Jan; 49(1): e31–e40.



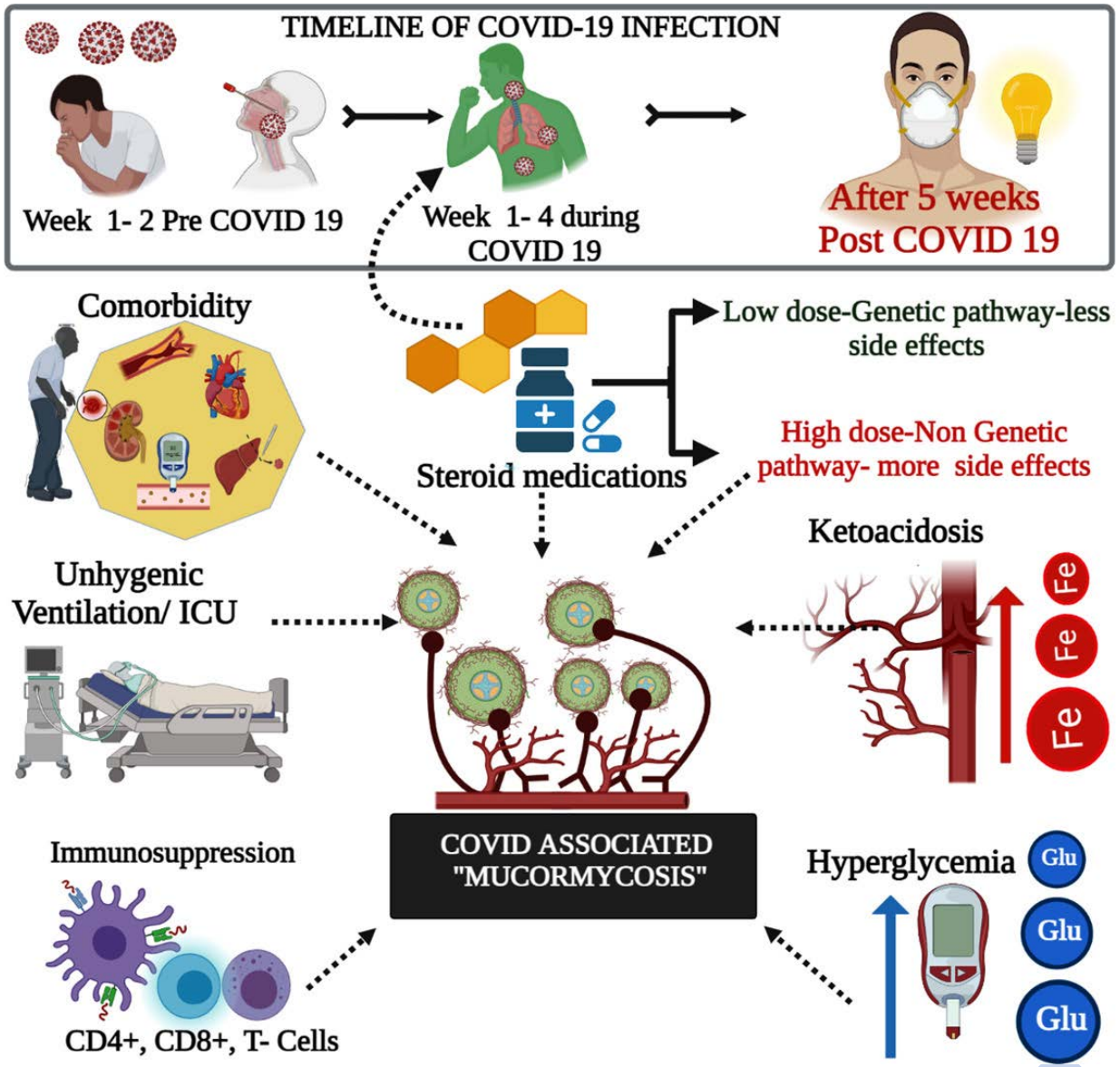
International Journal of Infectious Diseases DOI: (10.1016/j.ijid.2021.12.349)


SARS-COV-2 INFECTION
COMPLEMENT ACTIVATION (DIRECT ACTIVATION, ALTERNATIVE TLR-MEDIATED PATHWAYS)
VIRUS-INDUCED INFLAMMOSOME ACTIVATION IN MACROPHAGE SUBSETS
IMMUNE COMPLEXES (COMPLEMENT ACTIVATION)
TH17 CELL ACTIVATION
HOST IMMUNE SYSTEM ACTIVATION INCLUDING LYMPHOCYTES (B CELLS, T CELLS, AND/OR NATURAL KILLER CELLS) AND MYELOID CELLS (MACROPHAGES, DENDRITIC CELLS, AND MONOCYTES). RELEASE OF LYMPHOCYTE- (IFN GAMMA, IL-6, SIL-2R ALPHA, SIL-6R, AND GM-CSF) AND MONOCYTE/MACROPHAGE- (IL1- RECEPTOR ANTAGONIST, IL-10, IL-6, IP-10, MONOKINE, IFN ALPHA, MIP-1 ALPHA, MIP-1 BETA, AND SIL6R) DERIVED CYTOKINES
NEUTROPHIL AND MACROPHAGE -MEDIATED CYTOKINE RELEASE AND ACCUMULATION IN TISSUES
TLR-MEDIATED COMPLEMENT ACTIVATION
IL-6-MEDIATED ENDOTHELIAL CELL DAMAGE (TISSUE FACTOR EXPOSURE) AND COAGULATION AND VASCULATURE LEAKAGE
INTESTINAL BARRIER FAILURE AND BACTERIAL TRANSLOCATION, SYSTEMIC DAMP AND PAMP (LPS) RELEASE AND TLR ACTIVATION
Intestinal permeability changes with bacterial translocation

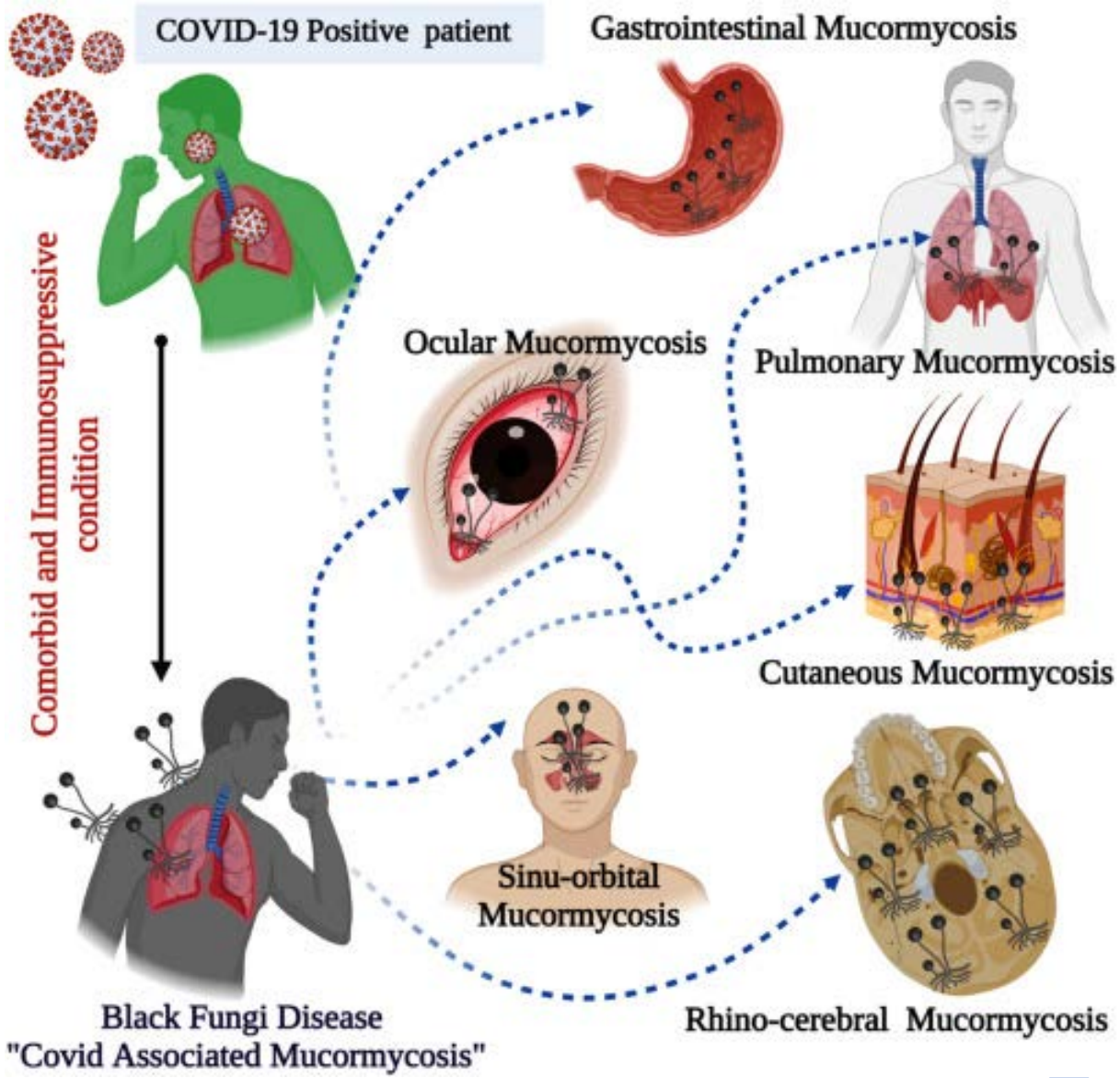
Opportunistic mycoses in COVID-19 patients/survivors: Epidemic inside a pandemic



J Infect Public Health. 2021 Nov;14(11):1720-1726



Sci Total Environ. 2022 Jan 20;805:150355.



Sci Total Environ. 2022 Jan 20;805:150355.

	Country	Case number in initial report	Age, years	Sex	Comorbidities	Length of illness, days	Invasive mechanical ventilation (days)	Extra-corporeal membrane oxygenation	Immuno-therapy	Antifungal	Mould identification	Autopsy type	Extent of fungal involvement
Borczuk et al (2020)[23]	Italy	29	79	Male	Dementia, congestive heart failure, intestinal ischaemia	9	Yes (6)	No	None	None	*Aspergillus*	Standard	Airway only
Borczuk et al (2020)[23]	Italy	39	61	Male	COPD, congestive heart failure, pharyngeal cancer	6	No	No	None	None	*Aspergillus*	Standard	Bronchopneumonia
Carsana et al (2020),[29] Antinori et al (2020)[72]	Italy	ND	73	Male	Diabetes, hypertension, hyperthyroidism, atrial fibrillation, obesity	ND	Yes (9)	No	None	Liposomal amphotericin B, then isavuconazole	*Aspergillus fumigatus*	Standard	Bronchial wall ulceration and focal necrotising pneumonia
De Michele et al (2020)[31]	USA	ND	ND	ND	ND	ND	No	No	ND	ND	*Aspergillus*	Standard	Bronchopneumonia, mycetoma
Deinhardt-Emmer et al (2020)[32]	Germany	3	78	Male	Hypertension, diabetes, chronic renal failure	30	Yes (7)	No	None	None	Fungus not specified	Standard	Fungal pneumonia
Hanley et al (2020)[42]	UK	5	22	Male	Obesity	27	Yes (22)	No	None	Caspofungin	Mucormycete	Standard	Lungs, hilar lymph nodes, brain, kidney
Rapkiewicz et al (2020)[57]	USA	2	60	Male	Coronary artery disease	7	No	No	None	None	Fungus not specified	Standard	Erosive bronchitis with hyphae; bronchopneumonia (fungal stain negative)
Remmelink et al (2020)[58]	Belgium	6	73	Male	Hypertension, chronic renal failure	11	Yes (ND)	Yes	Steroids	ND	*Aspergillus*	Standard	Lung and trachea
Remmelink et al (2020)[58]	Belgium	7	56	Male	None	7	No	No	None	ND	*Aspergillus*	Standard	Bilateral invasive aspergillosis (lungs)
Schaefer et al (2020)[63]	USA	4	50	Male	Relapsed B-ALL, febrile neutropenia, invasive aspergillosis	9	Yes (7)	No	None	ND	*Aspergillus**	Standard	Lung abscess
Schurink et al (2020)[65]	Netherlands	ND	ND	ND	ND	ND	ND	ND	ND	ND	*Aspergillus*	Standard	Massive aspergillosis involving lung parenchyma

B-ALL=b-cell acute lymphoblastic leukaemia. COPD=chronic obstructive pulmonary disease. ND=not documented. *Pre-existing diagnosis.

Table 2: Details of the 11 decedents with invasive mould disease

Lancet Microbe. 2021 Aug;2(8):e405-e414.

Conclusions…

- **Innate immune response to SARS-CoV-2 infection in a host triggers an inflammatory cascade**
- **The resultant immune exhaustion and organ damage may predispose the host to secondary infections**
- **Pandemic-imposed failure in ASP and IPC oversight likely added insult to this injury and made the host even more susceptible to secondary infections**
- **Incidence of secondary infections and attributable mortality has been poorly studied**
- **Antibiotic use has been staggeringly high in COVID-19 patients**
- **Effect of antibiotic use on antimicrobial resistance in these patients has also not been well studied**
- **In addition to predispositions inherent to COVID-19, several other preventable factors are at play**

…Conclusions

- MDRO outbreaks are underreported in the COVID-19 literature
- IPC and ASP assessments and corrections must be made widely to avoid further affronts.
- Findings that could distinguish viral pneumonia or ARDS from secondary bacterial or fungal pneumonia:
  - lobar consolidation or evidence of necrotizing pneumonia on chest imaging
  - rise in leukocyte counts, and
  - paying close attention to fever trends watching for recrudescence of fever after initial defervescence may help clinicians in making this distinction.
- Strict de-escalation protocols in COVID-19 patients


ANY
QUESTIONS?