



WEBINAR COVID-19 in the series: How to treat the disease

The characteristics of the disease

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History of SARS-CoV2 epidemic

- 01/12/ 2019: 1st case of severe pneumonia
- 31/12/2020: report of a cluster of unknown viral pneumonia around the « Huanan Seafood Wholesale Market » at Wuhan in China
- 01/01/2020: closing of this market specialised in selling fish, seafood but also wild and living animals (poultry, bats, snakes, game meat, woodchucks, etc.
- **Wuhan:** 11 millions inhabitants, 7th city in China, in Douth-Eeast, Hubei province



The SARS-CoV2

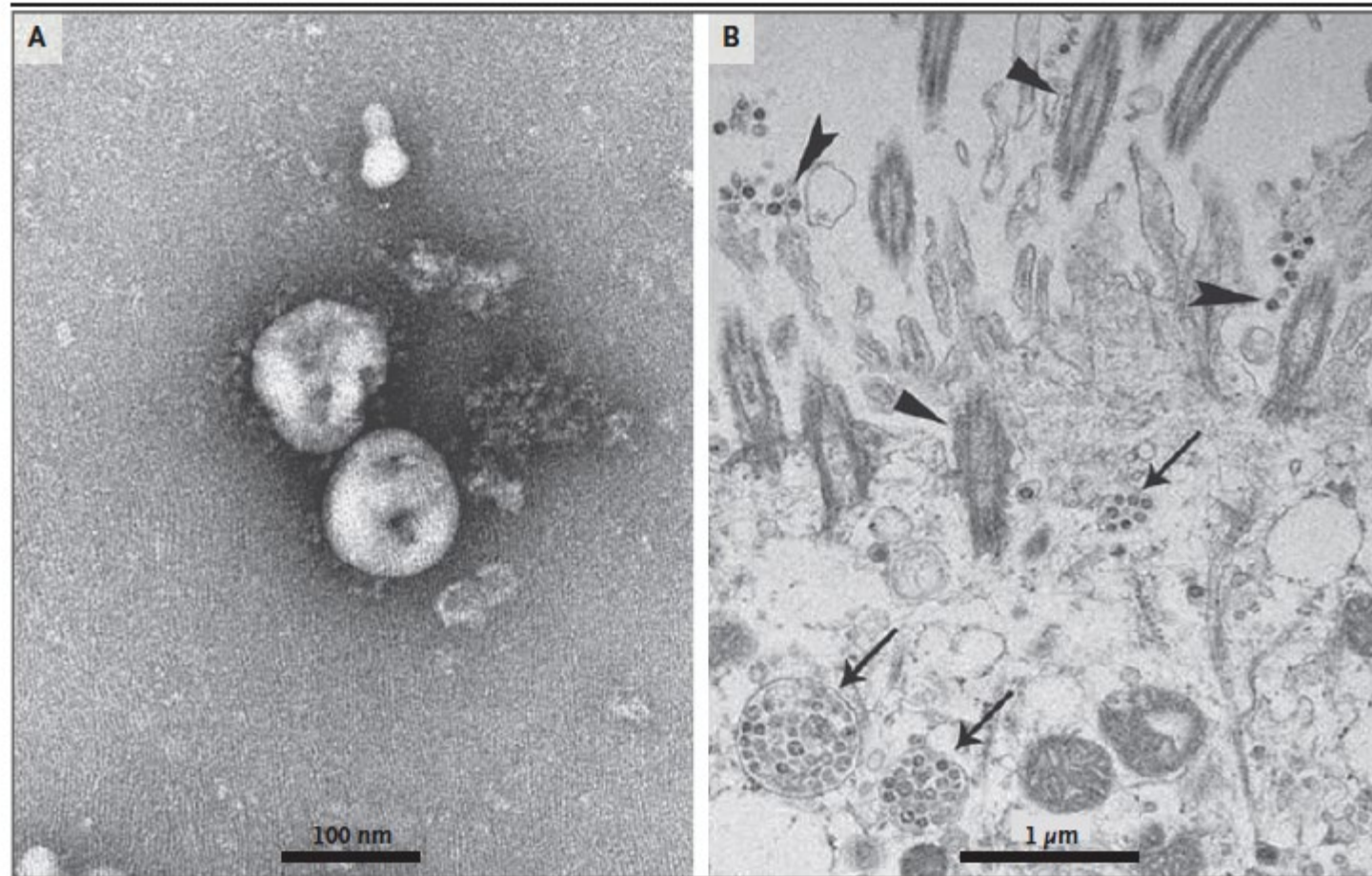
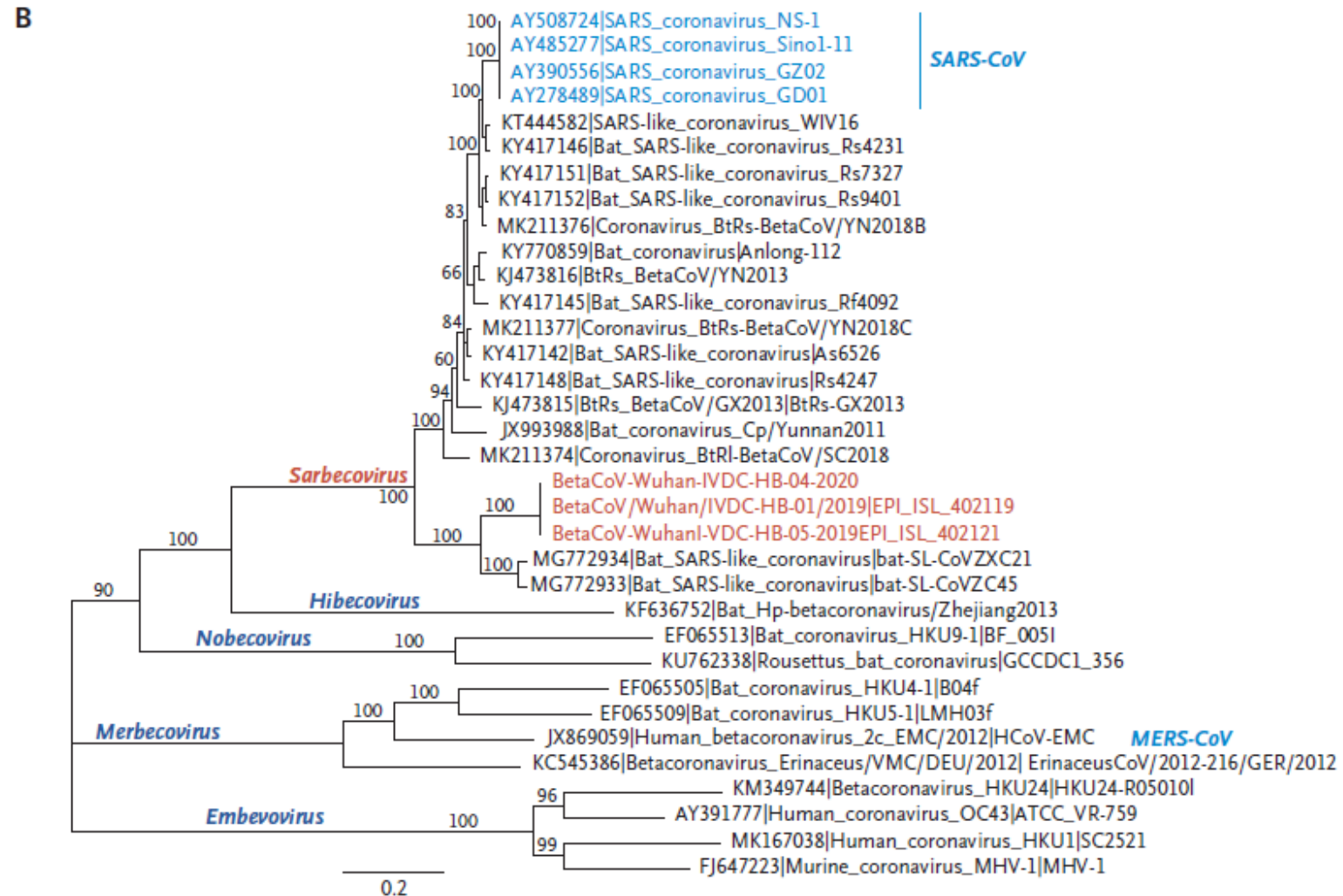


Figure 3. Visualization of 2019-nCoV with Transmission Electron Microscopy.

Negative-stained 2019-nCoV particles are shown in Panel A, and 2019-nCoV particles in the human airway epithelial cell ultrathin sections are shown in Panel B. Arrowheads indicate extracellular virus particles, arrows indicate inclusion bodies formed by virus components, and triangles indicate cilia.

The betacoronaviruses in the orthocoronavirinae subfamily



The family of Coronaviruses

4 coronavirus known for ENT infections (229E, OC43, NL63, HKU1)
+ 2 associated with severe pneumonia

- SARS CoV

Severe Acute Respiratory
Syndrome

2002-2004

- Transmission by bats via civet (Southern China)
- > 700 deaths, including Canada and the USA (fatality rate: 7 %)








- MERS CoV

• Middle East Respiratory
Syndrome

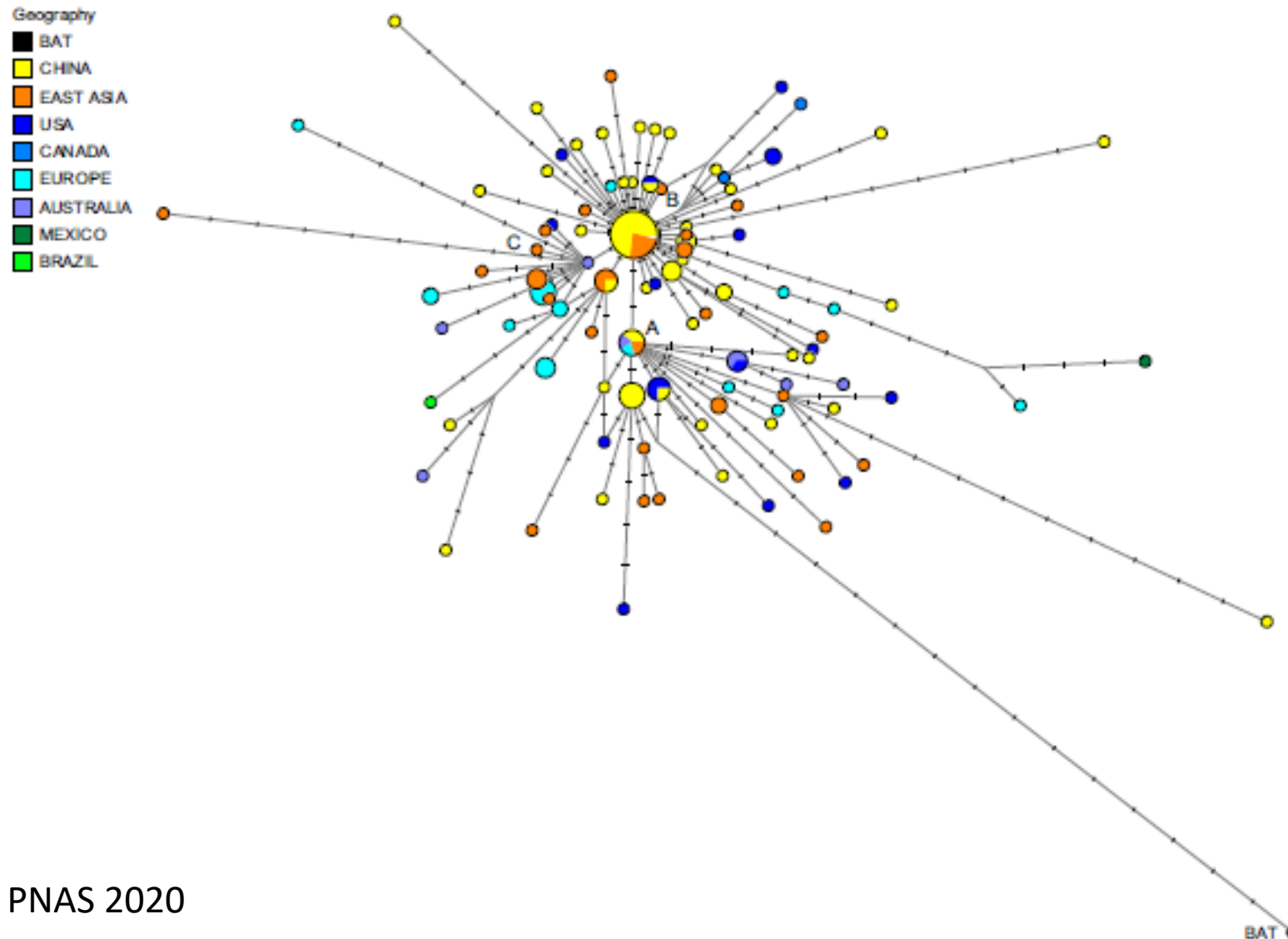
since 2012

- Transmission through camels
- In the Arabic Peninsula
- with 850 deaths in 27 countries, epidemic still going on:
 - Multiple epidemic flares: 2300 cases between 2012 and 2018 (35% fatality rate)
 - Last cases reported in December 2019

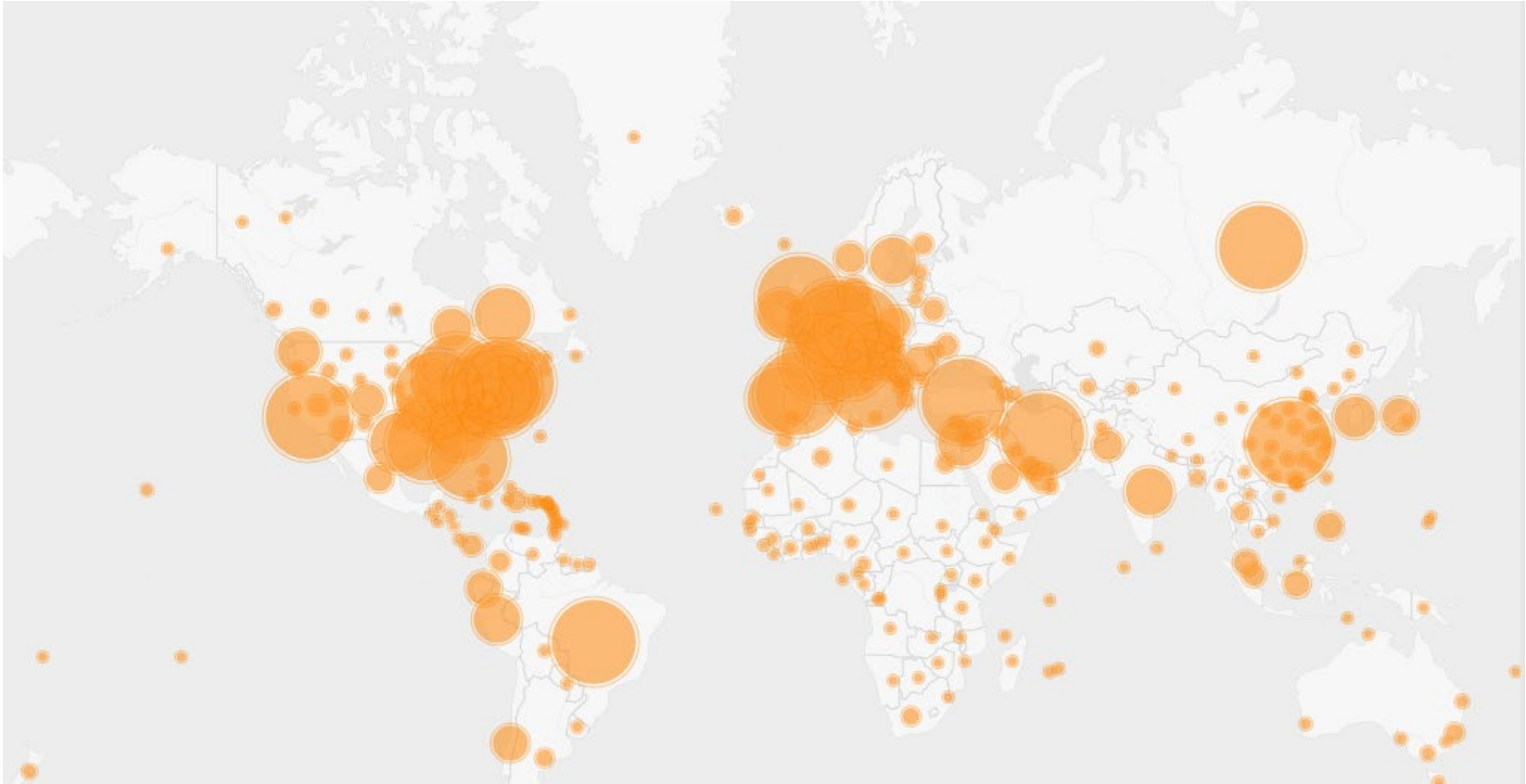
Suggested origin of SARS-CoV2: zoonosis

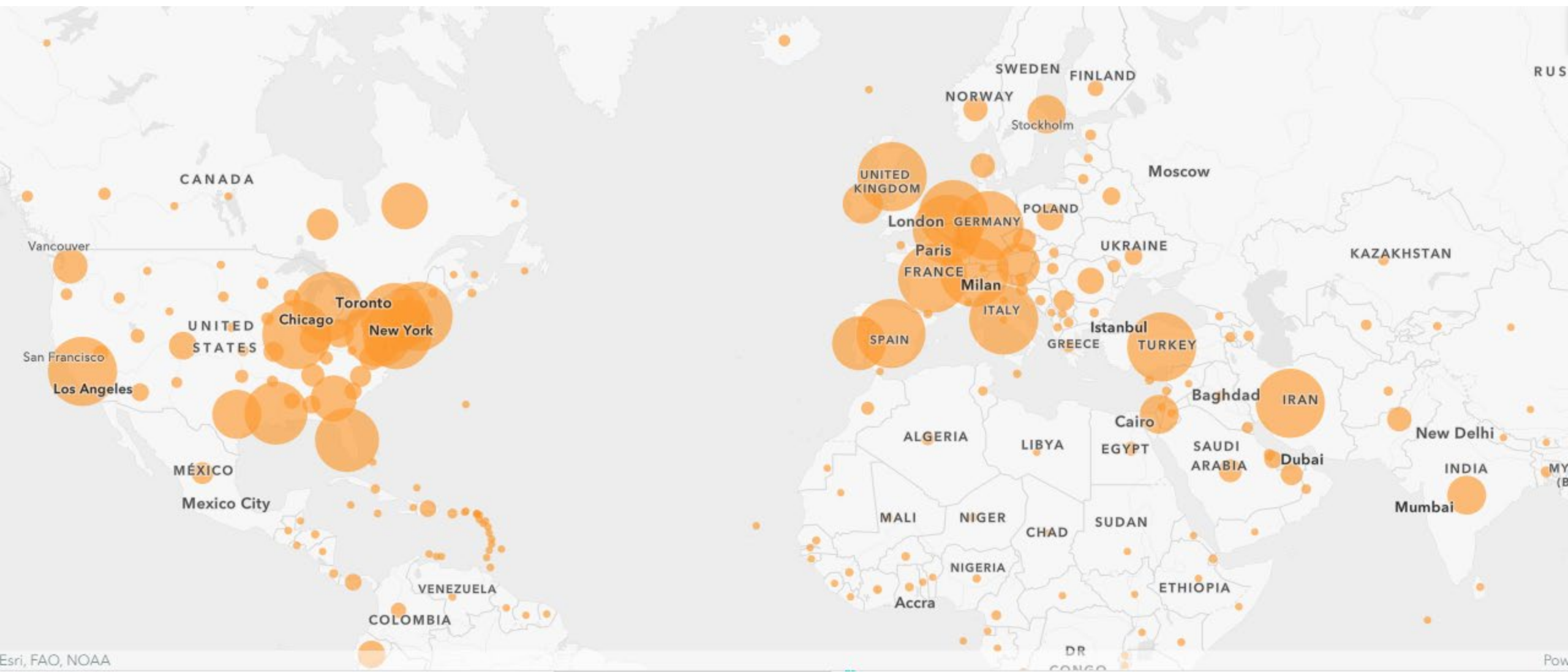
Virus (Disease)	Origin Virus	Intermediate host	Host
SARS-CoV-1 (SARS 2002)	 SARS-like Bat-CoV	 Civet Cat	 Humans
MERS-CoV (MERS 2012)	 SARS-like Bat-CoV	 Camel	
SARS-CoV-2 (COVID 2019)	 BaT-CoV RaTG13	 Pangolin (could be origin as well [Pangolin-CoV])	

Phylogenetic analysis of SARS-CoV2

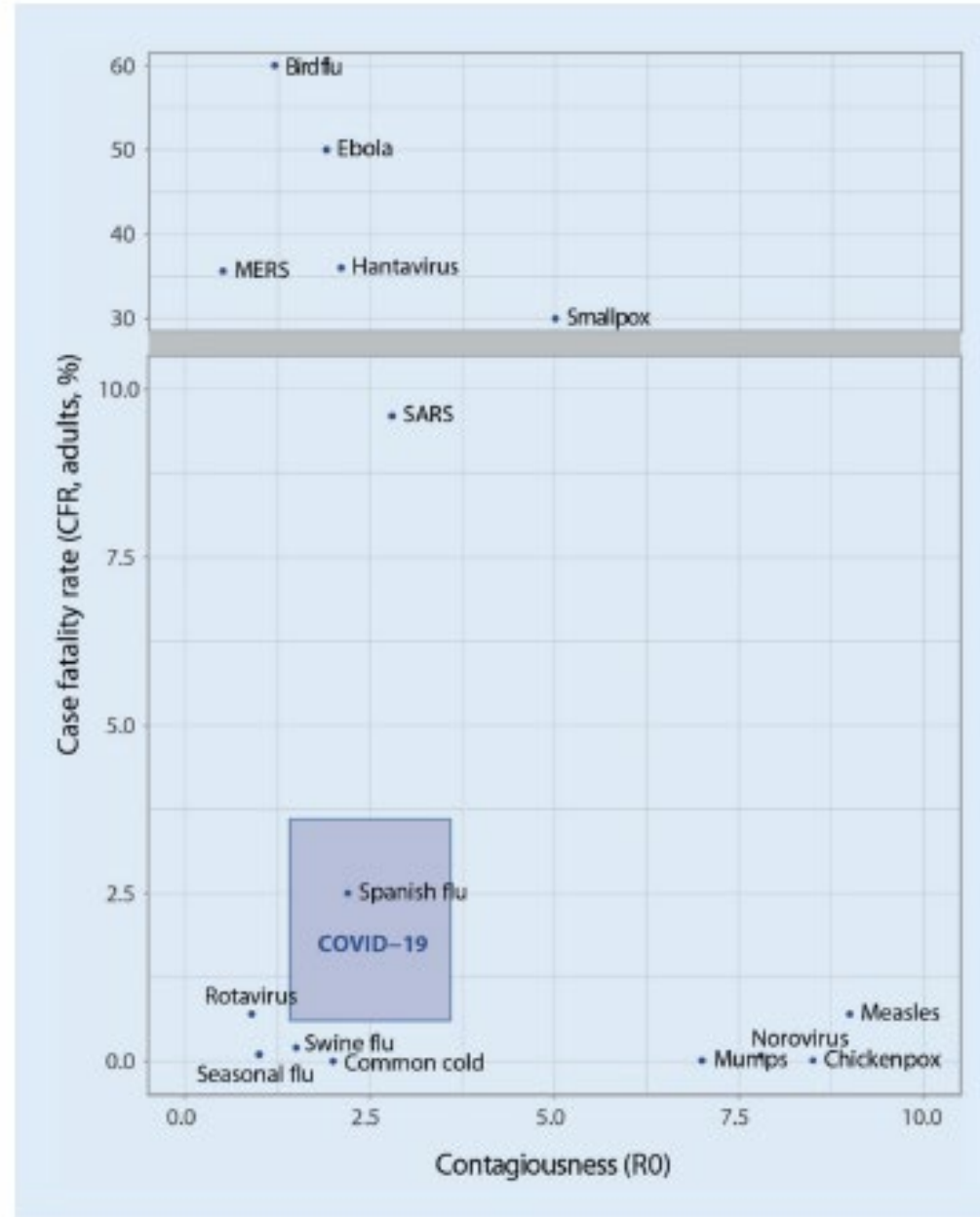


Global intensity of SARS-CoV2 epidemic

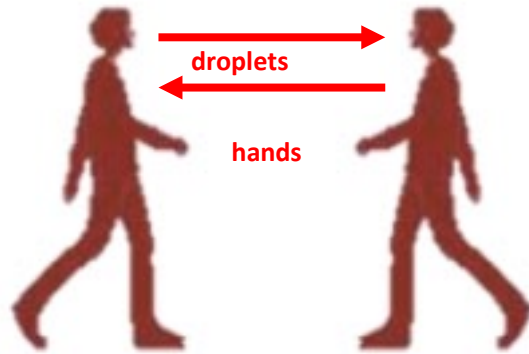




Mortality rates and contagiousness



Routes of transmission



Close contacts

≤ 1m away

≥ 15 minutes

+ if cough and sneezing

Droplets



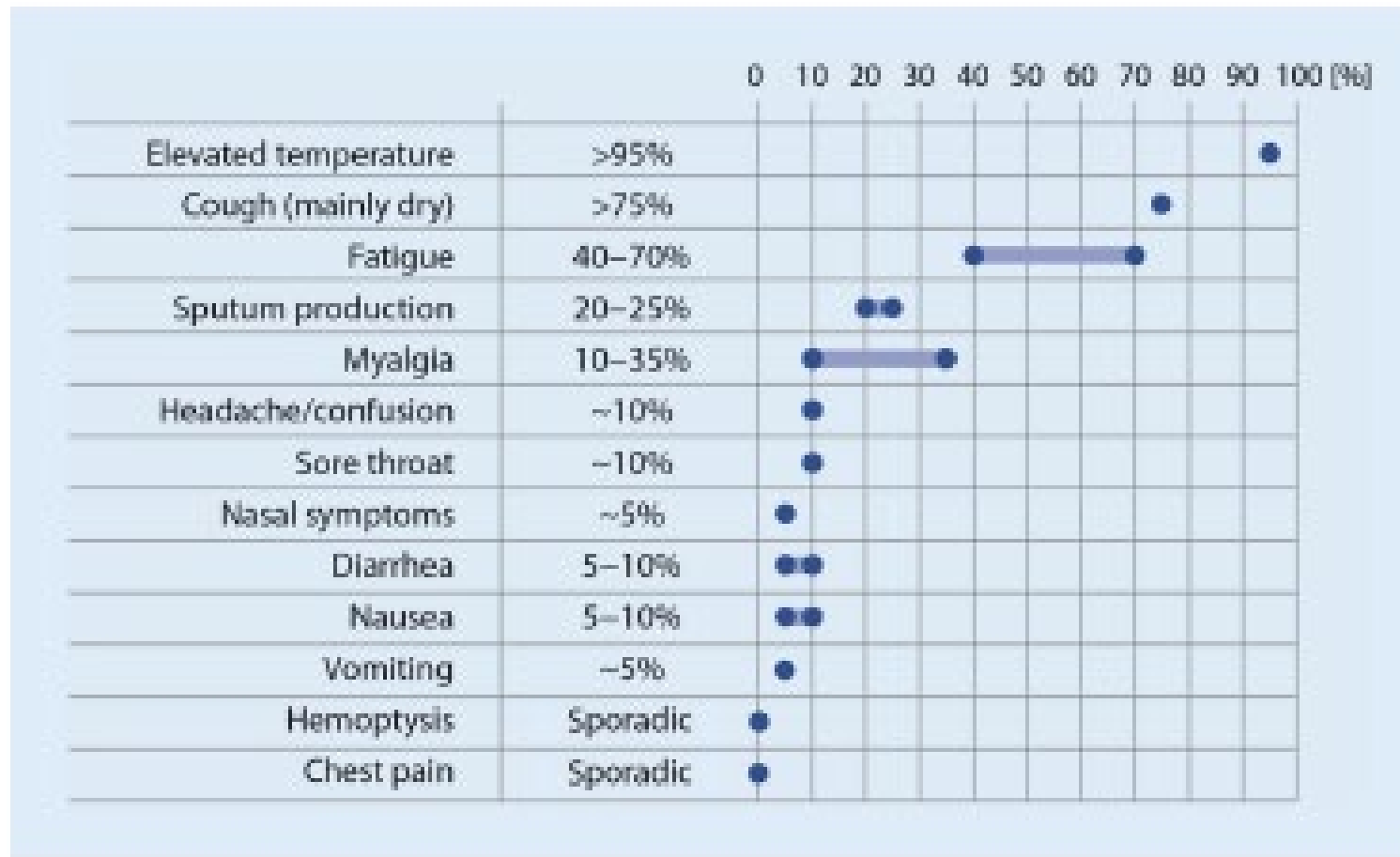
Hands



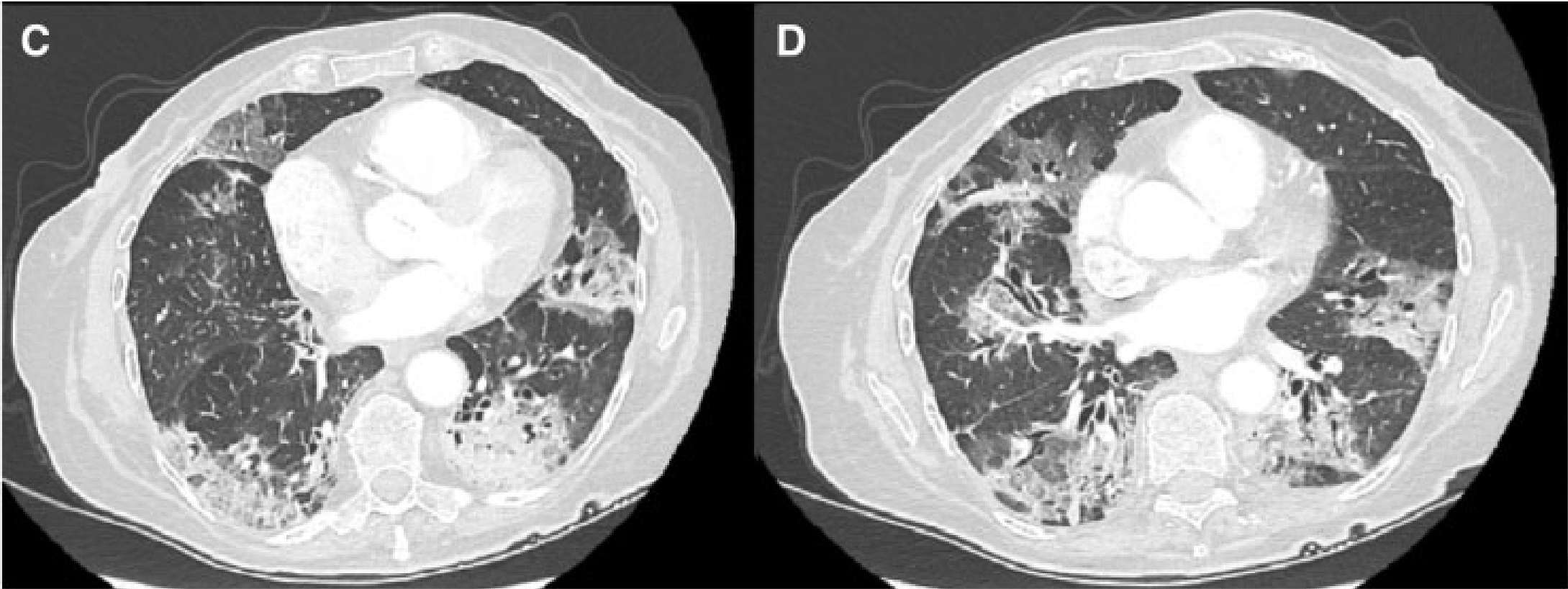
Routes: face mucosa: nose, mouth, eyes

- Virus present in biological liquids: pulmonary secretions, urines, stools.
- The close environment of the patient might be contaminated, however the virus does not survive on a replicative capacity on inert surfaces (< 3 hours) => Role of hands +++

Frequency of symptoms at initial presentation

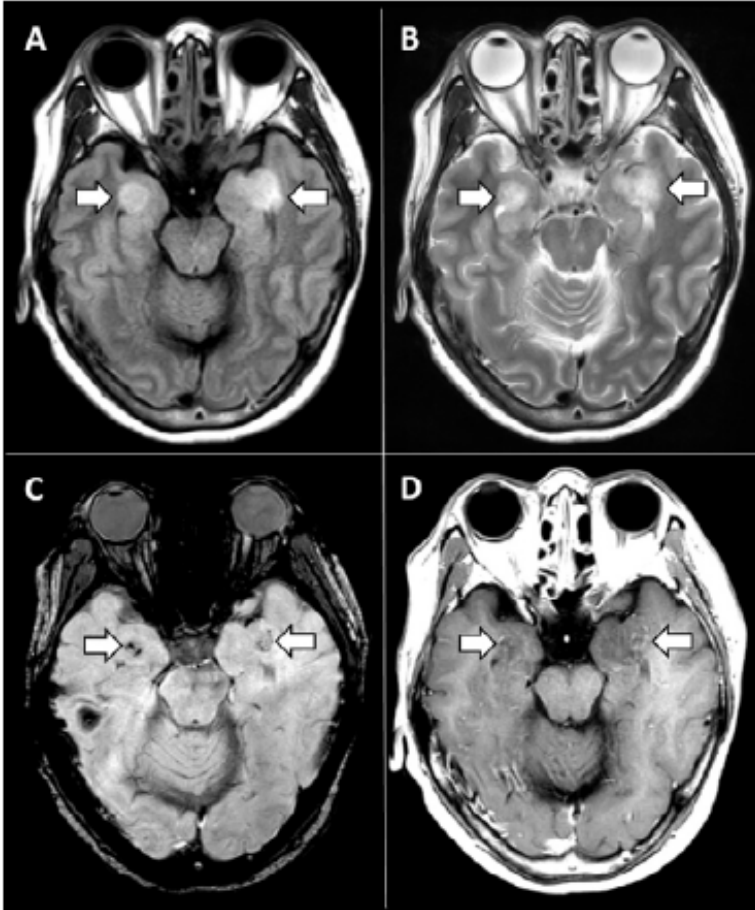


Typical lung injury / CT scan

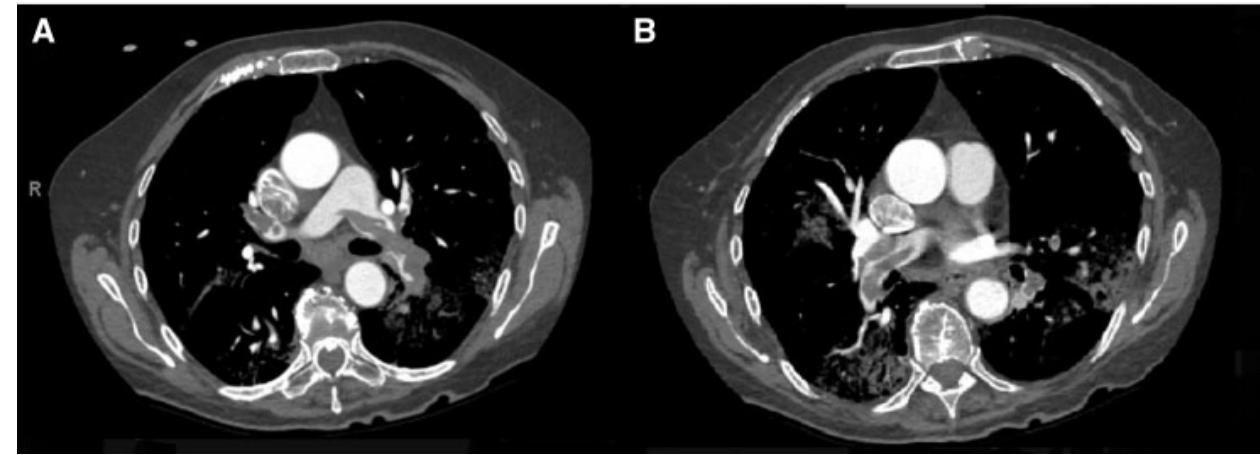


Extensive ground-glass opacifications of sub-pleural localisation

Other clinical /radiological signs



Necrotizing encephalopathy



Pulmonary embolism

Livedo reticularis

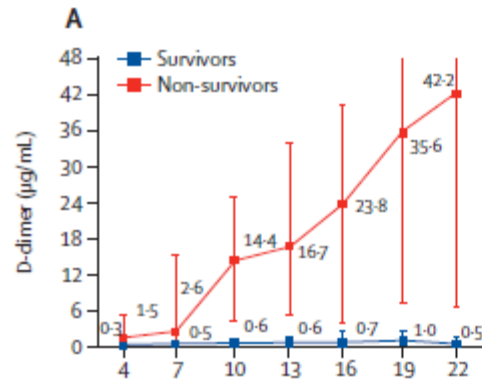


Figure 1. Patient described in Case 1 with transient unilateral livedo reticularis patch on the right thigh.

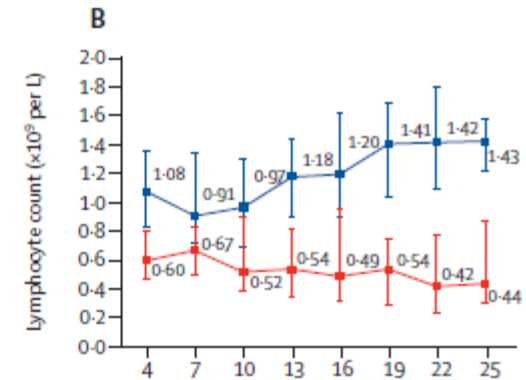
- Anosmia / agueusia
- Encephalopathy
- myocarditis

Temporal changes In laboratory markers

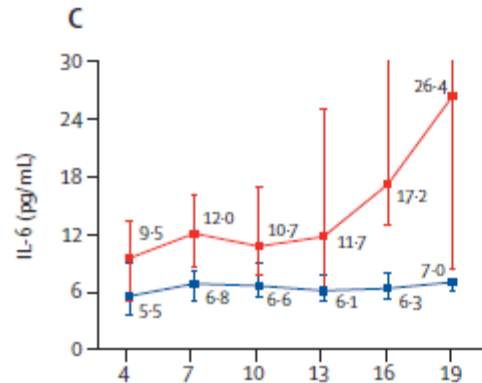
D-Dimers



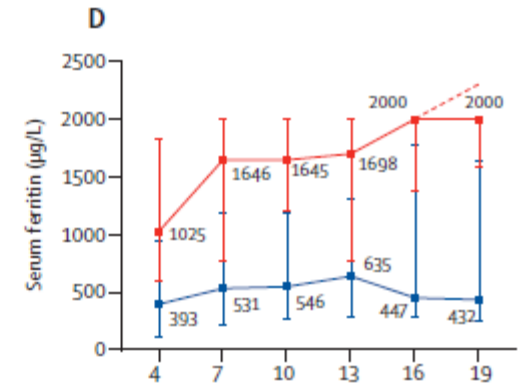
Lymphocytes



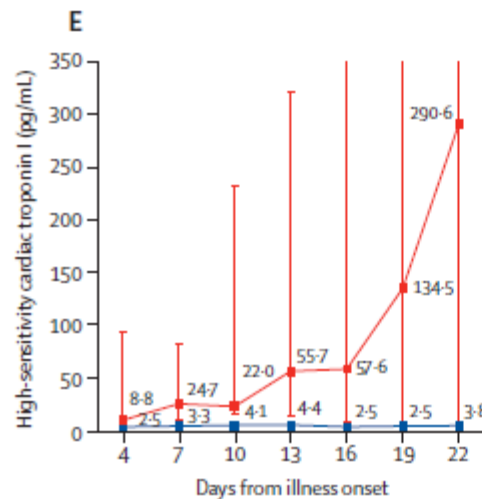
IL-6



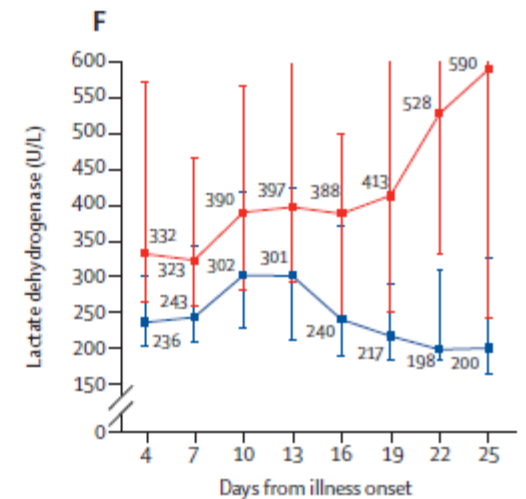
Ferritin



Troponin

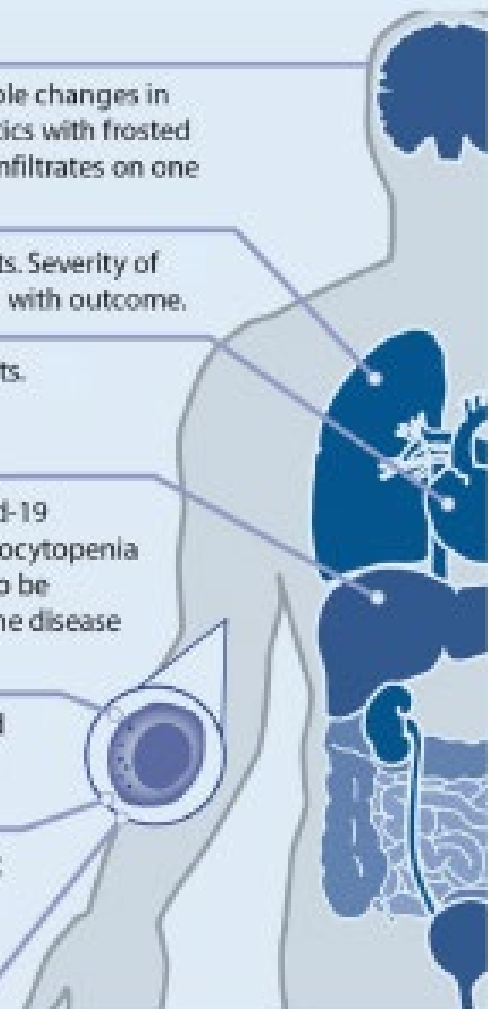


LDH



Biological findings

Findings	Frequency	Comment
Imaging – lungs		In thoracic X-ray no detectable changes in 40% of patients. CT-diagnostics with frosted glass-like changes, but also infiltrates on one or both sides.
Hypersensitive troponin	Increase in up to 12% of cases	More frequent in ICU patients. Severity of myocardial injury associated with outcome.
ASAT/ALAT (aspartate or alanine amino-transferase)	Increase in 22–38% of cases	More frequent in ICU patients. Significance unclear.
Lymphocytopenia	In 32–83% of cases	Occurs frequently with Covid-19 infections. Severity of lymphocytopenia and lacking recovery seem to be associated with severity of the disease and outcome.
Lactate dehydrogenase (LDH)	Increase in 21–76% of cases	Level seems to be associated with severity of disease and outcome.
Procalcitonin (PCT)	Relevant increase in less than 10% of cases	PCT-increase apparently not obligatory in COVID. Might hint at co-infection.

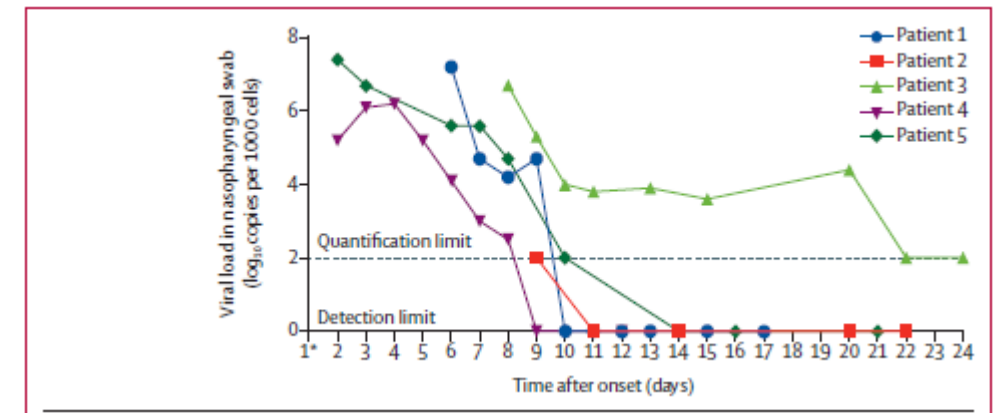
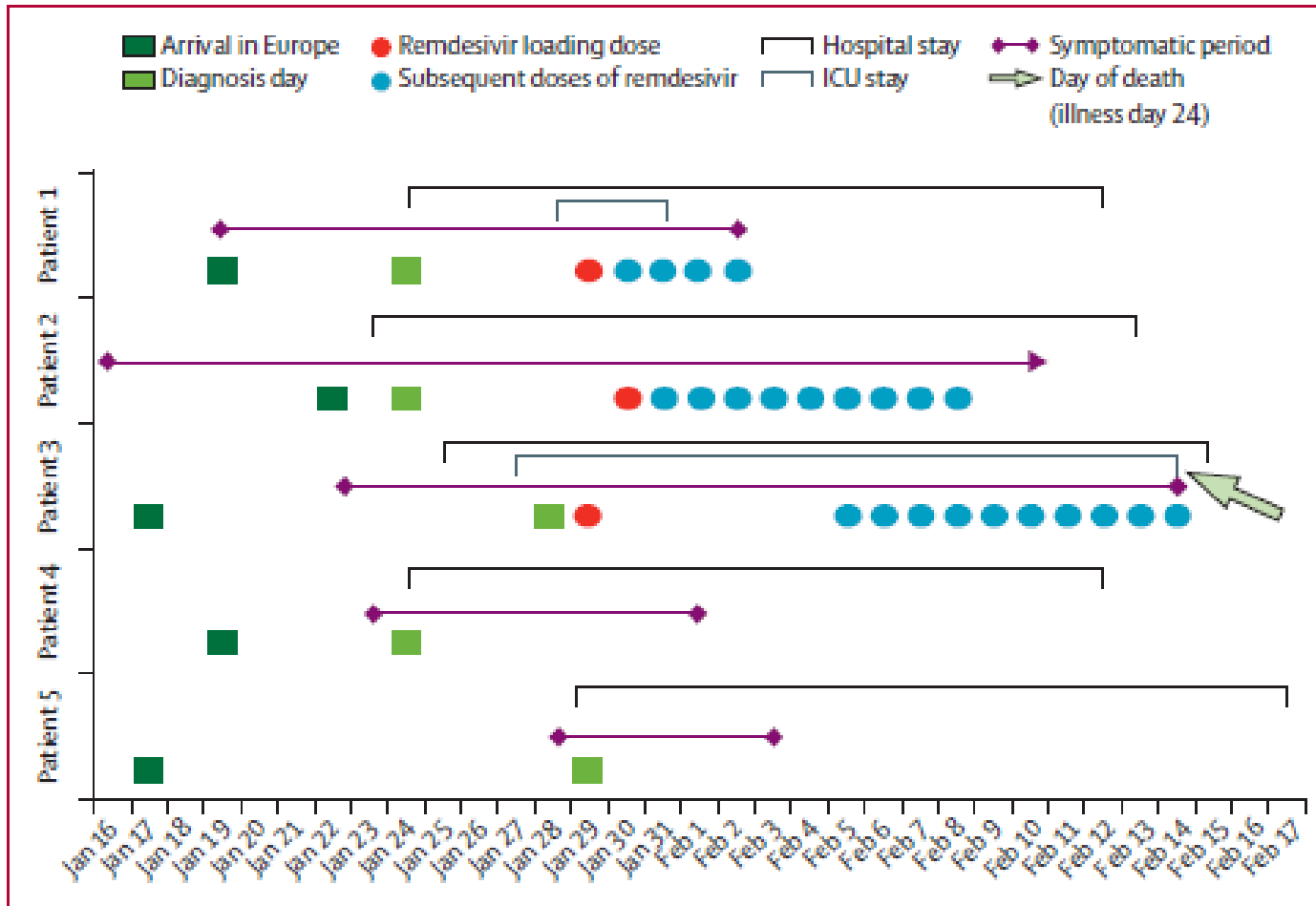


Major risk factor for unfavorable outcome: BMI

Cohort study on 3615 patients (USA)

Age \geq 60 years	N (%)	Admission to acute (vs discharge from ED)	P-value	N (%)	ICU Admission (vs discharge from ED)	P-value
BMI 30-34	141 (19%)	0.9 (95% CI 0.6-1.2)	0.39	57 (22%)	1.1 (95% CI 0.8-1.7)	0.57
BMI \geq 35	99 (14%)	0.9 (95% CI 0.6-1.3)	0.59	50 (19%)	1.5 (95% CI 0.9-2.3)	0.10
Age < 60 years						
BMI 30-34	173 (29%)	2.0 (95% 1.6-2.6)	<.0001	39 (23%)	1.8 (95% CI 1.2-2.7)	0.006
BMI \geq 35	134 (22%)	2.2 (95% CI 1.7-2.9)	<.0001	56 (33%)	3.6 (95% CI 2.5-5.3)	<.0001

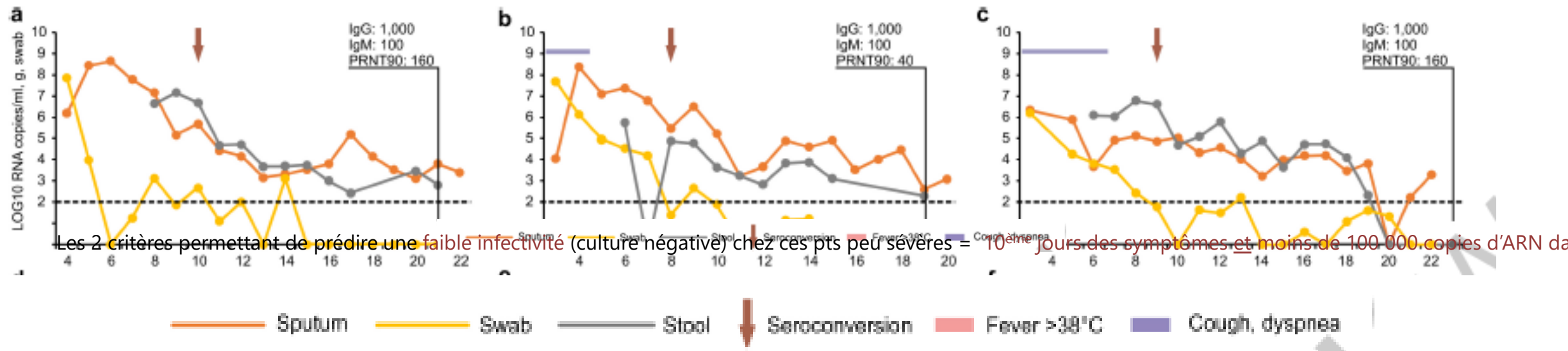
Natural history



- 1) High viral shedding in pharynx for 7 days, mild symptoms, young age
- 2) High viral shedding, persistence after 7 days, ICU
- 3) High viral shedding, clearance, then aggravation at day 7 with pneumonia

➔ **80-85% asymptomatic/mild, 15% moderate expression, 5% severe with IC need, fatality rate differing between countries**

Viral shedding and persistence



- High level of RNA between D1 and D5 in pharynx, then negative at D14
- In sputum and stools, persistence until D21 in some patients, no RNA in urine and serum
- No living virus after D8
- Viral replication in upper respiratory tractus (unlike SARS-CoV) and lung (like SARS-CoV)
- IF IgM and IgG anti Spike protein and neutralising Ab = seroconversion = 50% at D7 and 100% at D14



Take home messages

- New betacoronavirus baptised SARS-CoV2, zoonosis of bat/pangolin? Origin, that has emerged in China at the end of 2019
- Europe and the USA = epicenter of the global epidemic as of Mid April 2020
- High rate of transmission ($R_0 \approx 3$)
- Pleiotropic clinical manifestations
- Viral and immunological disease not completely deciphered yet



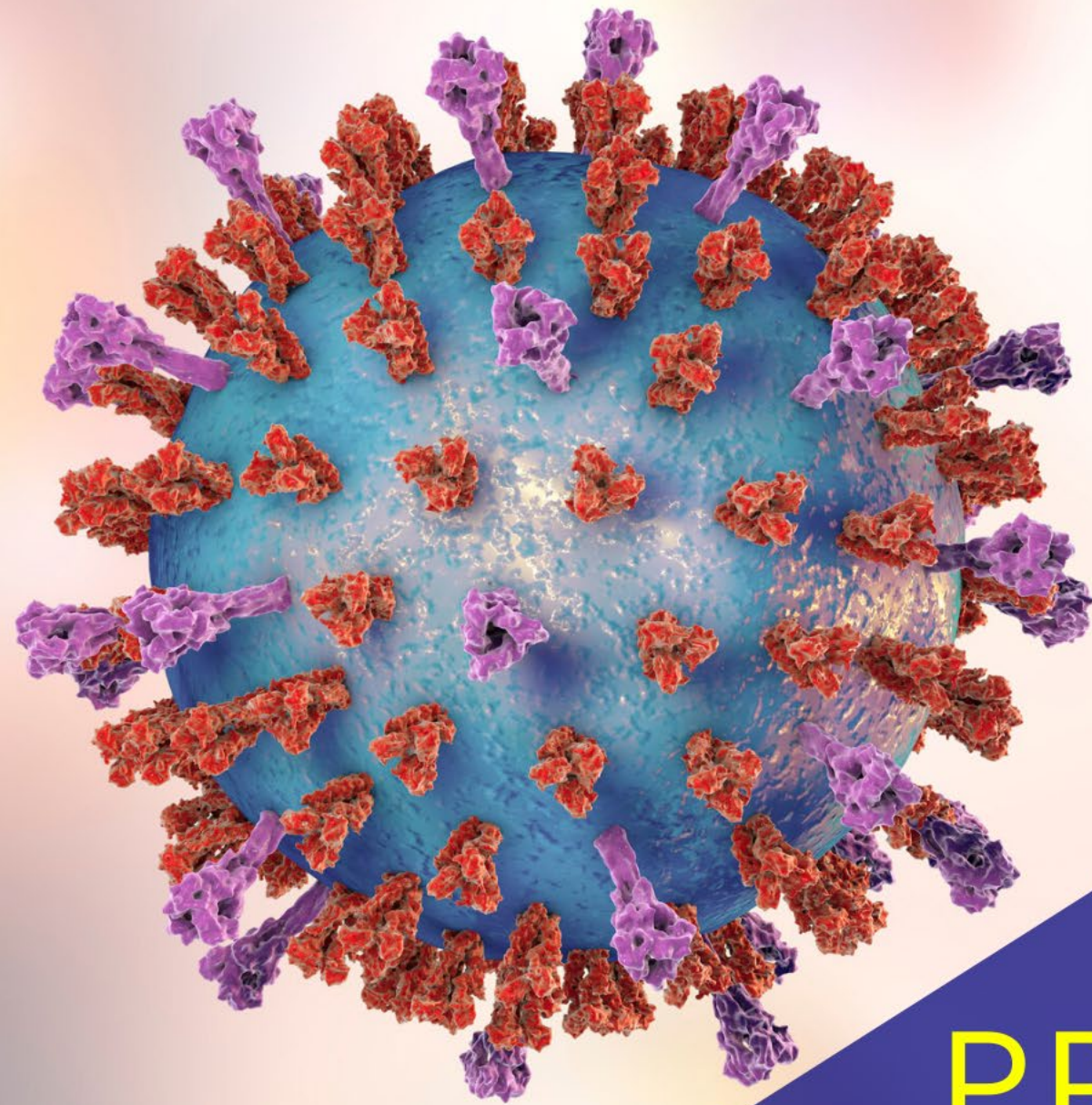
WEBINAR COVID-19 in the series: How to treat the disease CLINICAL MANAGEMENT

Name: Rick Body
Position: Professor of Emergency Medicine
Country: UK

DISCLOSURES

Over the past 24 months:

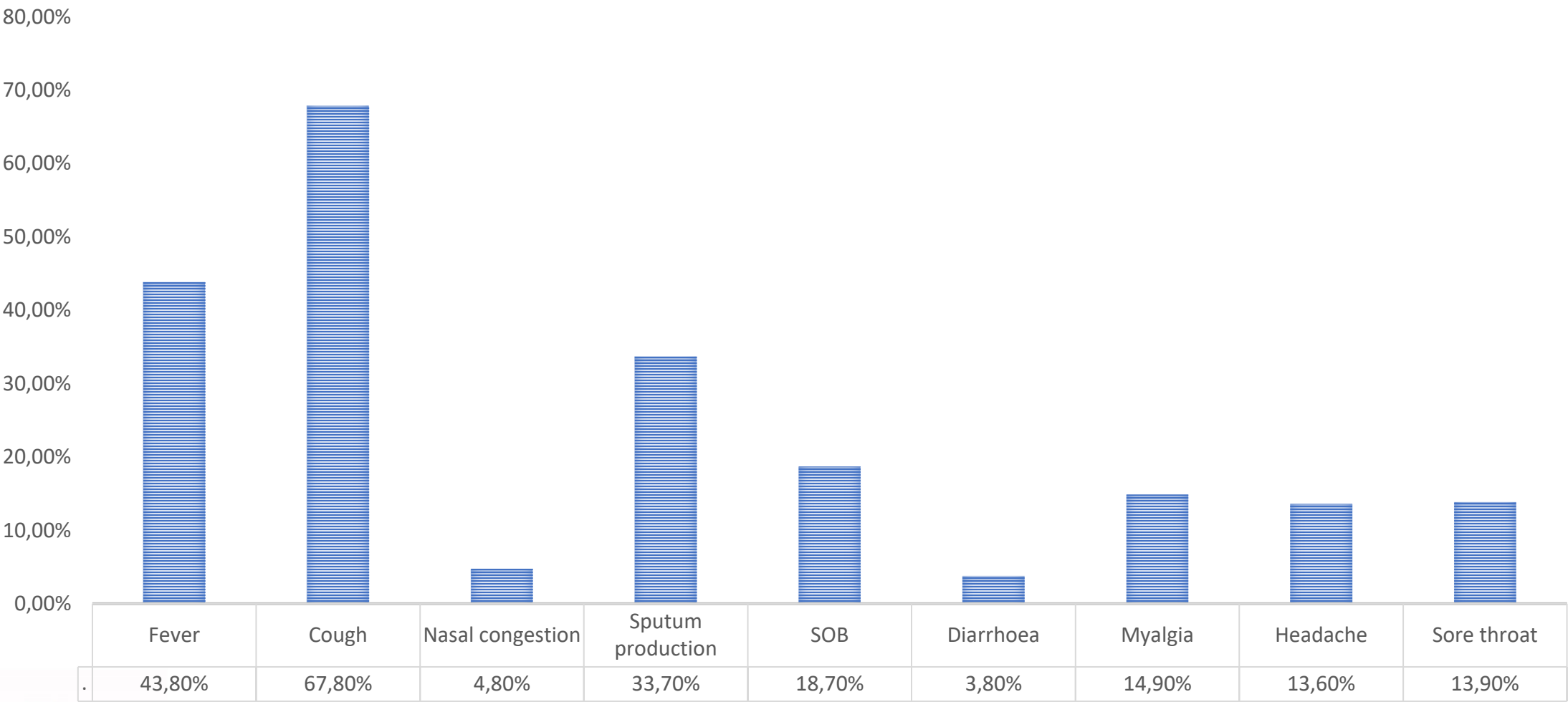
- Rick Body has advised
 - Siemens, Abbott Point of Care, LumiraDx
- Rick Body has chaired the Trial Steering Committee for a clinical study sponsored by Creavo
- Rick Body's institution has accepted research grants or donation of reagents for research from
 - Roche, Alere, Abbott Point of Care



CLINICAL PRESENTATION

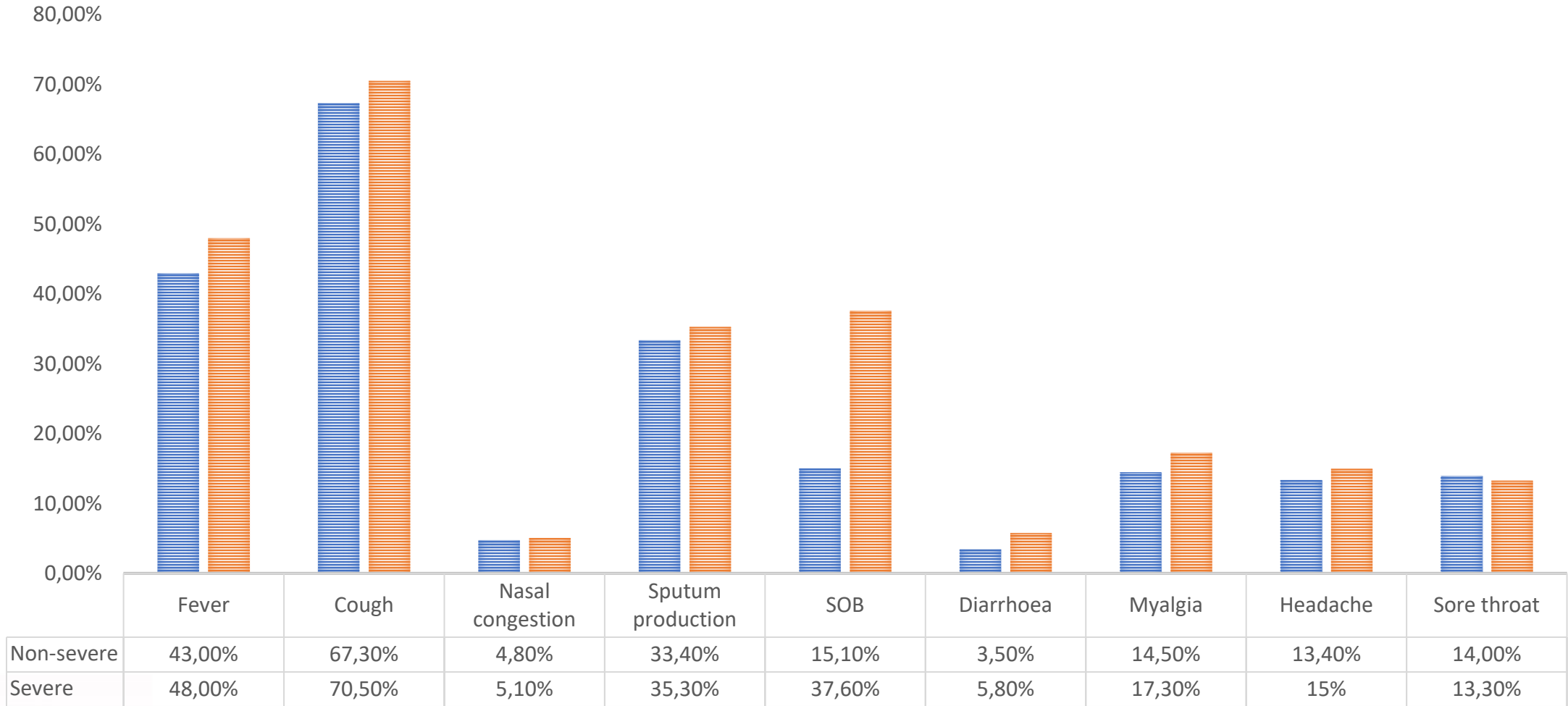
CLINICAL FEATURES OF COVID-19

Guan et al, NEJM 2020



CLINICAL FEATURES OF COVID-19

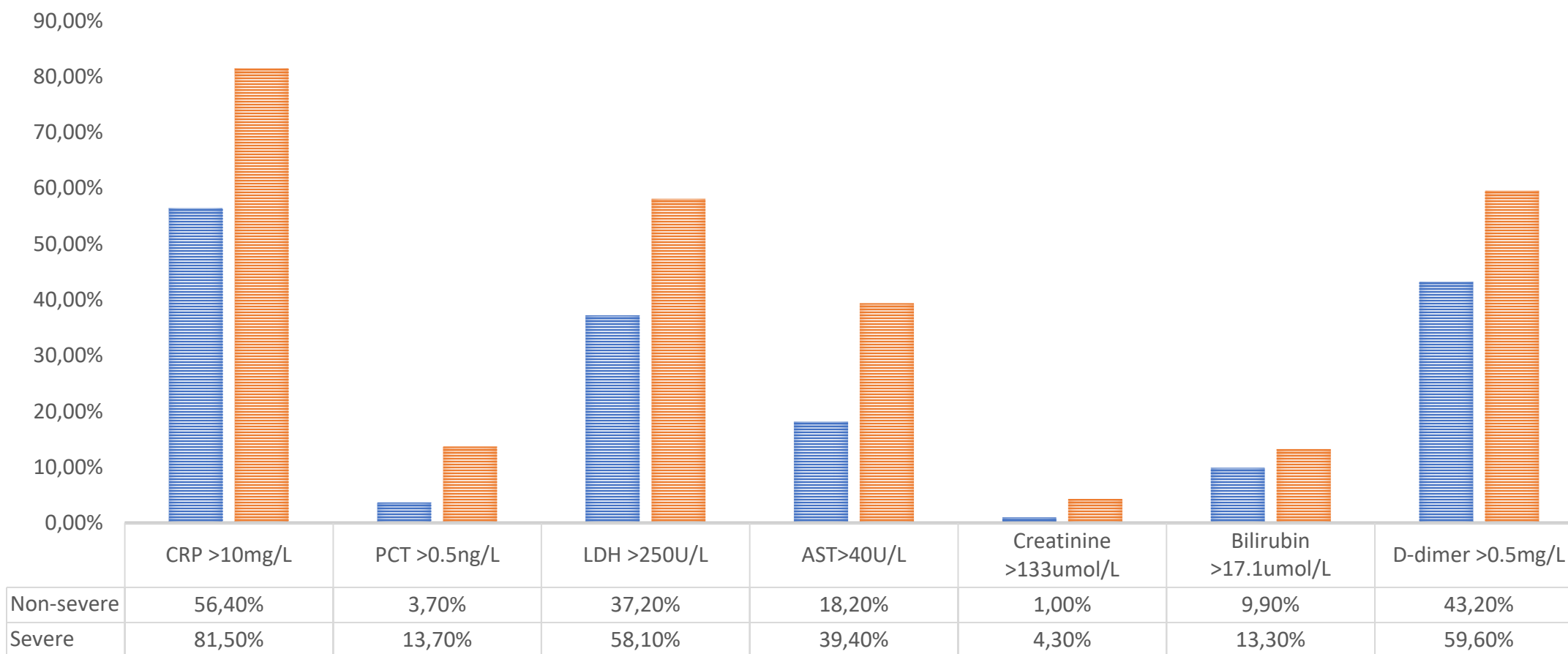
Guan et al, NEJM 2020

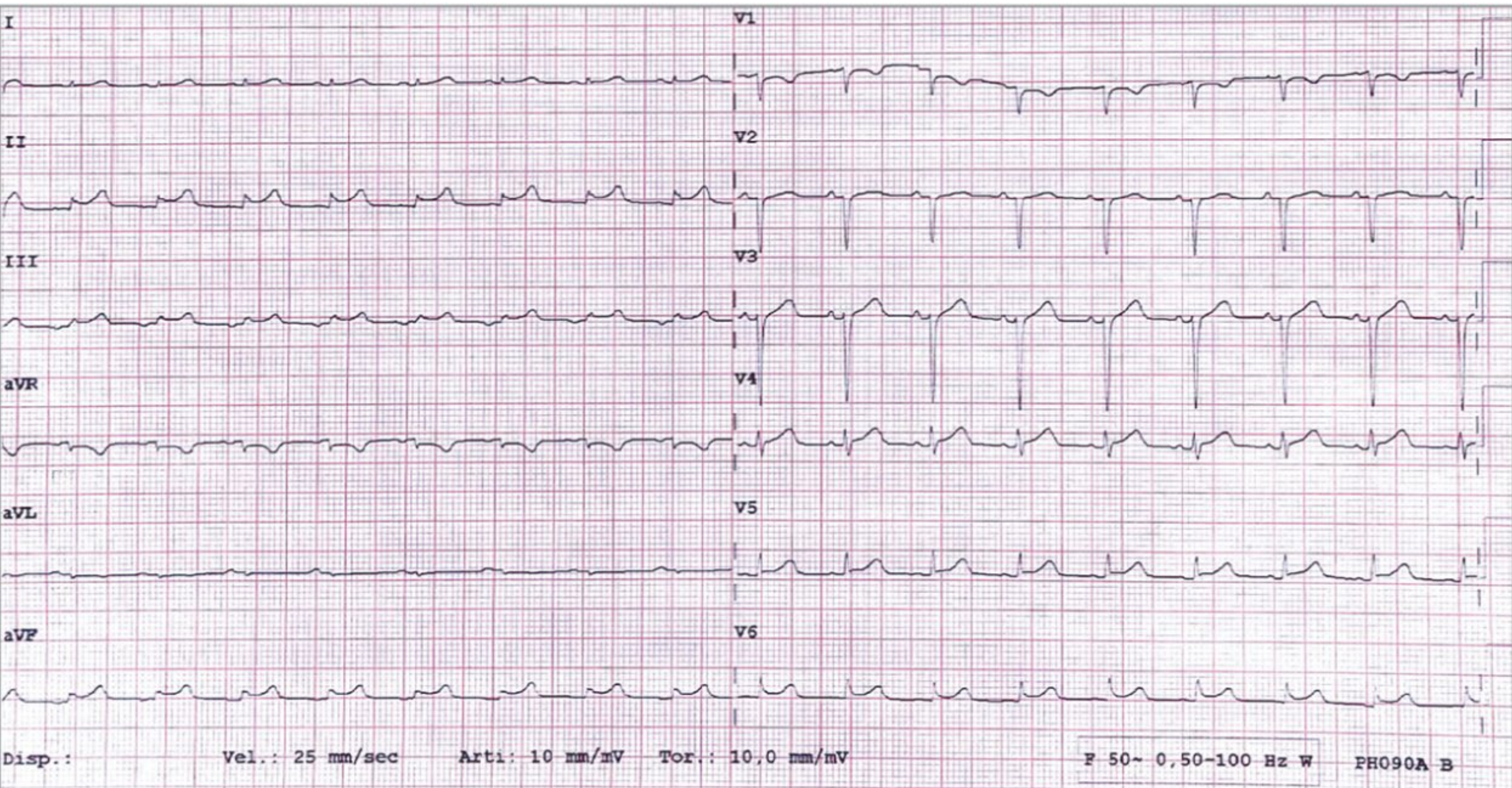


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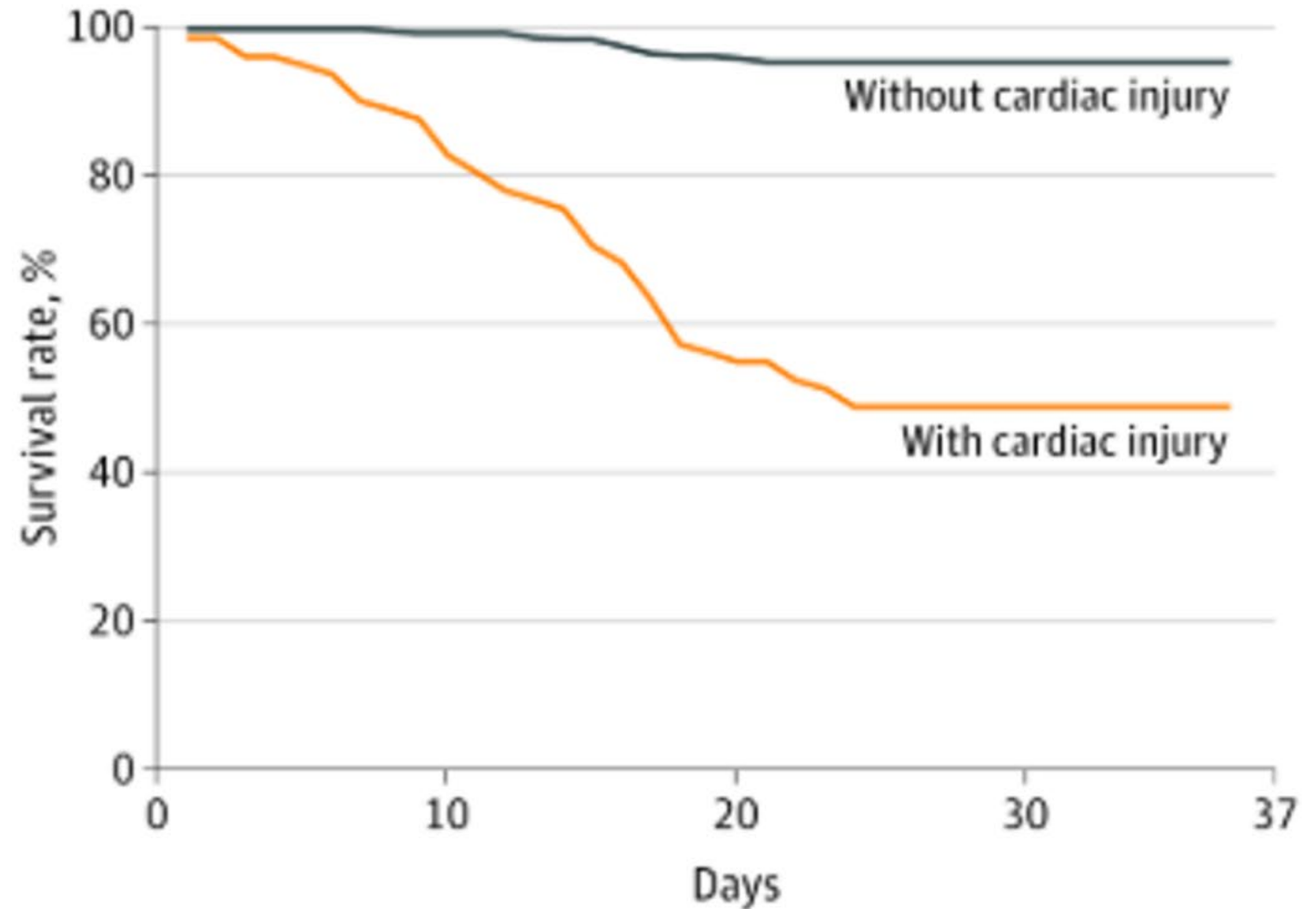
BIOMARKERS AND PROGNOSIS IN COVID-19

Guan et al, NEJM, 2019

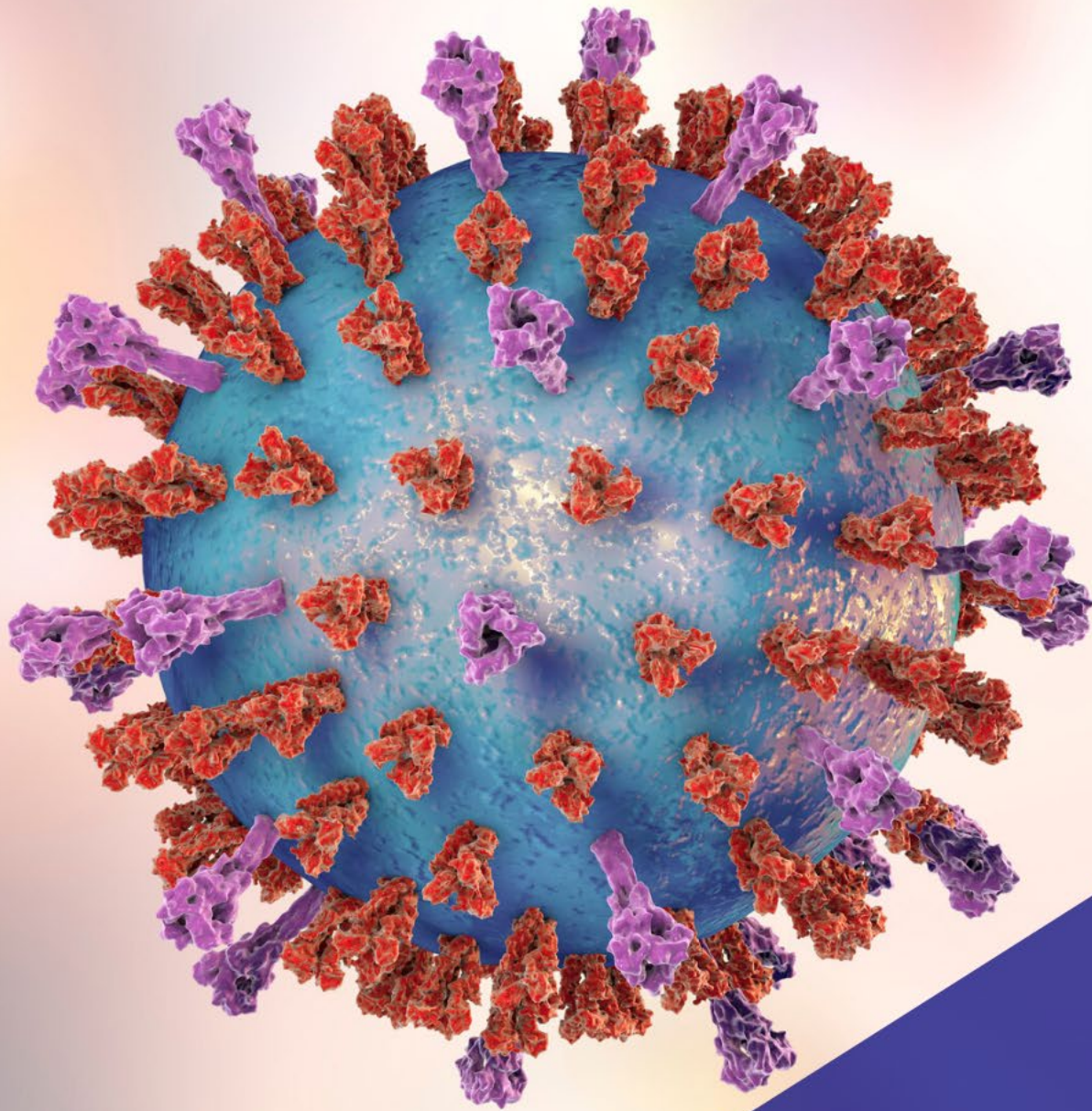




Patients with
COVID-19 and
myocardial injury
have substantially
worse prognosis



Shi et al, JAMA Cardiology 2020



DIAGNOSIS

DIAGNOSTIC PIPELINE

A timeline of the COVID-19 pandemic

JAN 10TH

SARS-CoV-2
genome
sequenced &
published



JAN 17TH

First RT-PCR
assay for
SARS-CoV-2
reported
online



FEB 4TH

1st FDA
emergency
approval for
RT-PCR assay



MAR 17TH

1st point of
care test
receives
emergency
FDA
authorization



APR 4TH

1st antibody
test receives
emergency
FDA
authorisation



PRESENT

FindDx lists
247 CE
marked assays
relating to
COVID-19



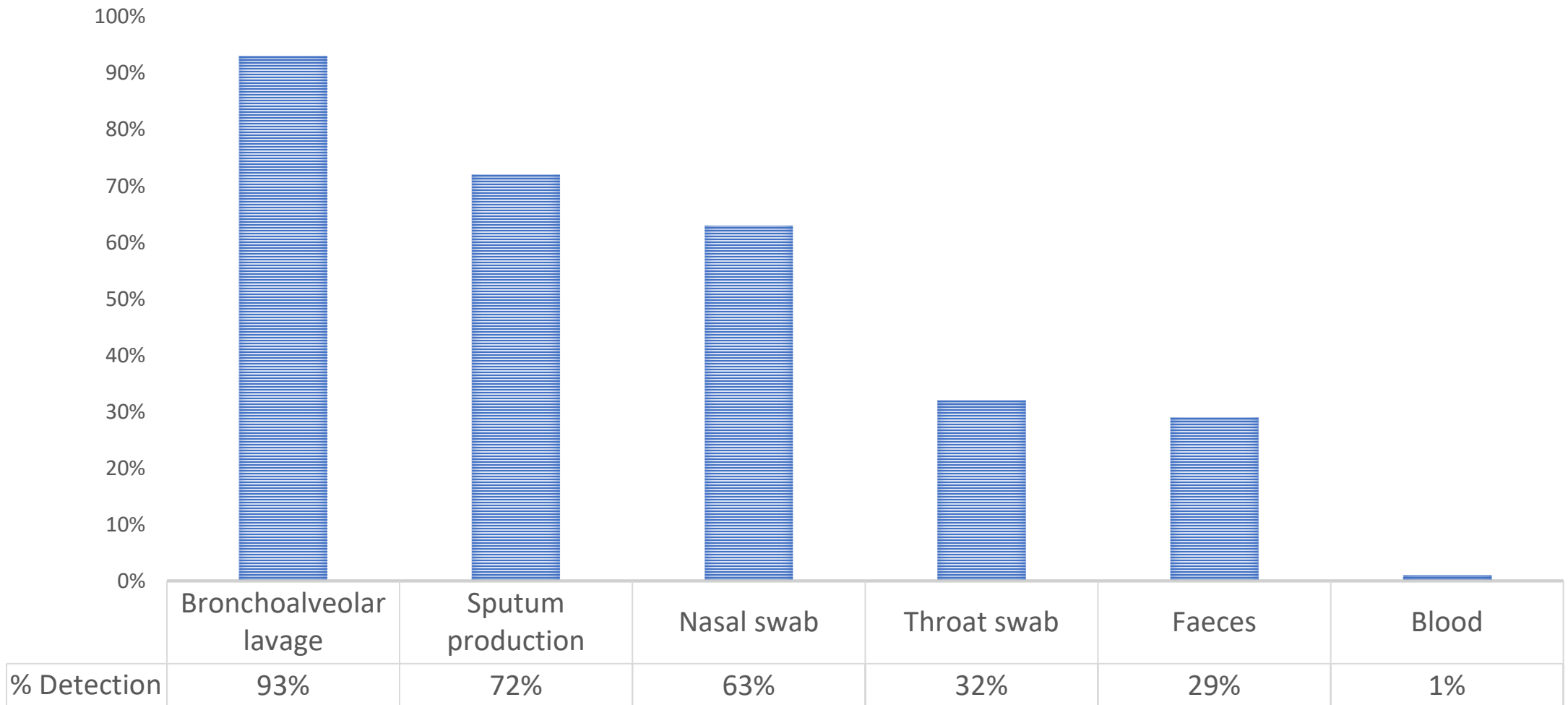




EUSEM does not advocate any particular commercially supplied products

DETECTION OF SARS-COV-2 IN DIFFERENT SAMPLE TYPES

Wang et al, JAMA 2020. n=205



CT SCAN vs RT-PCR

1,014 patients
Compared with RT-PCR, CT had:



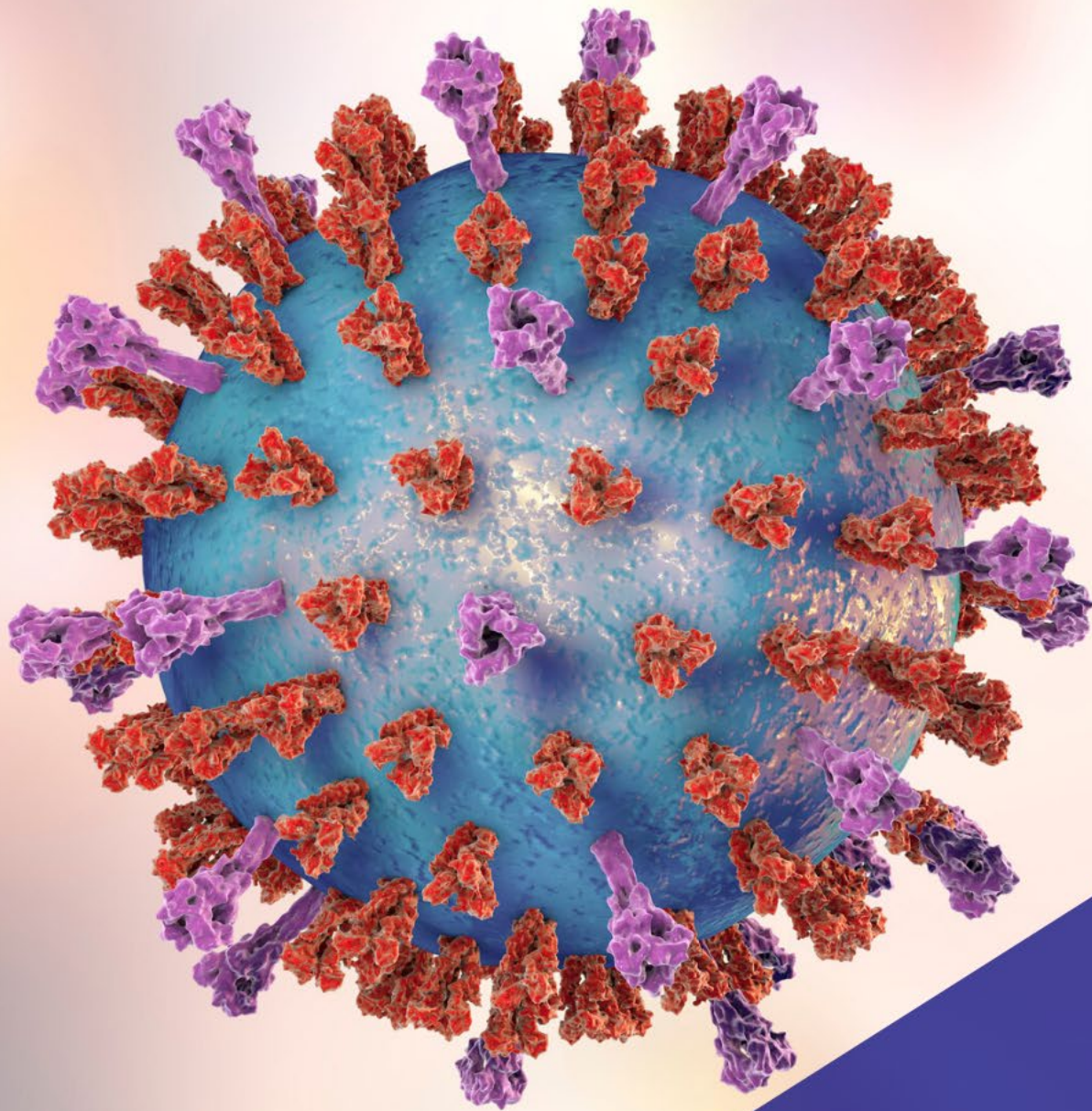
97% sensitivity

95% CI 95 - 98%

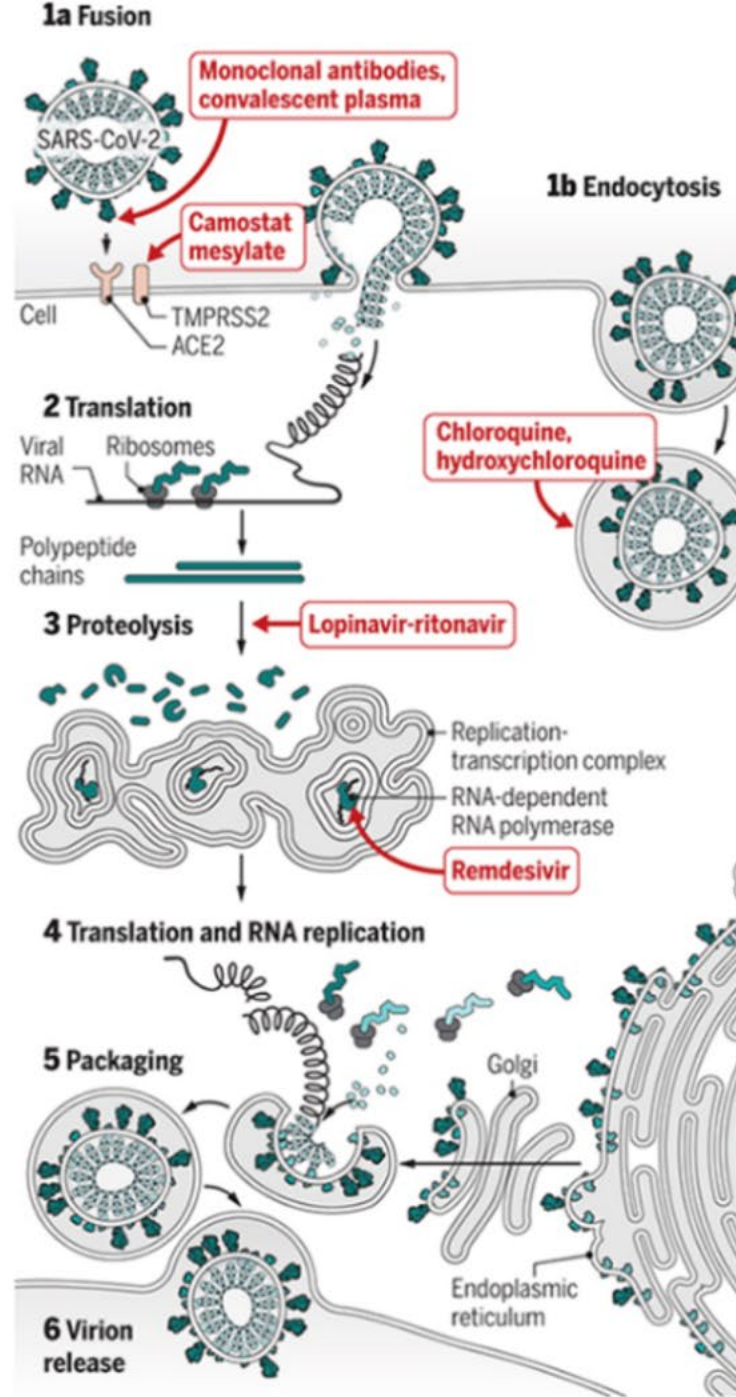
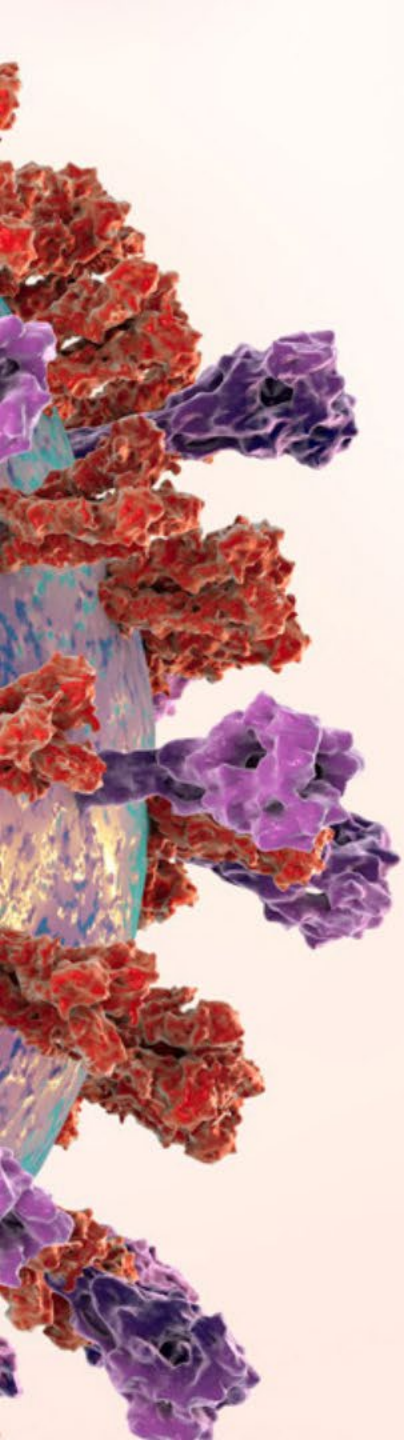


25% specificity

95% CI 22 - 30%



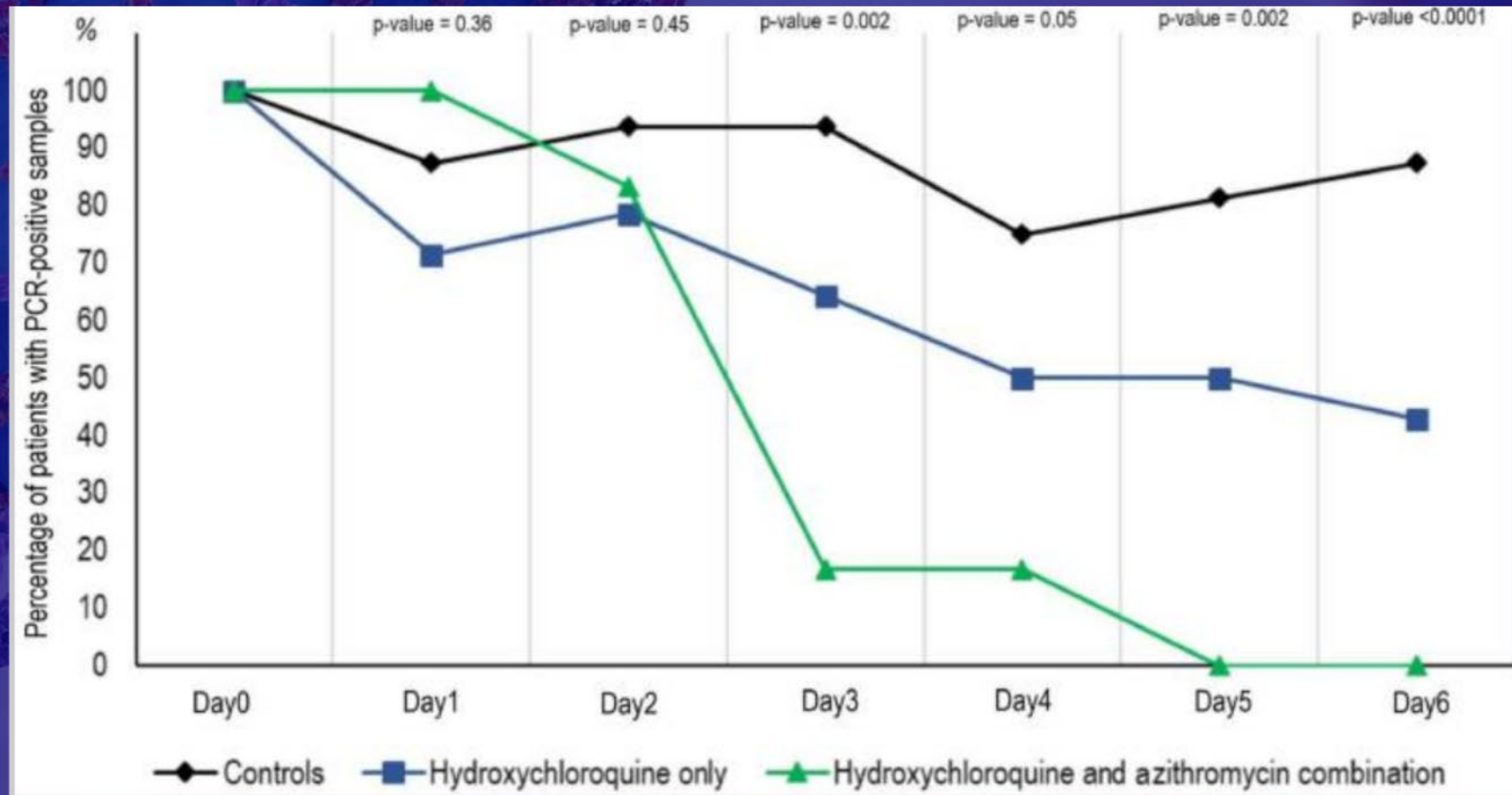
TREATMENT



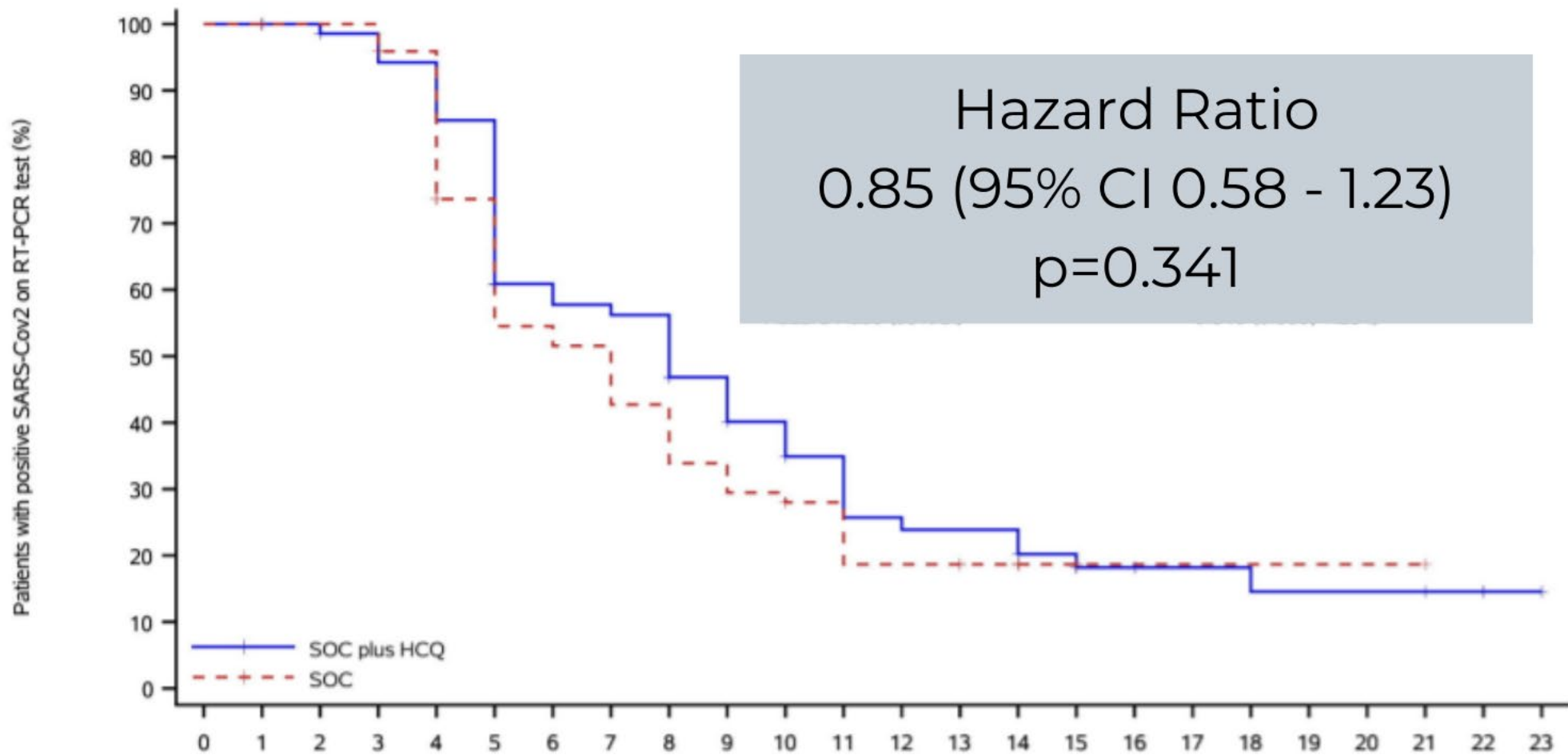
POTENTIAL NEW TREATMENTS FOR COVID-19

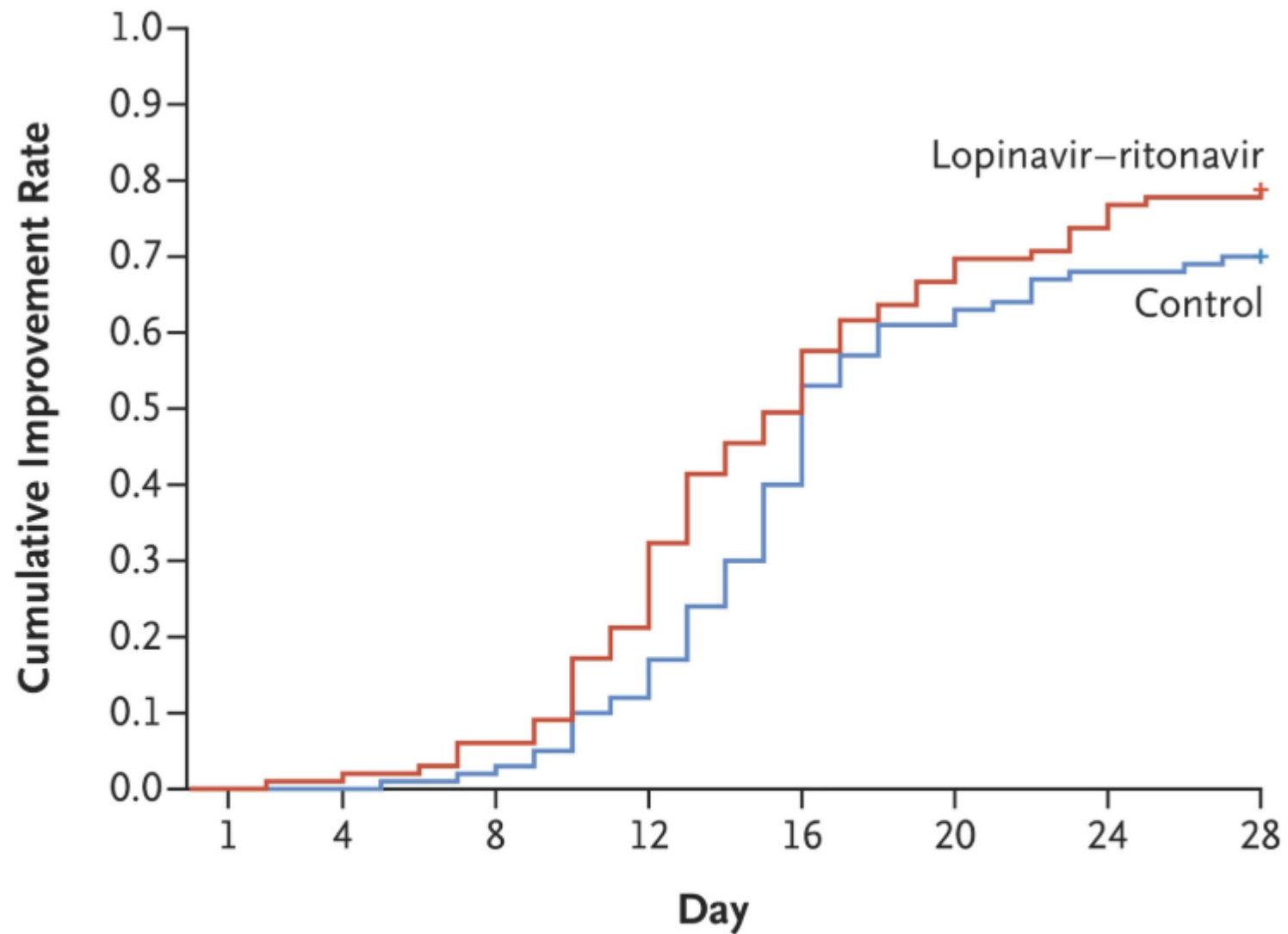
HYDROXYCHLOROQUINE

Non-randomised, open label study. N=26 (6 had azithromycin)



HYDROXYCHLOROQUINE





No. at Risk

Lopinavir-ritonavir	99	98	93	78	50	33	26	22
Control	100	100	98	88	60	39	32	30

<https://www.nejm.org/doi/full/10.1056/NEJMoa2001282>

OTHER PROMISING (BUT UNPROVEN) TREATMENTS FOR COVID-19



Convalescent plasma



Tocilizumab, sarilumab



Acetazolamide, nifedipine



Low-dose steroids



Anakinra (interleukin-1 receptor antagonist)

ONGOING TRIALS: Ventilation Strategies



Awake proning: ProCOV
Pilot Study



Early CPAP: RECOVERY-RS;
EC-COVID



COVID-19 has diverse clinical presentations

Many routinely used biomarkers have
important prognostic value

There has been rapid progress in
diagnostic technology

Many clinical trials are in progress; but to
date **no treatments** have been proven to
be effective