Specifika virových pneumonií z pohledu intenzivní péče a aktuální pandemie

Jan Máca
FNO a LF OU

akutne.cz, 2020

COVID-19

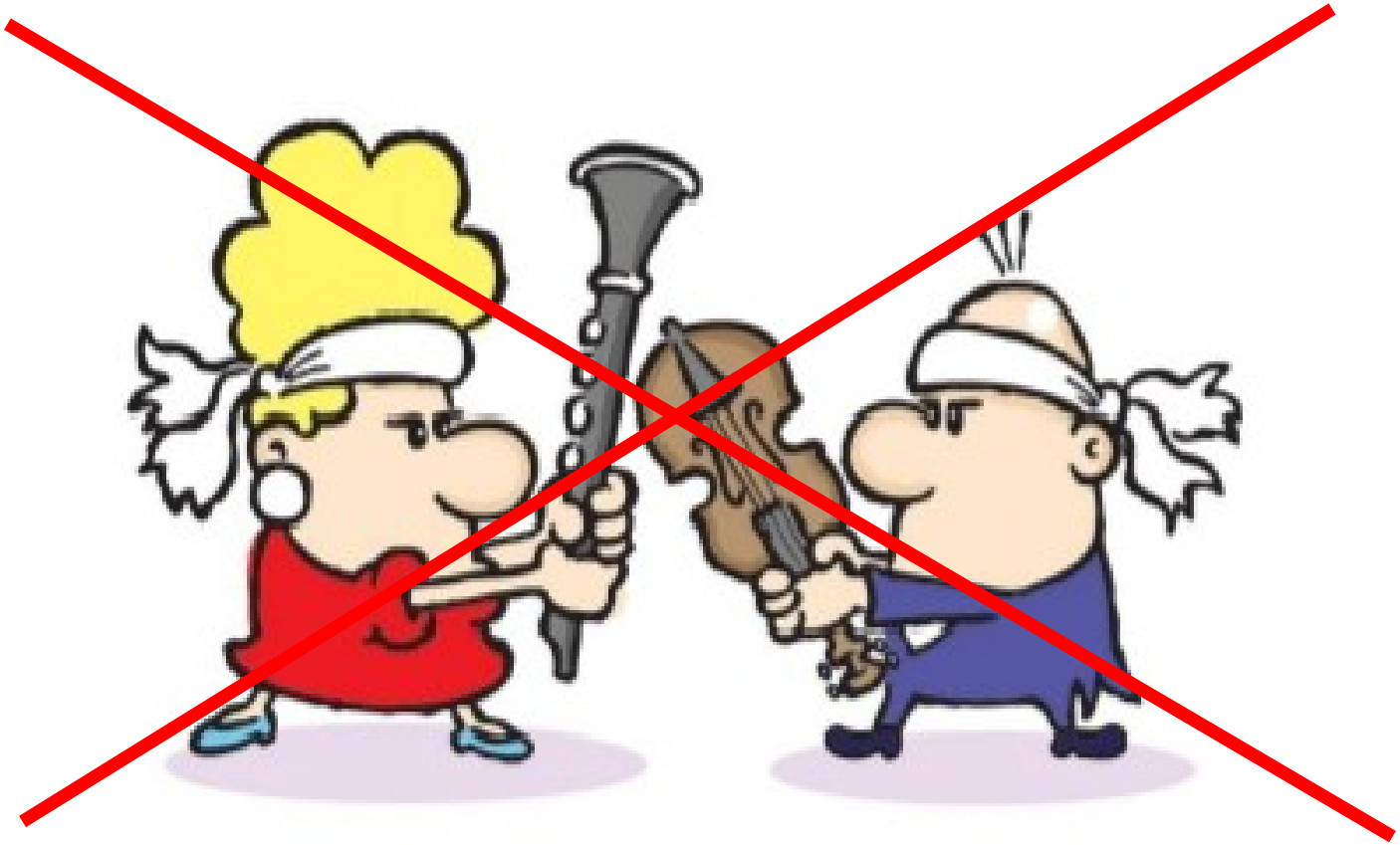
specifika virové pneumonie v intenzívní péči

Jan Máca
FNO a LF OU

akutne.cz, 2020

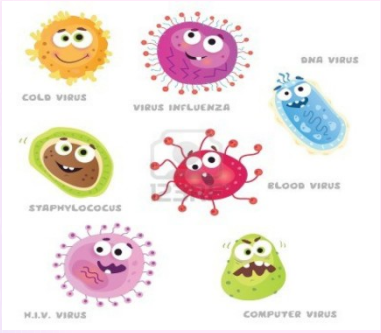
COVID-19	Pubmed	**75 002**
	Google	**5 050 000 000**/0.71s
SARS-CoV-2	Pubmed	**44 600**
	Google	**140 000 000**/0.65s

NO Conflict of Interest



virové pneumonie

- Virus chřipky typu A
- Virus chřipky typu B
- Koronaviry (SARS, MERS, SARS-CoV-2, sezónní koronaviry)
- Respiračně syncytiální virus
- Lidský metapneumovirus
- Adenoviry
- Rhinovirus
- Coxsackieviry
- Echoviry
- Hantaviry
- Epstein-Barr virus
- Cytomegalovirus
- Parainfluenza virus
- Herpes simplex virus
- Lidský herpes virus 6
- Varicella-zoster virus



SARS-CoV-2

Influenza A

H3N2, H1N1

Influenza B

COVID-19

Influenza A

H3N2, H1N1

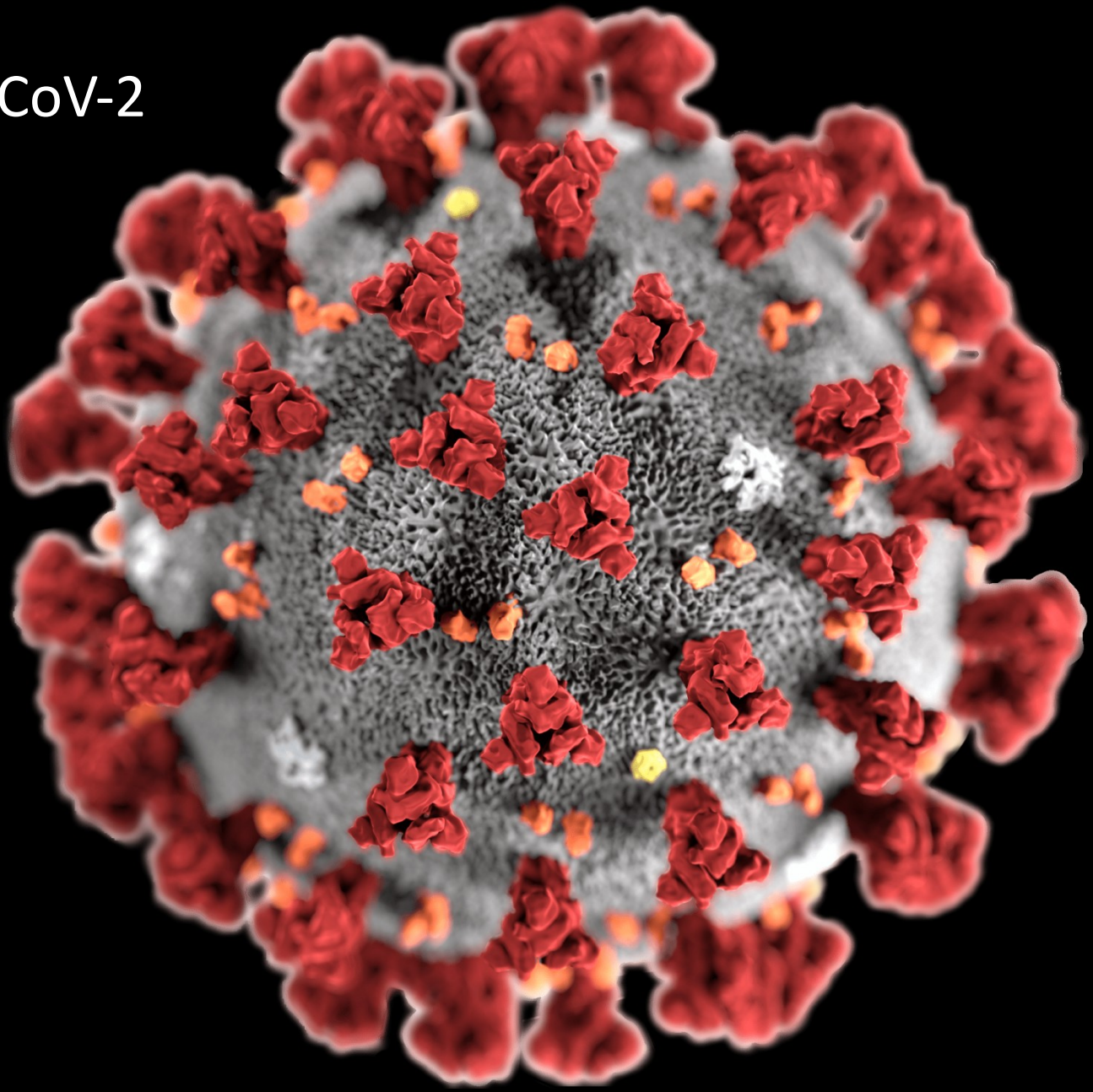
Influenza B

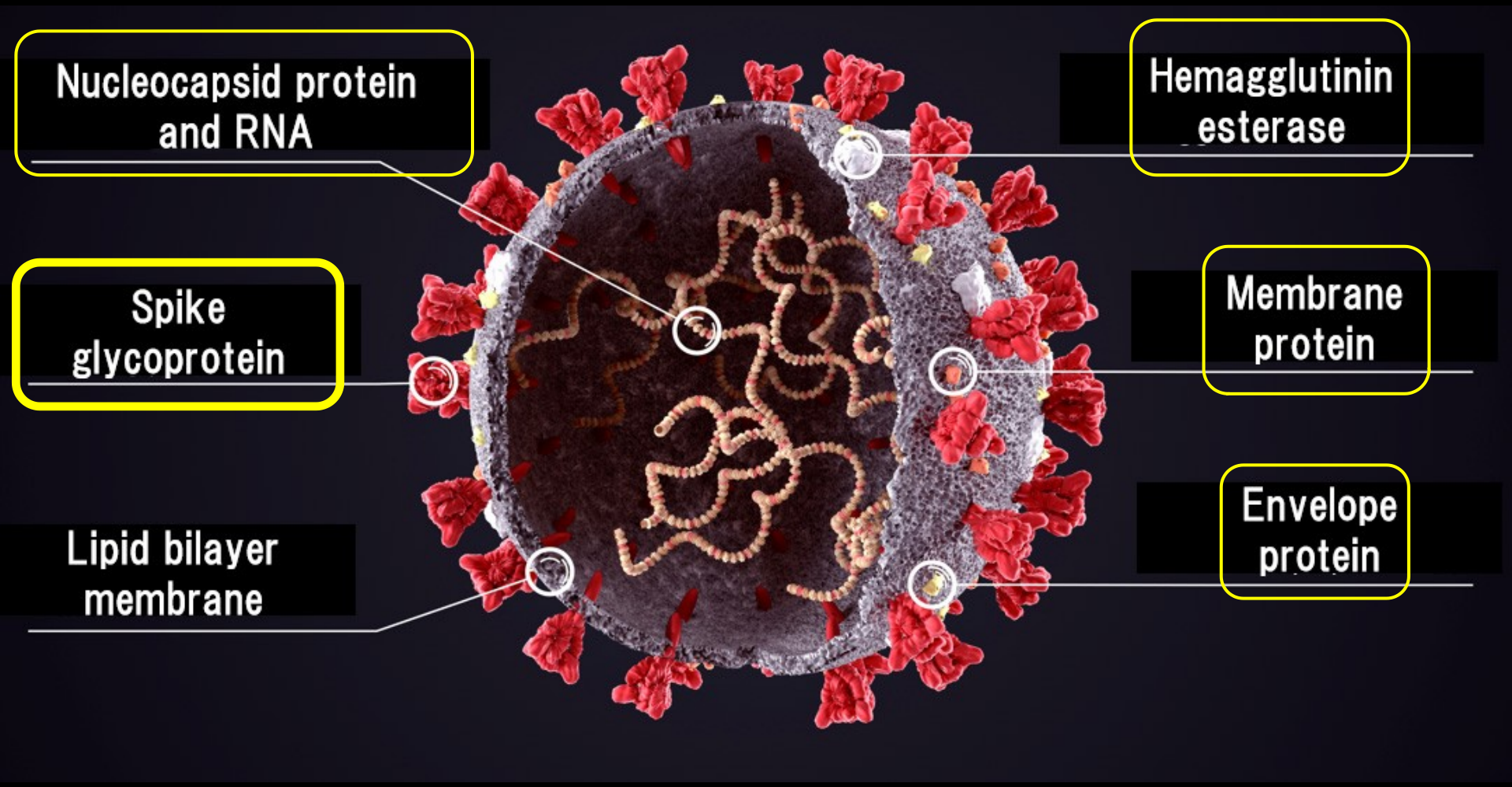
COVID-19

COrona**VI**rus **D**isease - 20**19**

SARS-CoV-2

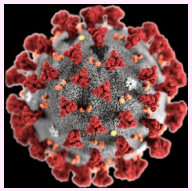
SARS-CoV-2



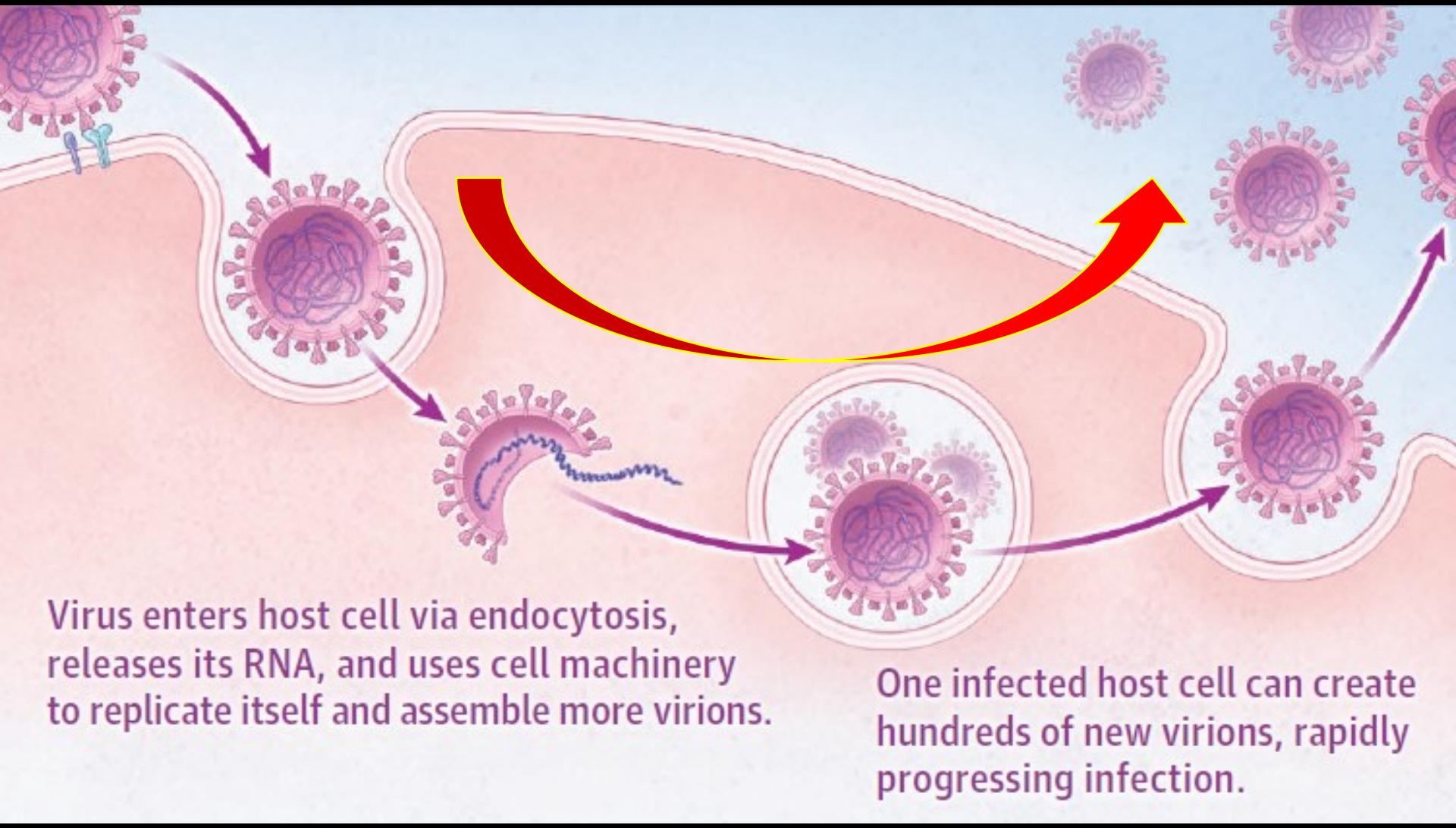


virion 60-140 nm

spike protein 9-12 nm



patogeneze

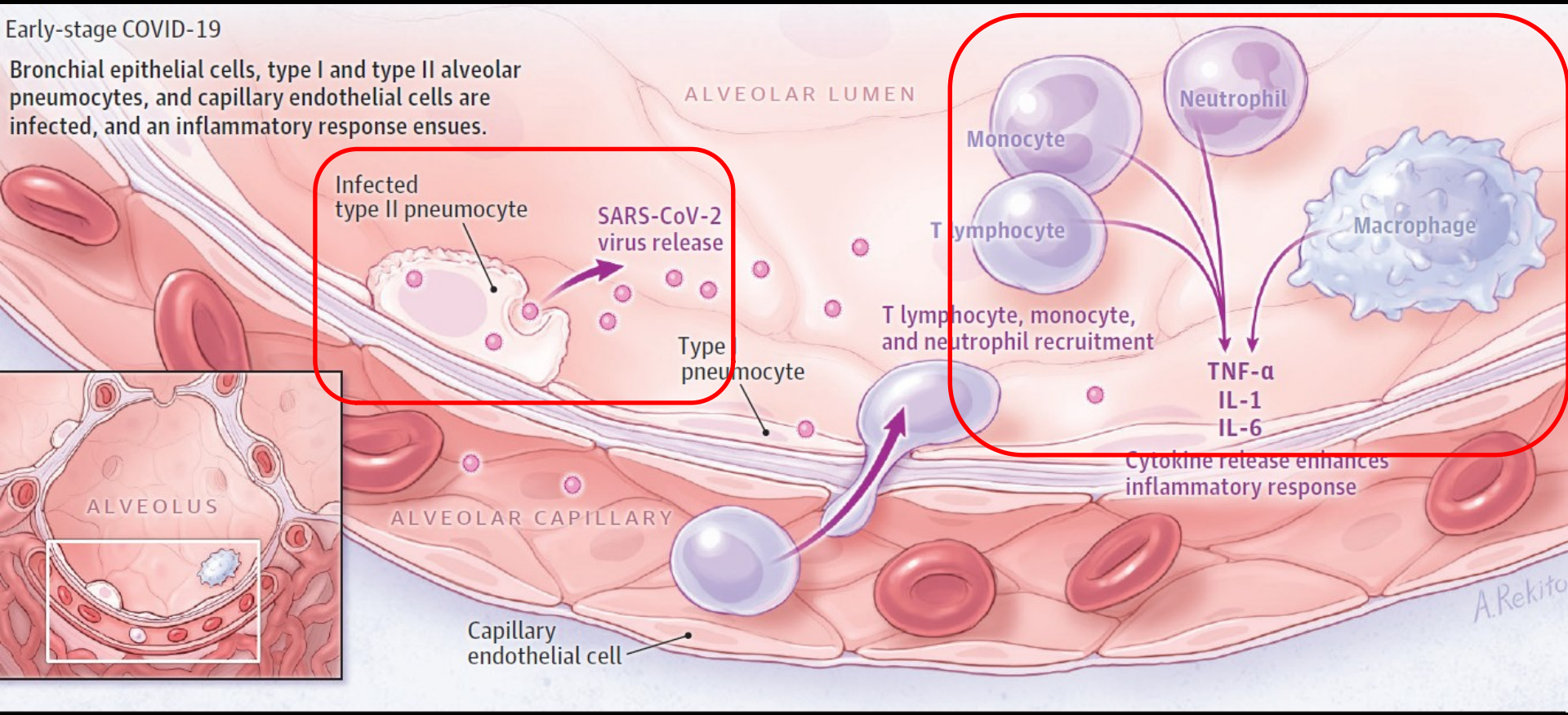


Trans**M**embrane **PR**otea**S**e, **S**erine 2, TMPRSS2 a ACE2

downregulace ACE2

časná fáze

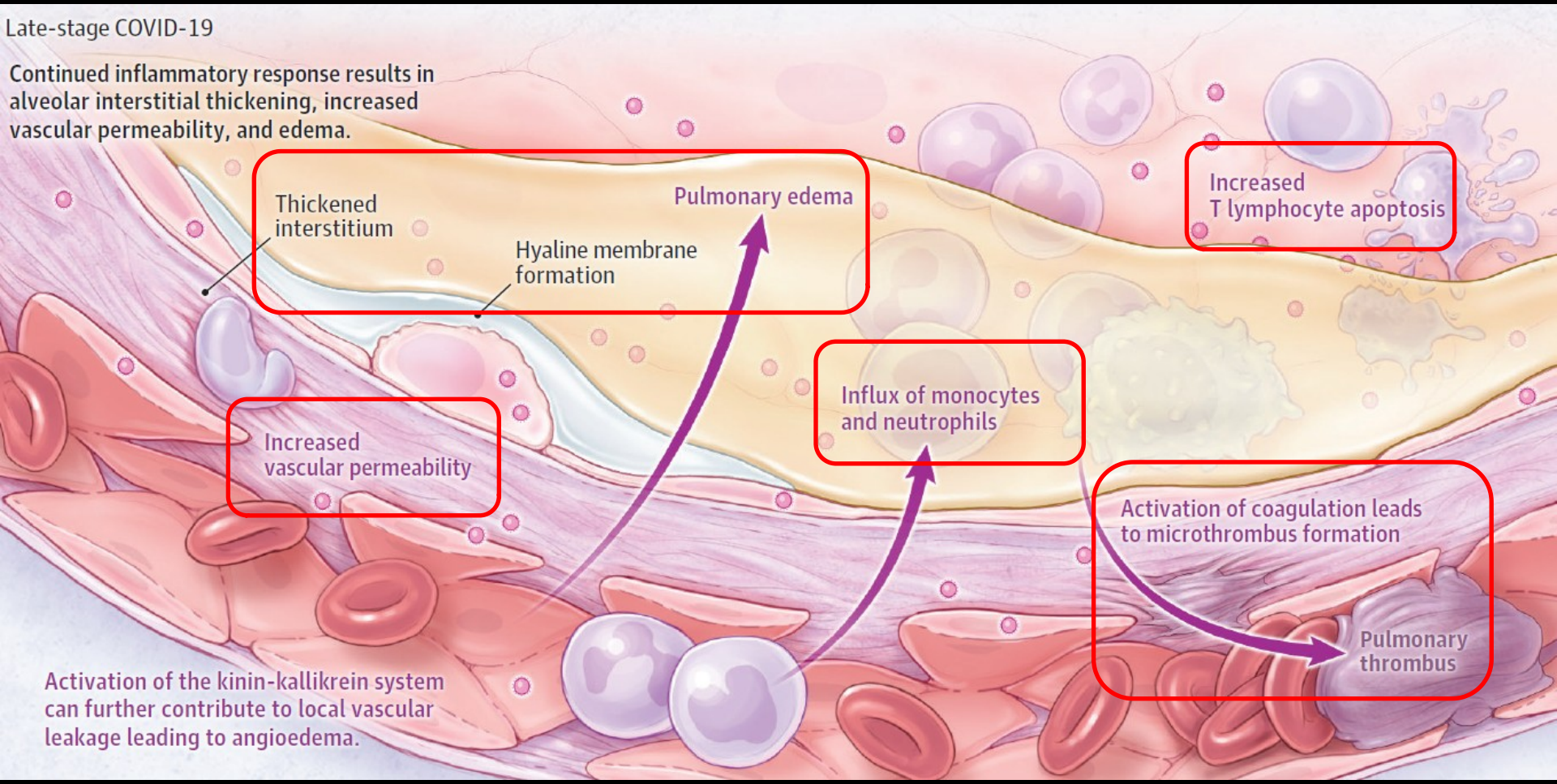
alveolitis
ground glass (mléčné sklo) opacity



PnII, PnI, endotel, bronchiální epitel, lymfocyty

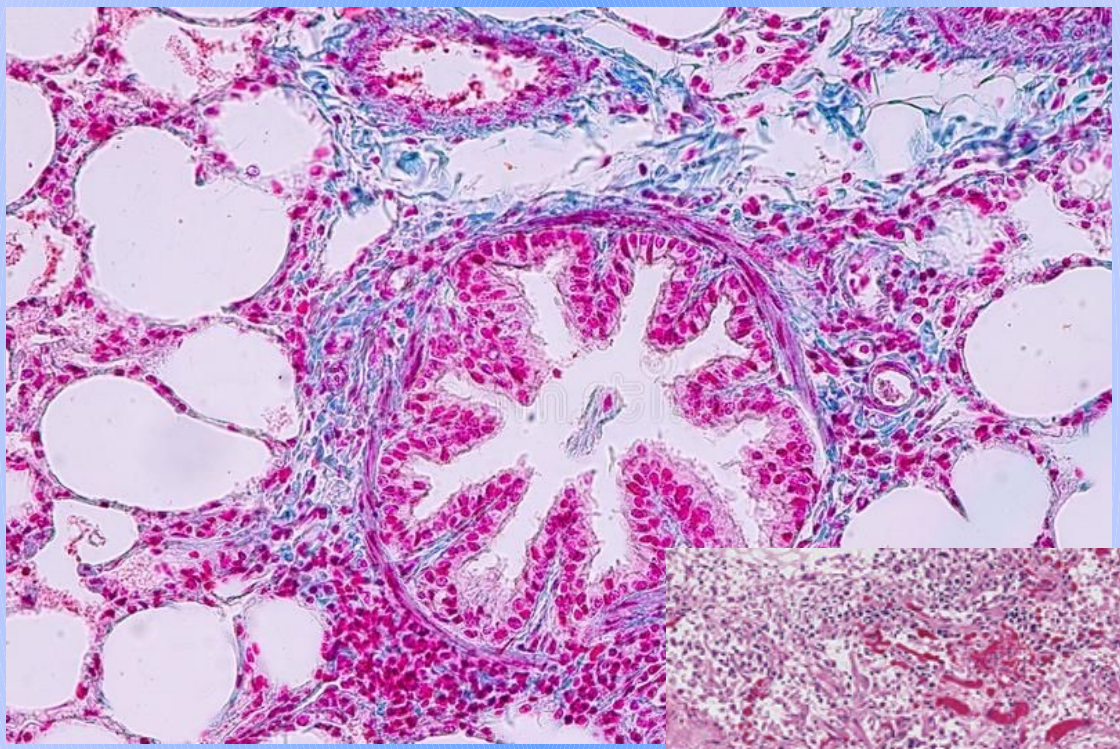
pozdní fáze

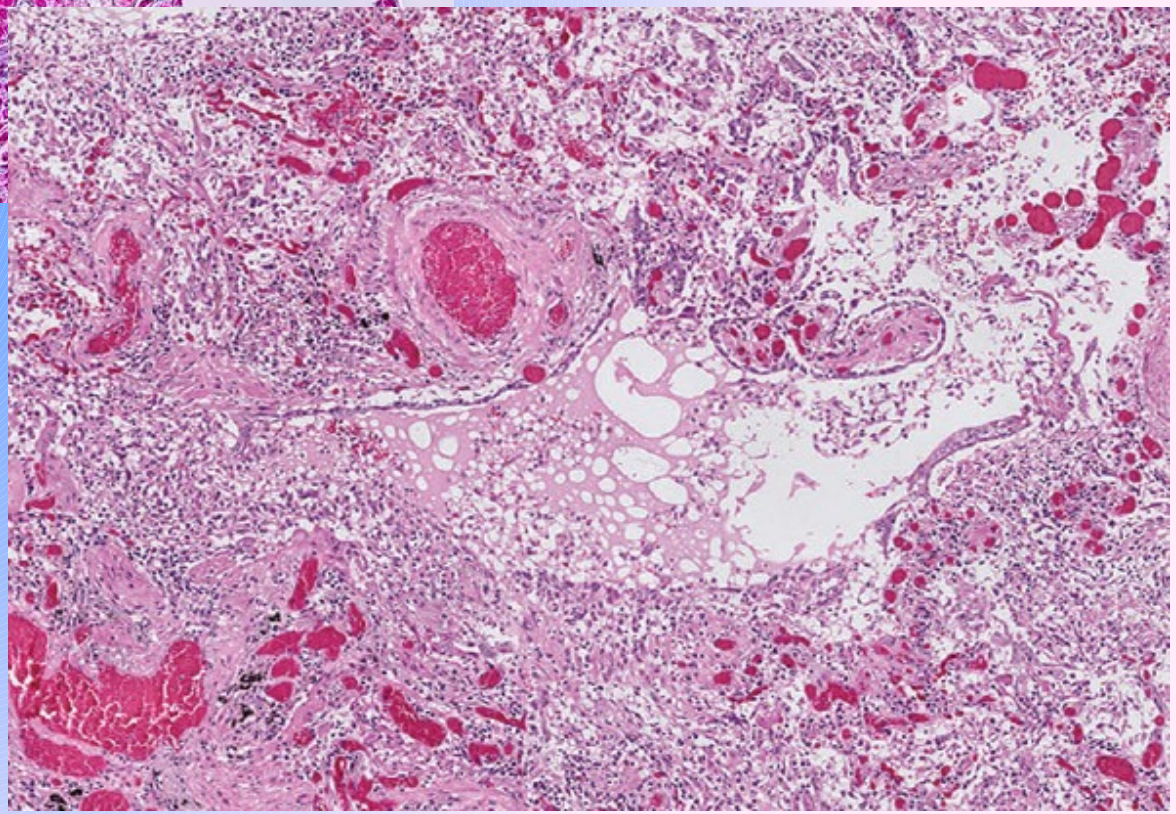
endotelialitis, angioedém, hyperkoagulace, fibroproliferace



KKS, komplement

ARDS ↔ sepse/MODS

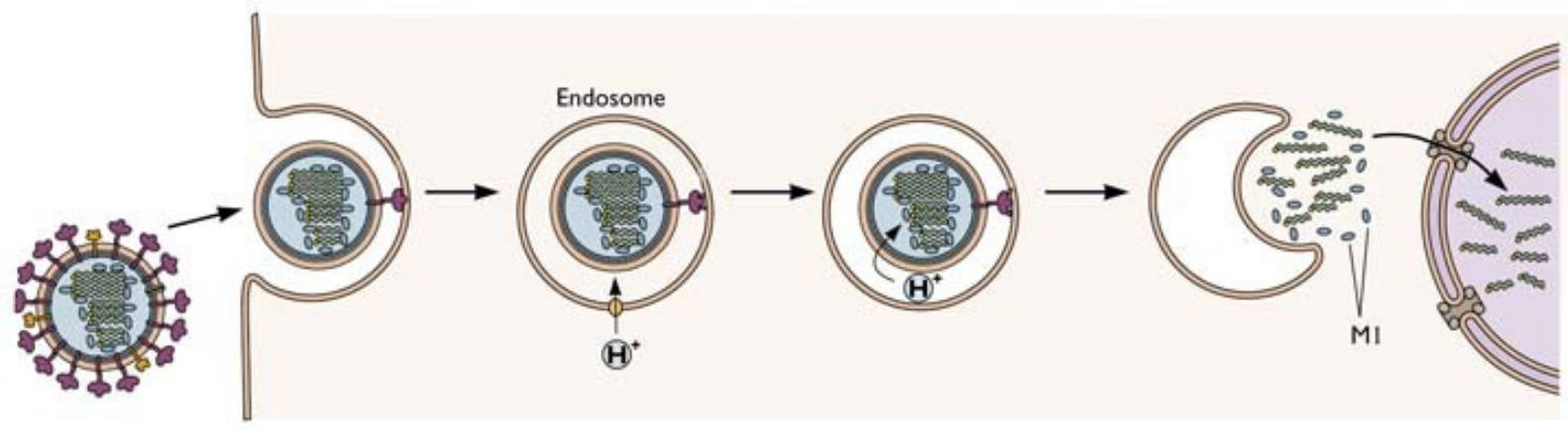


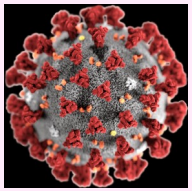


Influenza A

cílové buňky: respirační epitel, Pn II. typu, alveolární makrofágy

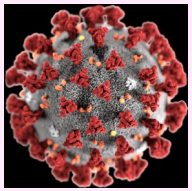
průnik do bb., množení





COVID-19
specifika ve vztahu k IM

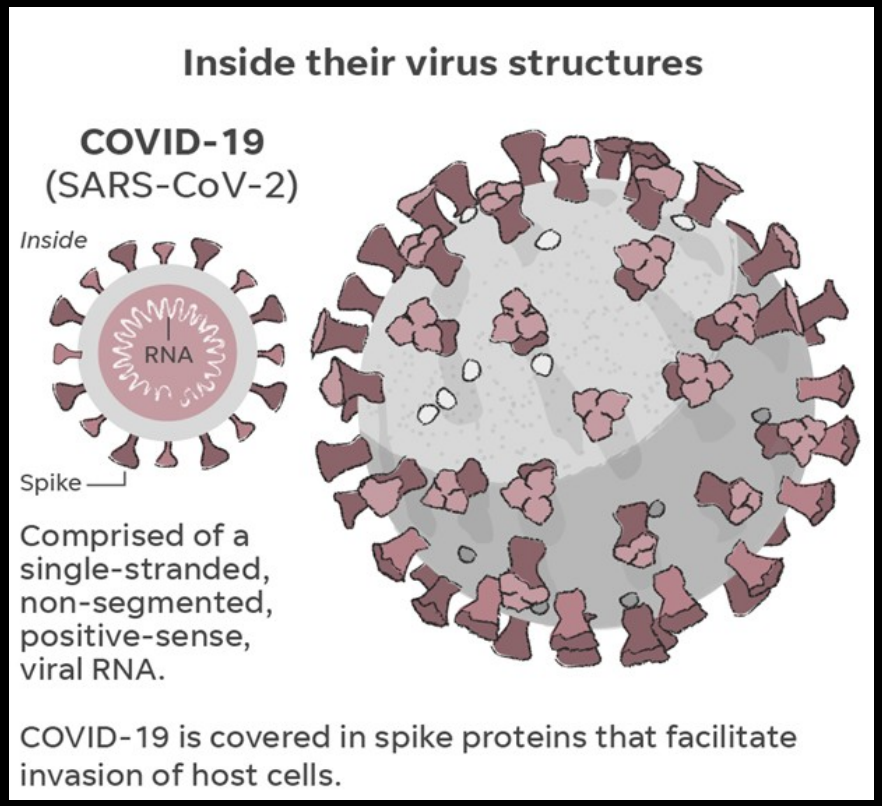
COVID-19 specifika



1. epidemiologie
2. symptomatologie
3. terapie (UPV)

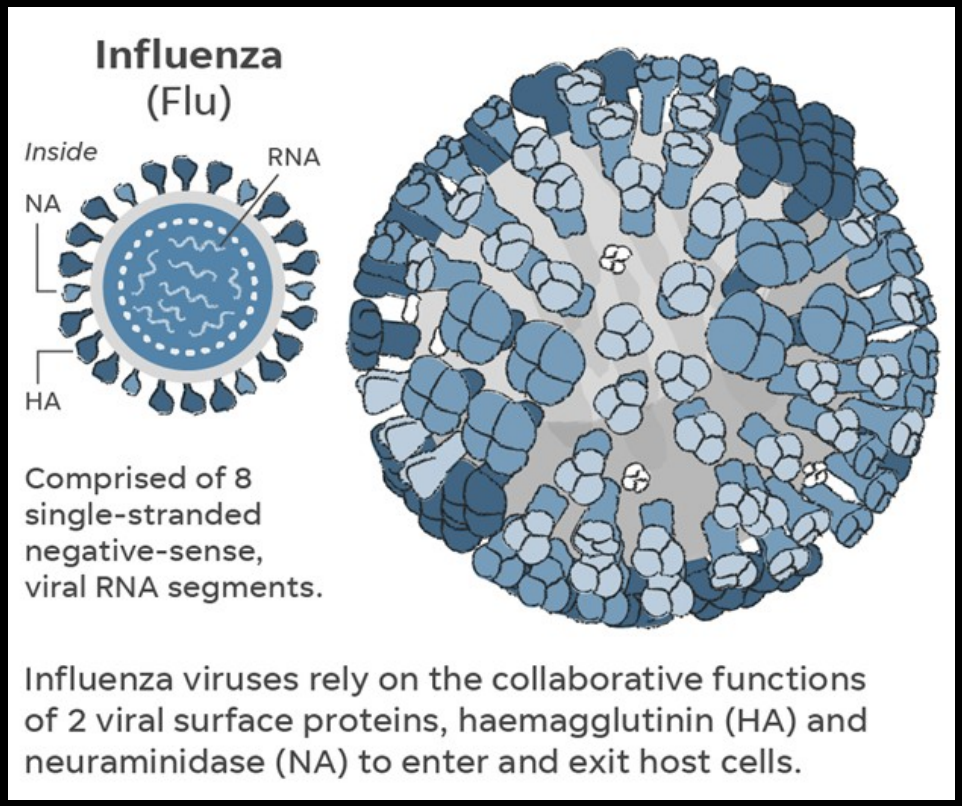
+ srovnání s chřipkou

SARS-CoV-2



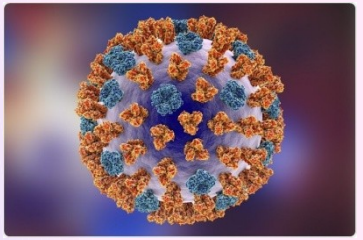
spike protein

IV



neuraminidáza (sialidáza)
hemaglutinin

chřipka - dělení



Influenza A, B, C

dle antigenicity nukleokapsidy a proteinů jádra

Influenza A

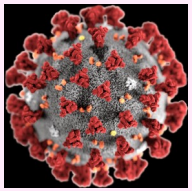
dle povrchových proteinů hemaglutinin (H) a neuraminidáza (N)

sezónní chřipka
Influenza A (H3N2, H1N1)
Influenza B

prasečí chřipka
Influenza A H1N1

ptačí chřipka
Influenza A H7N9
Influenza A H3N5
Influenza A H5N1

nové formy virů
…



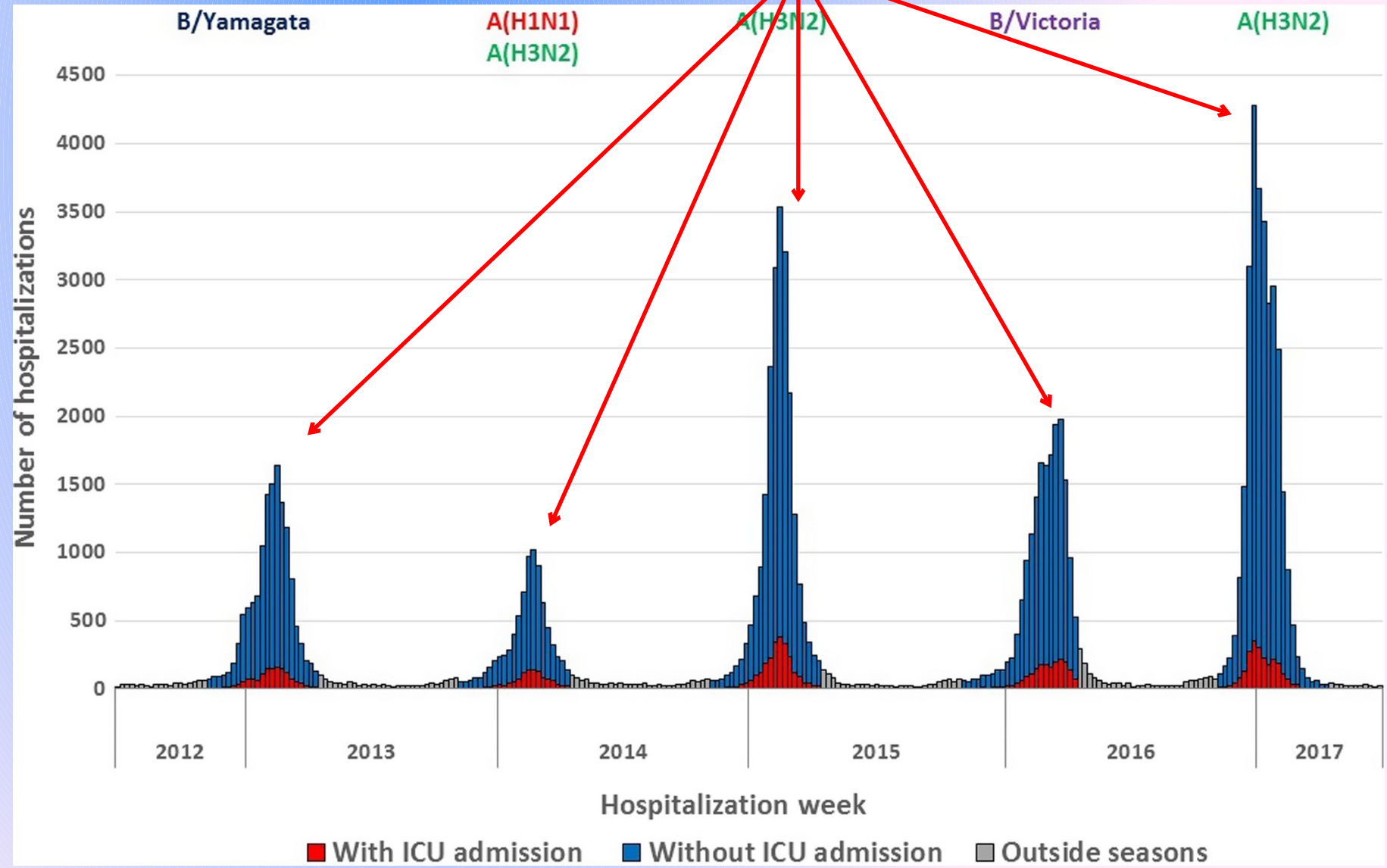
epidemiologie

sezónnost

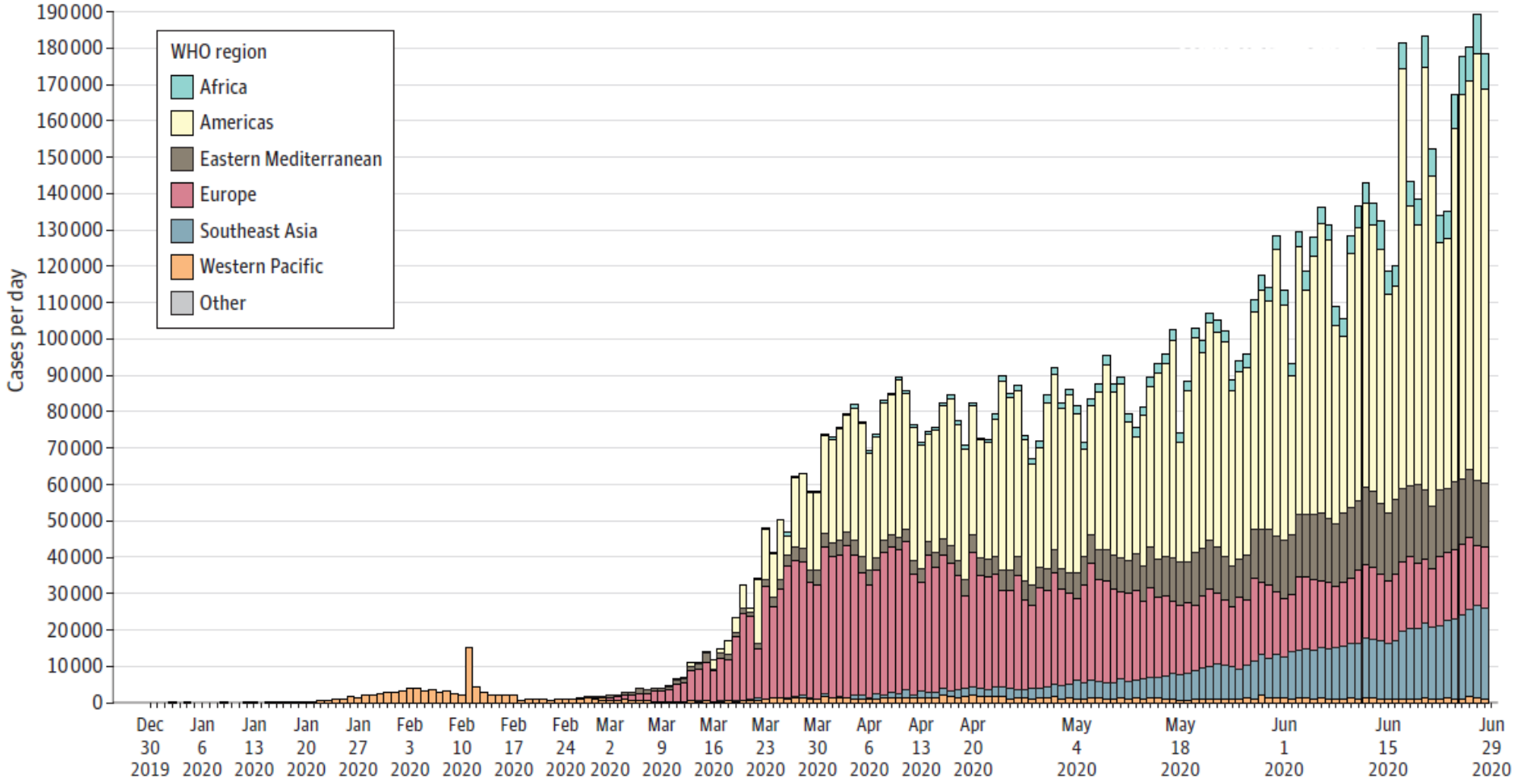
konsekvence: počty pacientů v IM

IV

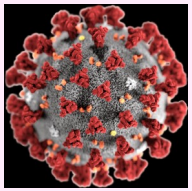
sezónní charakter



SARS-CoV-2



kontinuálnost, nesezónnost

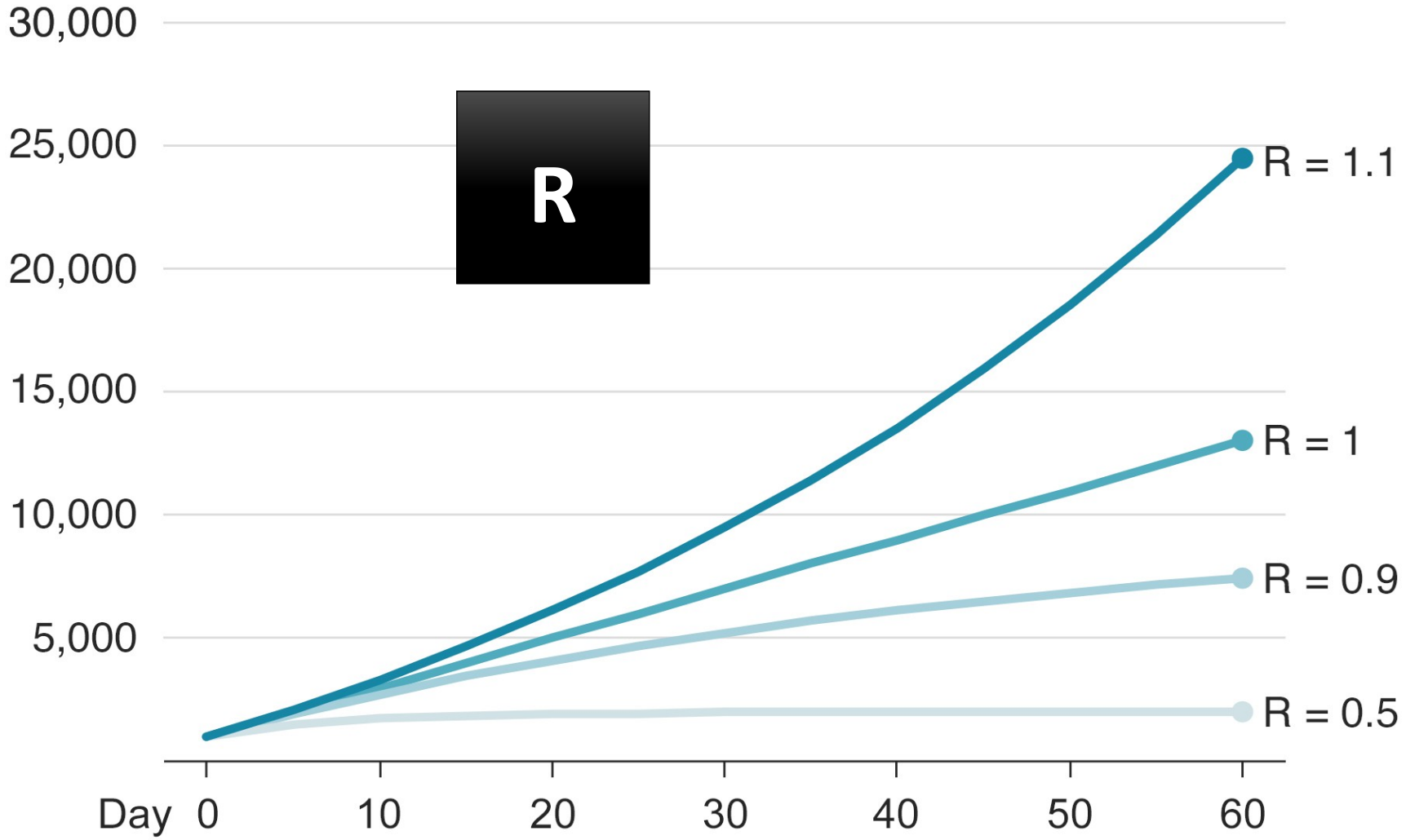


epidemiologie

R, inkubace, mortalita

konsekvence: počty pacientů v IM

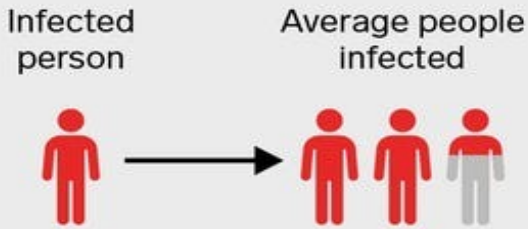
How 1,000 cases would increase under different infection rates



BBC

The average number of people that one person with a virus infects, based on the R0 scale

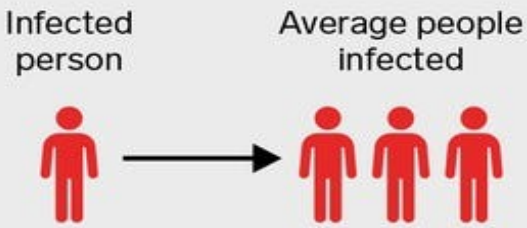
COVID-19: 2–2.5*



H1N1: 1.2–1.6

Ebola: 1.6–2

SARS: 2–4



MERS: 2.5–7.2**

*As of February 28, 2020 **R0 calculated solely during the 2015 outbreak in South Korea

Sources: ScienceMag; WHO; Journal of the ISIRV

BUSINESS INSIDER

How influenza compares to COVID-19

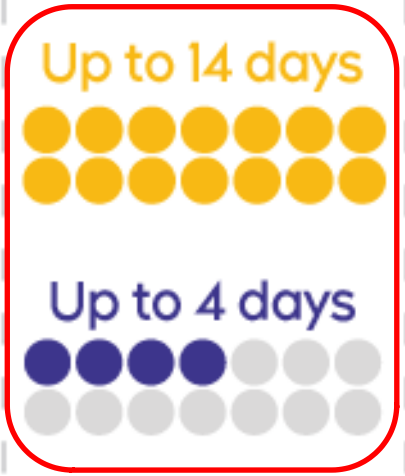
The seasonal flu and the novel coronavirus may have similar symptoms, but they differ in key ways.

Deaths

Number of annual deaths from flu and number of COVID-19 deaths since March

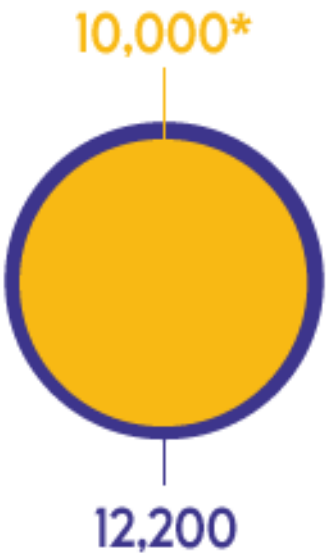
Incubation period

Length of time before symptoms appear



Hospitalizations

Number of patients requiring hospitalization



Reproduction number

Or R0, number of expected cases from one infected

Case Fatality Rate

Percentage of deaths among infected people

1.6%

0.1%

*Hospitalization status information was only available for 65 per cent of case reports

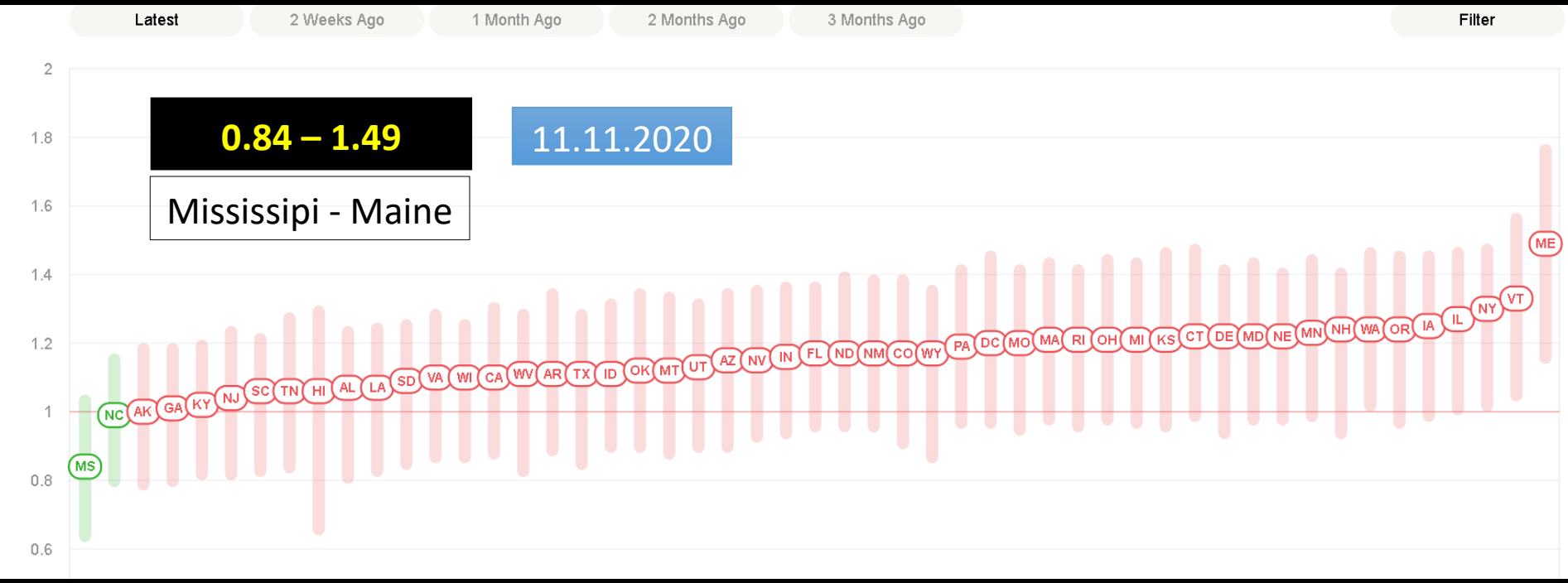
COVID-19 deaths approximately as of June 25

Sources: Public Health Agency of Canada, Canadian Medical Association Journal, Infection Prevention and Control

CTV NEWS

USA

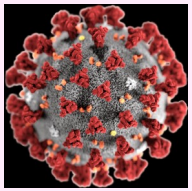
R



ČR

R rate = 0.7

18.11.2020



epidemiologie

přežití viru

konsekvence: rizika managementu IM

SARS-CoV-2

How long does coronavirus survive on surfaces?

3 hours:

This is the amount of time we know that coronavirus can survive and remain infectious in **airborne droplets**, but we don't know if humans produce enough in a single cough to infect another person.

Up to 72 hours:

This is the amount of time coronavirus can stay active on **hard, shiny surfaces**. Think things like play equipment, door and public transport handles and your phone.

The virus does degrade over time, but you should avoid touching these surfaces in shared spaces, and if you can't do that, avoid touching your face afterward before thoroughly washing your hands.

Up to 24 hours:

This is the amount of time it took for researchers to find no more viable traces of the virus on cardboard. This is also a good guide for other **porous surfaces**.

Porous surfaces are much less likely to hold viable amounts of the virus.

hard and shiny vs. porous

HOW LONG THE NEW CORONAVIRUS CAN LIVE ON SURFACES

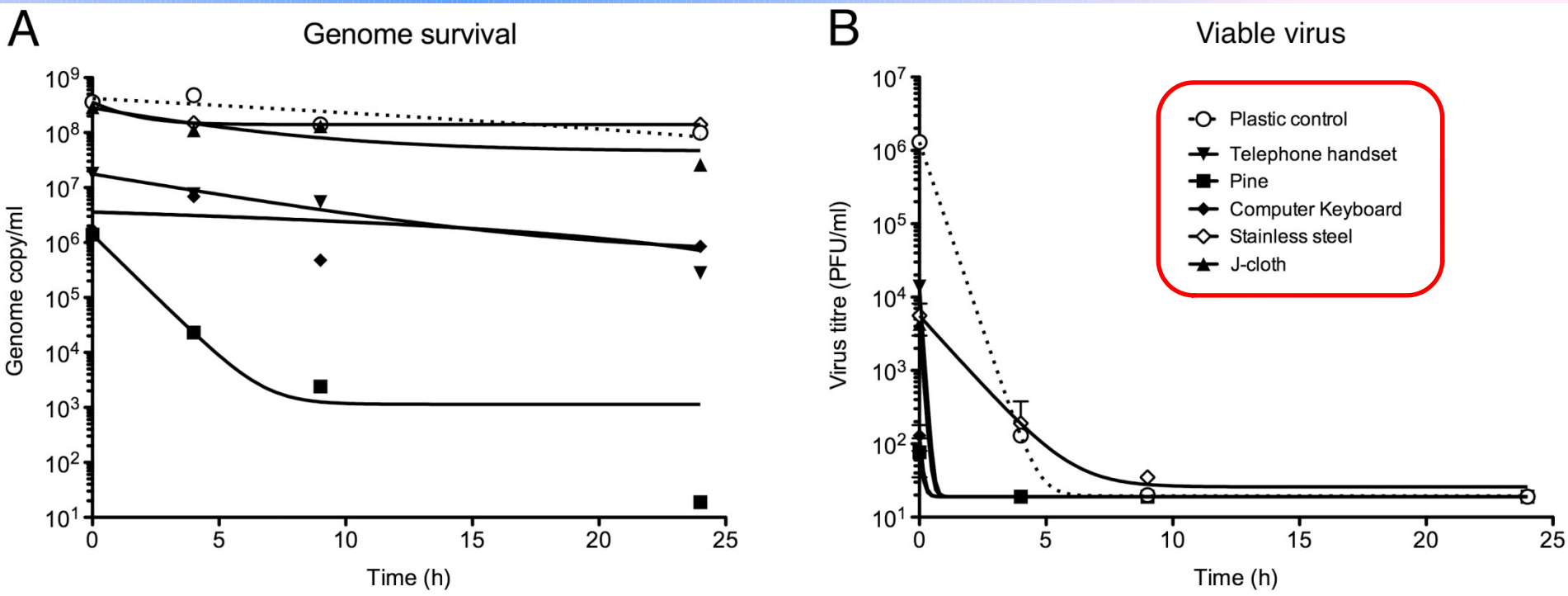
SURFACE	LIFESPAN OF COVID -19 VIRUS
Paper and tissue paper**	3 hours
Copper*	4 hours
Cardbord*	24 hours
Wood**	2 days
Cloth**	2 days
Stainles steel*	2 -3 days
Polypropylene plastic*	3 days
Glass*	4 days
Paper money**	4 days
Outside of surgical mask**	7 days

*At 69.8 to 73.4°F (21 to 23°c) and 40% relative humidity

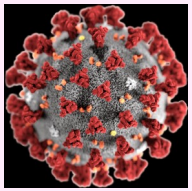
**At 71°F and 65% relative humidity

Source:New England Journal of Medicine *; The Lancet Microbe**

IV


A
Genome survival
Genome copy/ml
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10^1
0
5
10
15
20
25
Time (h)
B
Viable virus
Virus titre (PFU/ml)
10^7
10^6
10^5
10^4
10^3
10^2
10^1
Plastic control
Telephone handset
Pine
Computer Keyboard
Stainless steel
J-cloth
0
5
10
15
20
25
Time (h)

hodiny



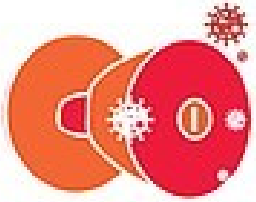
epidemiologie

tramsmise

konsekvence: počet případů a rizika managementu IM

CORONAVIRUS TRANSMISSION

FOMITES

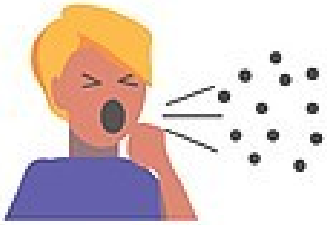


Fomites are **contaminated objects and surfaces** that transmit coronavirus from your **hands** to your **eyes, nose or mouth.** Fomite spread is more likely on hard, non-porous materials like metals and plastics. Regular use of **hand sanitizer** and vigorous **hand-washing** can prevent fomite spread.

Hand washing

Hand sanitization

DROPLETS



Droplets are **moist particles** expelled from **speaking, breathing, coughing and sneezing.** They are considered to be the primary vector of COVID-19 infection. Virus-bearing droplets can spread coronavirus through your **eyes, nose or mouth.** Droplets do not remain airborne long: **6 feet of distance** limits exposure, but **masks covering the mouth and nose** are the best prevention.

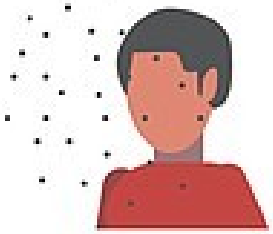
Mask wearing

Eye protection

Social distancing

Staying outdoors

AEROSOLS



Aerosols are **tiny particulates** that infected carriers exhale, especially when **shouting, singing, or speaking.** Aerosols are mostly **inhaled** as a means of transmitting the virus. Unlike droplets, aerosols can remain airborne for several hours, can travel further than 6 feet, and may accumulate, especially in **poorly ventilated, closed spaces. Masks,** worn snugly and properly, are extremely effective at containing aerosols. **Remaining outdoors,** where aerosols cannot accumulate, also prevents transmission

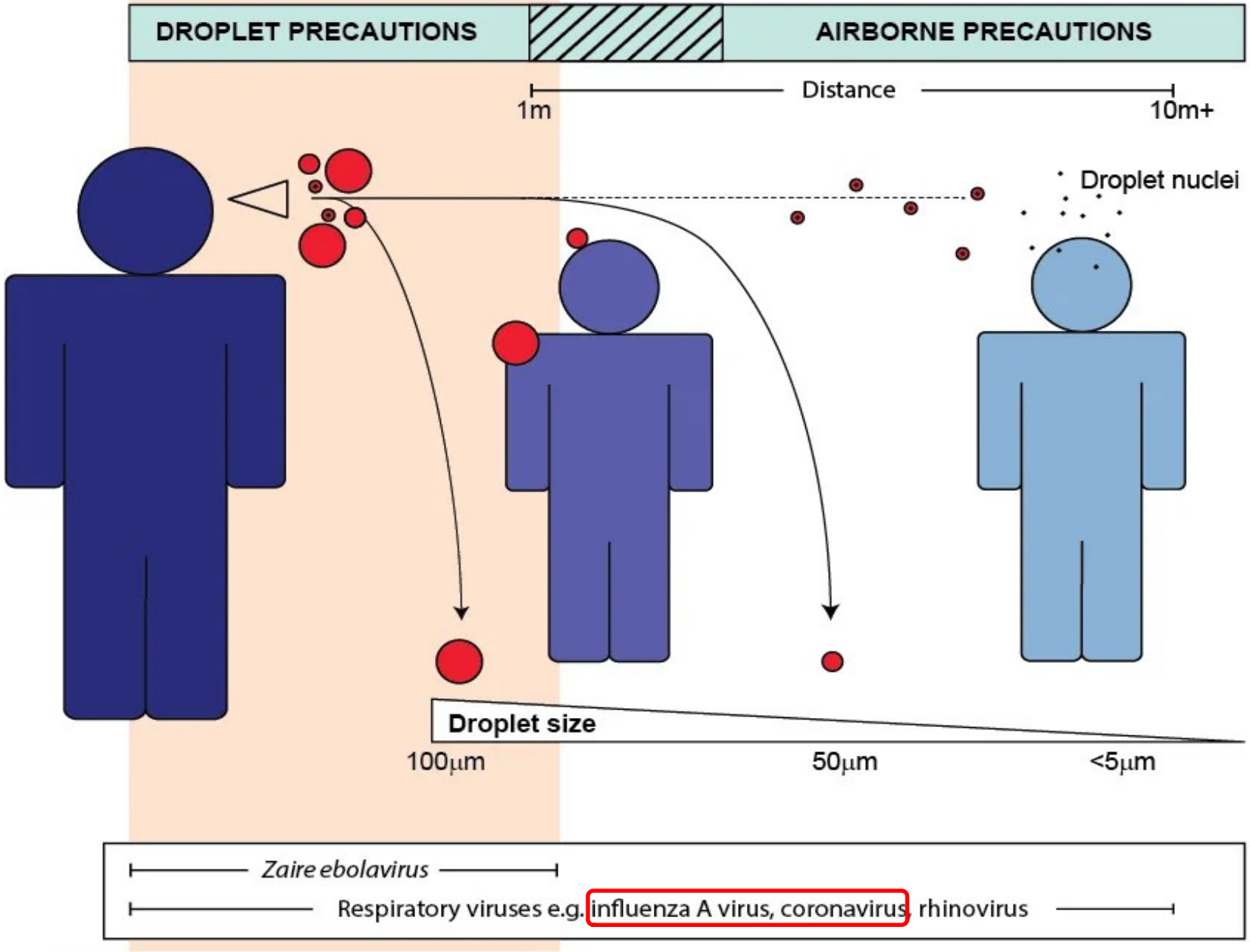
Mask wearing

Staying outdoors

Ventilation

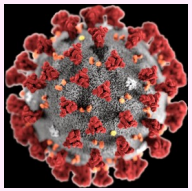
Social distancing

Source: CDC / UMMC



SIMPLE SKETCH OF DROPLET & AIRBORNE VIRUS AND BACTERIAL TRANSMISSION

IAN M MACKAY, PHD
V6 15-AUG-2014
VIROLOGYDOWNUNDER.BLOGSPOT.COM.AU



epidemiologie

cílové skupiny

konsekvence: rizika managementu IM

IV

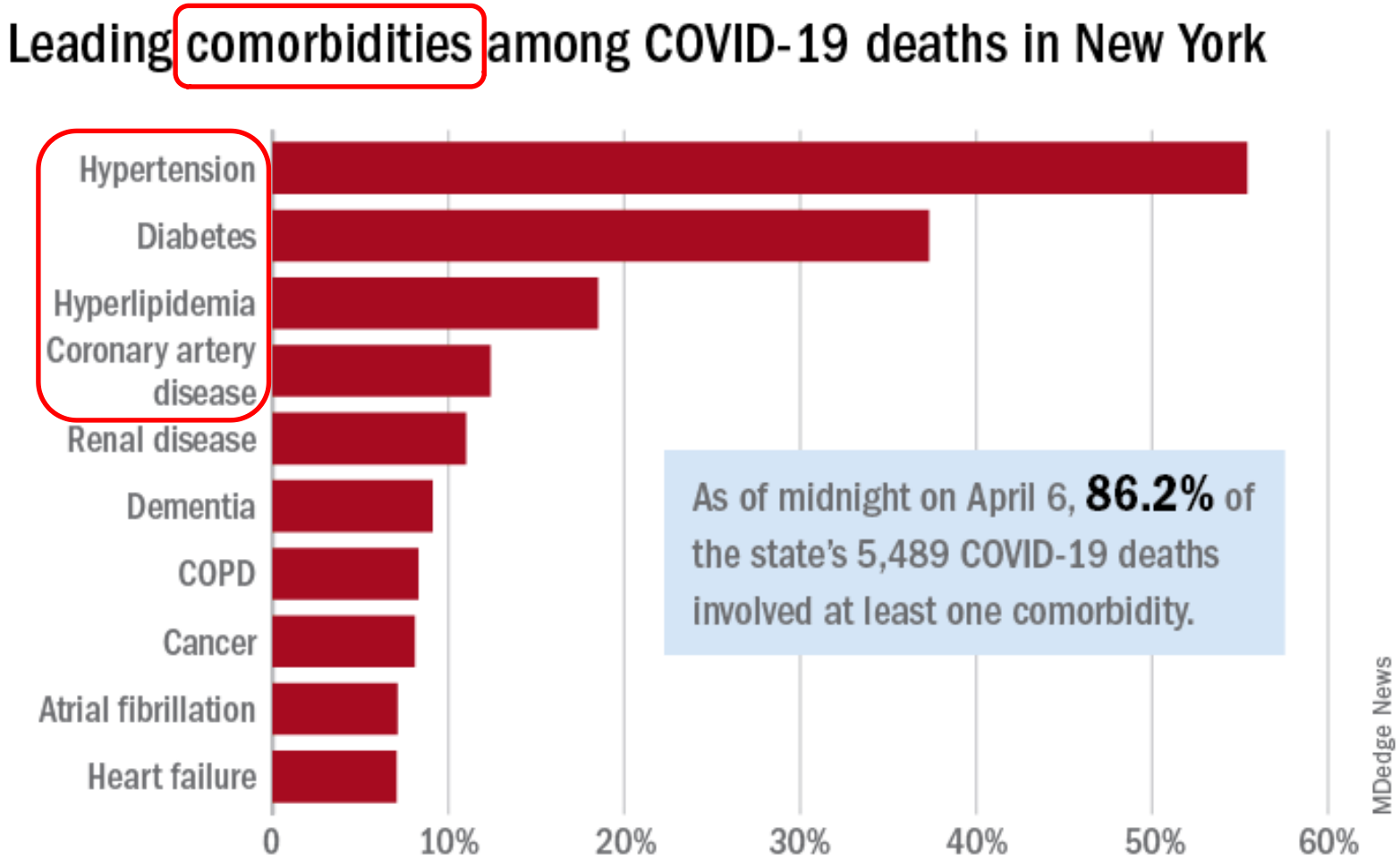
H1N1

Seasonal	Pandemic (2009–2010 Season only)
1. Individuals over 65 years old 2. Financially vulnerable persons 3. Handicapped individuals 4. Soldiers	1. Healthcare workers 2. Infants and pregnant women 3. Individuals over 65 years old 4. Individuals in high-risk groups aged 50 to 64 years 5. Students (elementary, middle, and high school) 6. Soldiers 7. Teachers (preschool and K-12) 8. Airport, infrastructure, and port workers 9.Social welfare and child care center residents and workers

SARS-CoV-2

- komorbidity
- obezita
- věk

SARS-CoV-2



Note: Data reported on a daily basis by hospitals, nursing homes, and other health care facilities.

Source: New York State Department of Health

Obesity and COVID-19

People with obesity are at higher risk of developing more severe COVID-19 than people who do not have obesity.[1–4]

People with obesity are a high-risk group that can develop severe illness from COVID-19:[3,5–7]

~x3

The presence of obesity was found to increase the risk of severe illness **~x3** with a consequent longer hospital stay.[7]

12%

Studies have shown that each 1-unit increase in BMI was also associated with a **12%** increase in the risk of severe COVID-19.[7]

People with obesity and COVID-19 are more likely to be hospitalised and admitted to critical care units[8]

48.3%
of people hospitalised for COVID-19 had a BMI ≥30 (kg/m²)

BMI >40 (kg/m²)
was the second strongest predictor of hospitalisation, after age

In addition to obesity being a common comorbidity in patients with severe COVID-19 illness, some of the common complications associated with obesity are also risk factors for serious illness:[9]

Obesity is the most prevalent complication among people <65 years with COVID-19.[8,10,11]

Obesity is associated with other health complications which can lead to serious illness, including:[9]


Cardiovascular disease


Diabetes


Hypertension

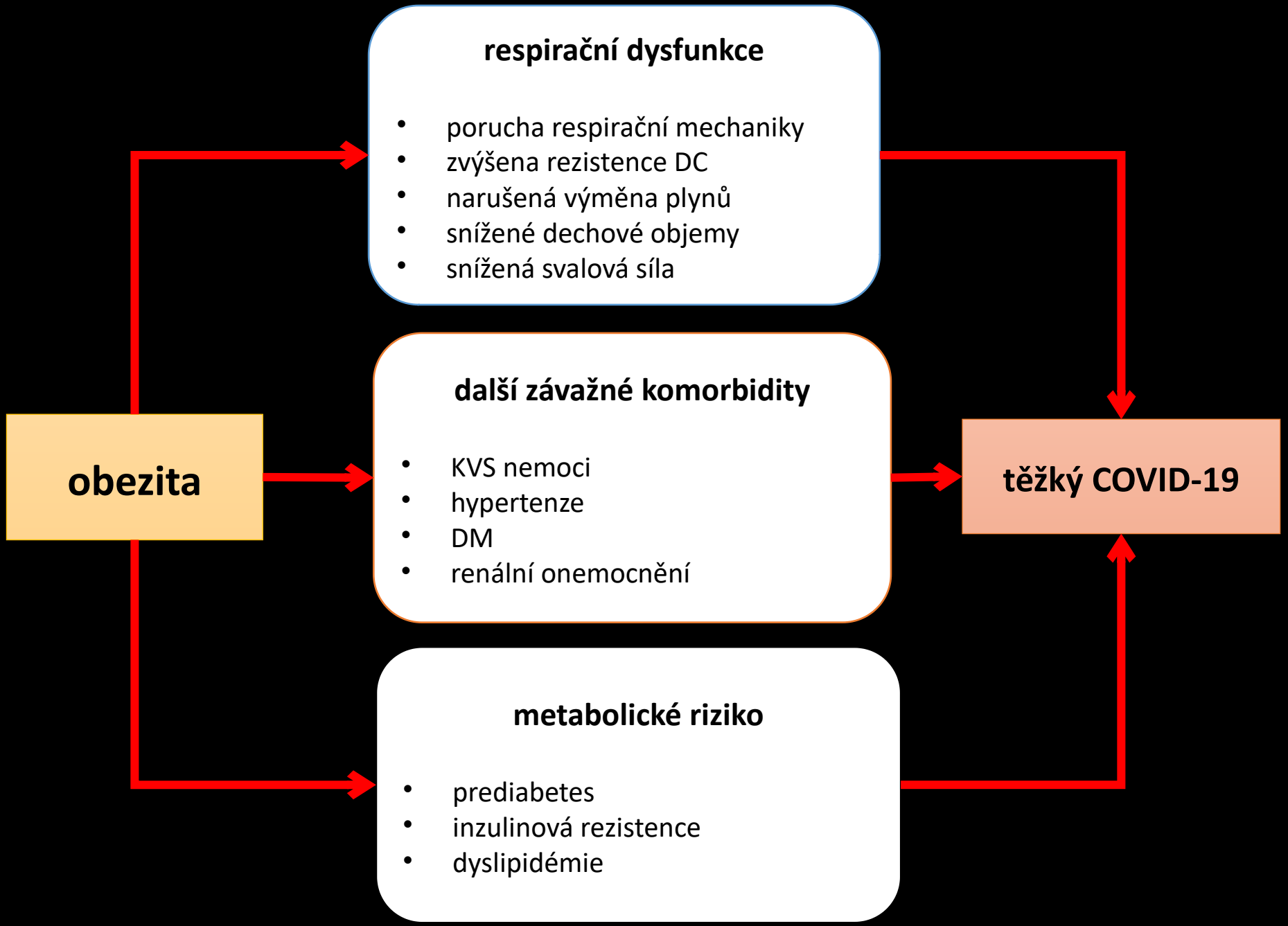
For more information about obesity and COVID-19, visit
global.rethinkobesity.com/obesity-and-covid19.html

Rethink Obesity®

novo nordisk®

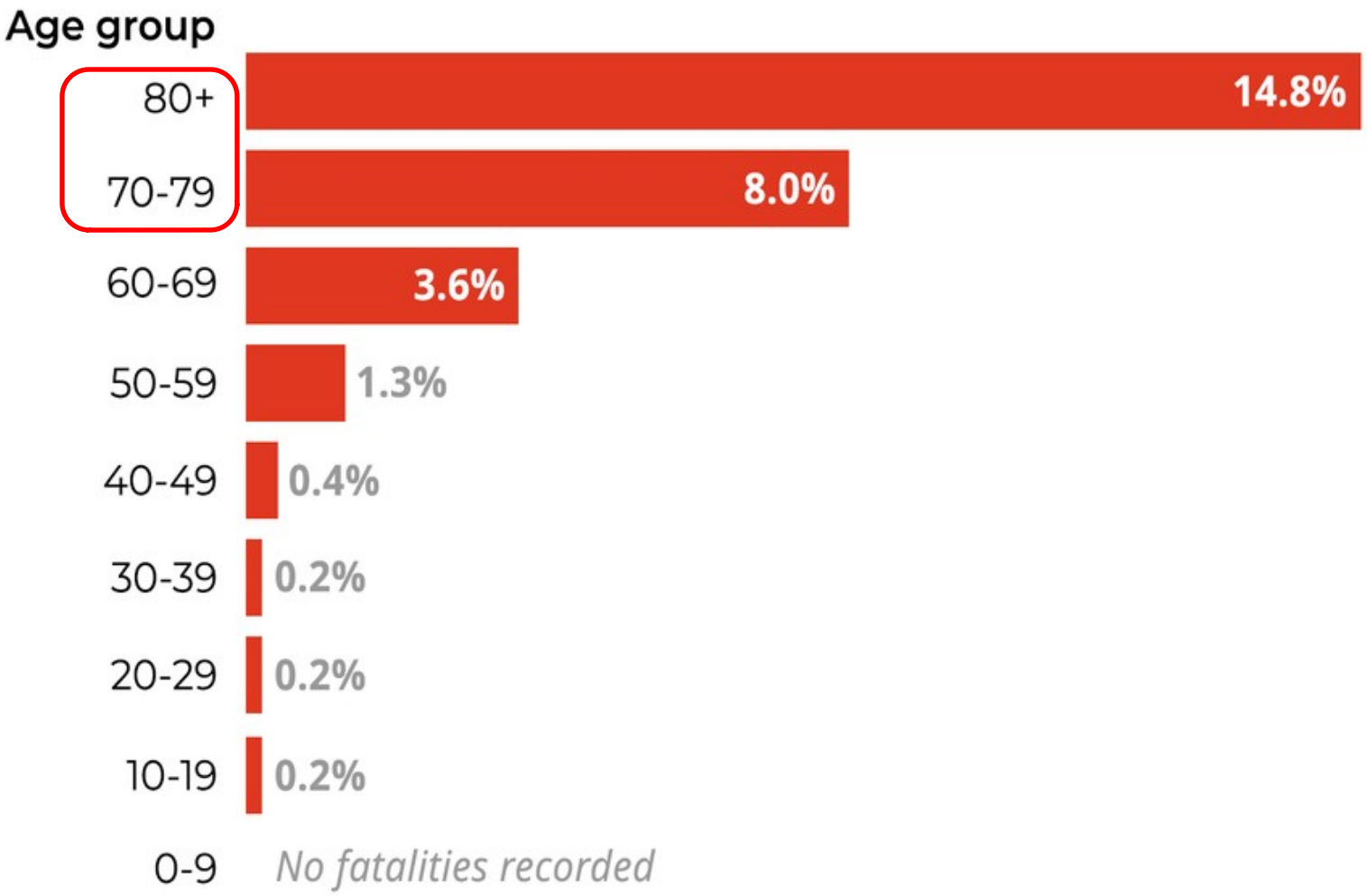
3x větší riziko těžkého průběhu
delší hospitalizace

na každý 1 bod BMI se zvedá riziko těžkého průběhu o 12%

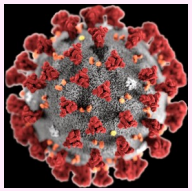

respirační dysfunkce
porucha respirační mechaniky
zvýšena rezistence DC
narušená výměna plynů
snížené dechové objemy
snížená svalová síla
obezita
další závažné komorbidity
KVS nemoci
hypertenze
DM
renální onemocnění
těžký COVID-19
metabolické riziko
prediabetes
inzulinová rezistence
dyslipidémie

COVID-19 death rate by age group

Death rate due to COVID-19 (all cases)



Source: Author provided



klinická symptomatologie

konsekvence: komplikovaná klinická diagnostika

Symptoms	Coronavirus Symptoms range from mild to severe	Cold Gradual onset of symptoms	Flu Abrupt onset of symptoms
Fever	Common	Rare	Common
Fatigue	Sometimes	Sometimes	Common
Cough	Common* (usually dry)	Mild	Common* (usually dry)
Sneezing	No		No
Aches and pains	So		Common
Runny or stuffy nose			Sometimes
Sore throat		mon	Sometimes
Diarrhea	Ra	No	Sometimes for children
Headaches	Sometimes	Rare	Common
Shortness of breath	Sometimes	No	No

ageuzie
parageuzie
anosmie

Sources: World Health Organization, Centers for Disease Control and Prevention

Clinical Presentation of Covid-19

Asyntomatic Infection	Absence of clinical signs and symptoms of the disease and normal chest X-ray or CT scan associated with a positive test for SARS-CoV-2
Mild Infection	Upper airway symptoms such as fever, fatigue, myalgia, cough, sore throat, runny nose and sneezing. Pulmonary clinical exam is normal. Some cases may not have fever and others may experience gastrintestinal symptoms such as nauseas, vomiting, abdominal pain, and diarrhea.
Moderate Infection	Clinical signs of pneumonia. Persistent fever, initially dry cough, which becomes productive, may have wheezing or crackles on pulmonary auscultation but shows no respiratory distress. Some individuals may not have symptoms or clinical signs, but chest CT scan reveals typical pulmonary lesions.
Severe Infection	Initial respiratory symptoms may be associated with gastrointestinal symptoms such as diarrhea. The clinical deterioration usually occurs in a week with the development of dyspnea and hypoxemia (blood oxygen saturation [SaO_2] <94%)
Critical Infection	Patients can quickly deteriorate to acute respiratory distress syndrome or respiratory failure and may present shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction.

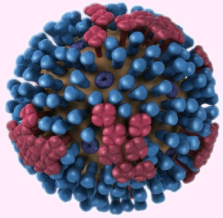
Clinical Presentation of Covid-19

dušnost a pokles SpO_2

ARDS
AHF (MI), DIC, AKI, encefalopatie
MODS

Severe Infection	Initial respiratory symptoms may be associated with gastrointestinal symptoms such as diarrhea. The clinical deterioration usually occurs in a week with the development of dyspnea and hypoxemia (blood oxygen saturation [SaO_2] <94%)
Critical Infection	Patients can quickly deteriorate to acute respiratory distress syndrome or respiratory failure and may present shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction.

pH1N1 2009 influenza A



těžká nebo komplikovaná forma

- ✓ **ARDS**
- ✓ **encefalitida**, encefalopatie
- ✓ šok + orgánové dysfuknce
- ✓ **myokarditida**
- ✓ rhabdomyolýza
- ✓ invazivní **sekundární bakteriální infekce** (perzistentní horečka a další symptomy)
- ✓ chybí koagulopatie

symptomatologie

fenomén silent hypoxemia

SARS-CoV-2

CRITICAL CARE PERSPECTIVE

Why COVID-19 Silent Hypoxemia Is Baffling to Physicians

Martin J. Tobin, Franco Laghi, and Amal Jubran

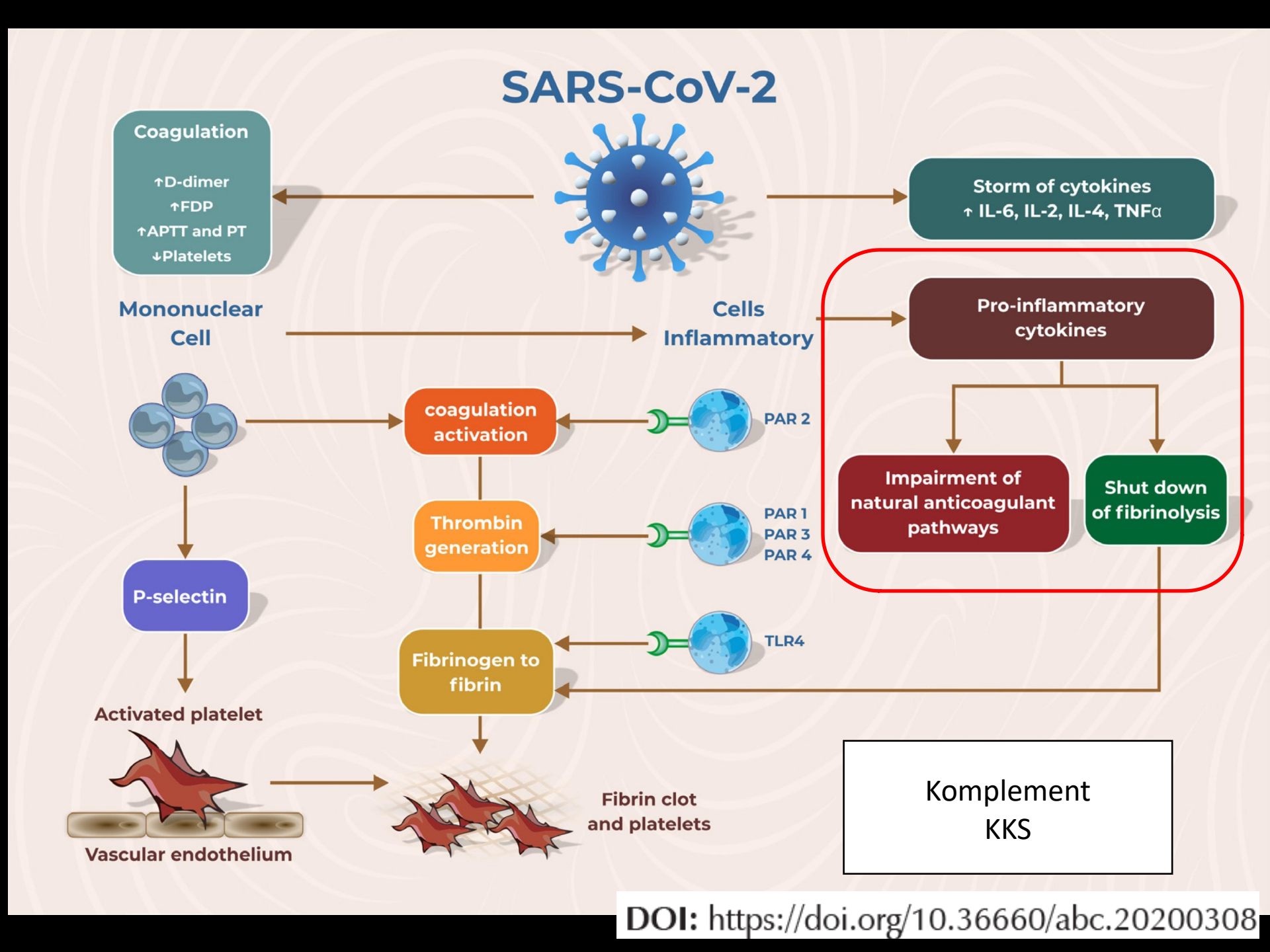
„happy hypoxia“

diskrepance mezi klinickým stavem (↓ dušnost) a extrémní hypoxémií (SpO_2 ≈ 80%)

subjektivní vnímání dušnosti, aference CNS, vliv CO_2, problémy měření SpO_2, posun disociační křivky

symptomatologie

fenomén imunokoagulace



DOI: https://doi.org/10.36660/abc.20200308

CRITERIA FOR SEVERITY

- Respiratory rate ≥ 30 bpm
- Arterial O_2 saturation ≤ 93% at rest
- $PaO_2/FiO_2 \leq 300$
- Radiological evidence of pulmonary impairment greater than 50% over 24-48 hours

ISTH SIC score

Criterion	Points	Parameter
Platelet count ($x10^9/L$)	1	100-150
	2	<100
INR	1	1.2-1-4
	2	>1.4
SOFA score	1	1
	2	≥2

SIC – sepsis-induced coagulopathy

COVID-19
(confirmed diagnosis)

↓

Criteria for severity
(1 or more criteria)

↓

SIC score ≥ 4/DIVC
and/or D-dimer > 6x ULRR

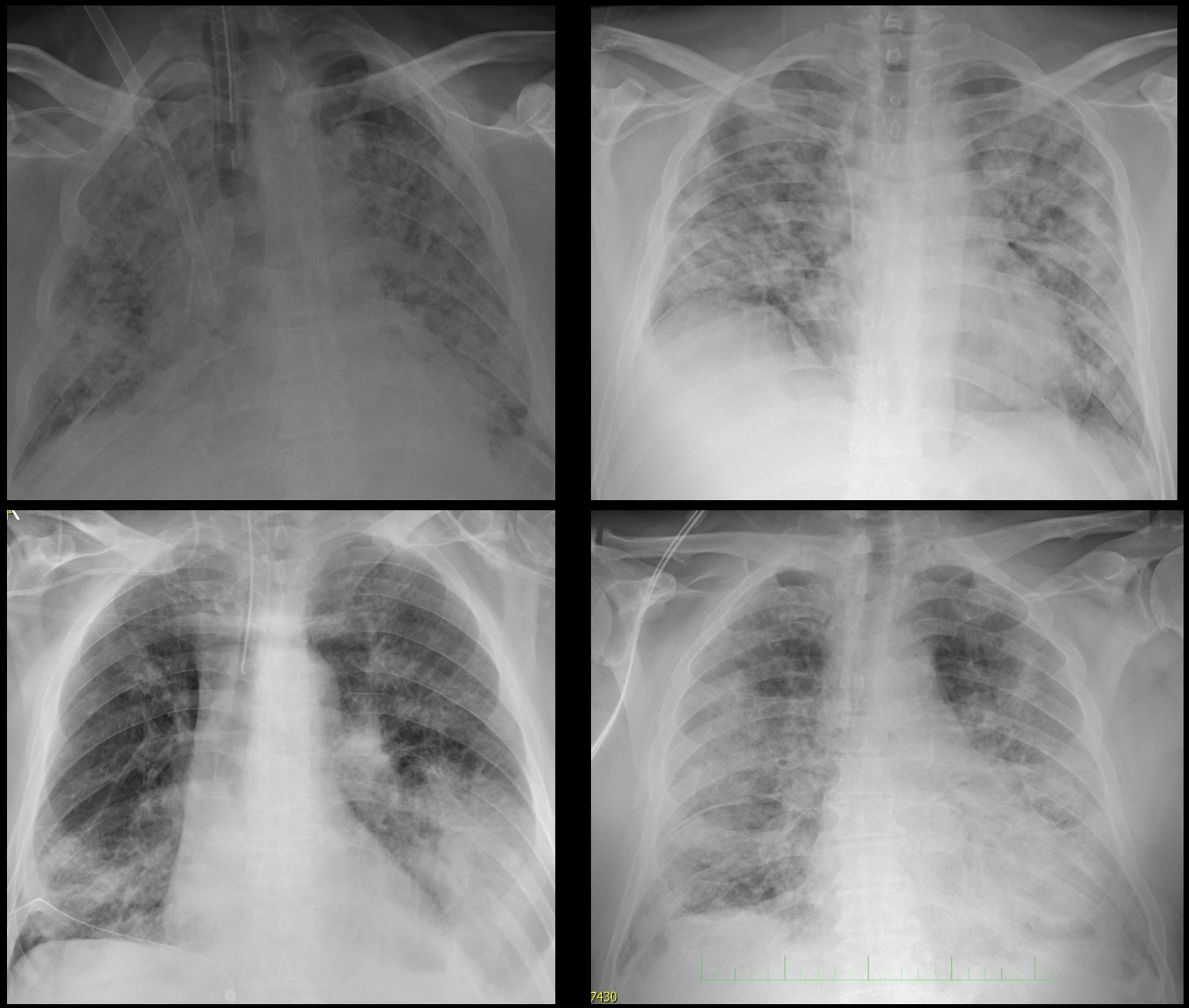
↓

ANTICOAGULANT THERAPY
MIGHT BE CONSIDERED
(in the absence of contraindications)

DOI: https://doi.org/10.36660/abc.20200308

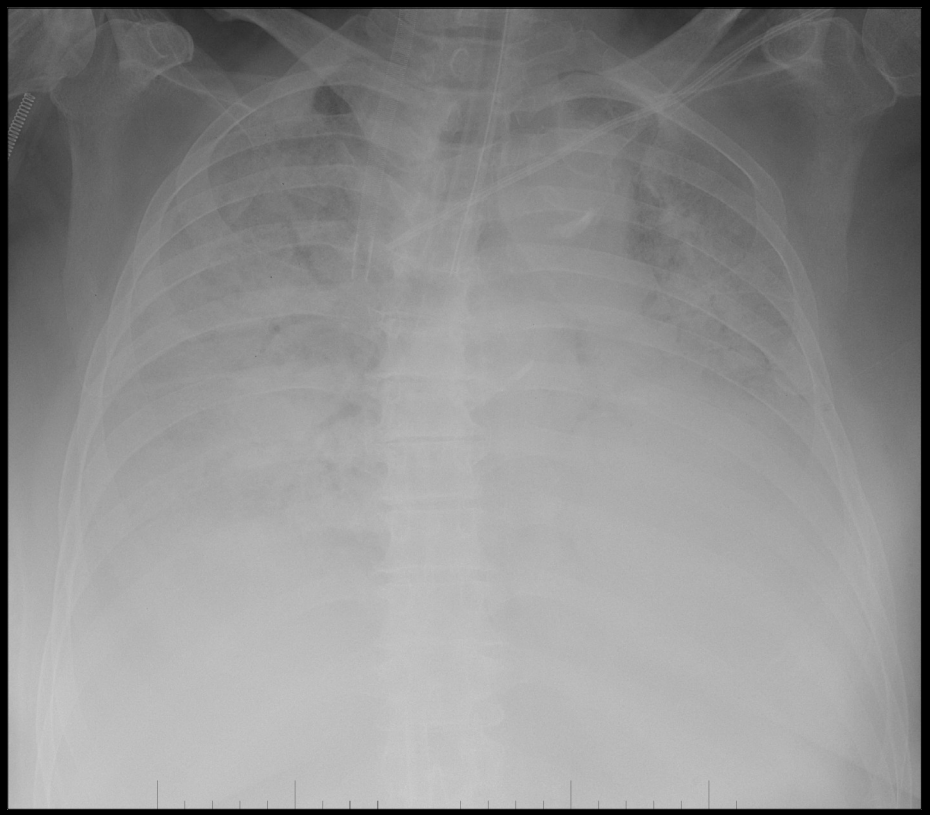
rtg

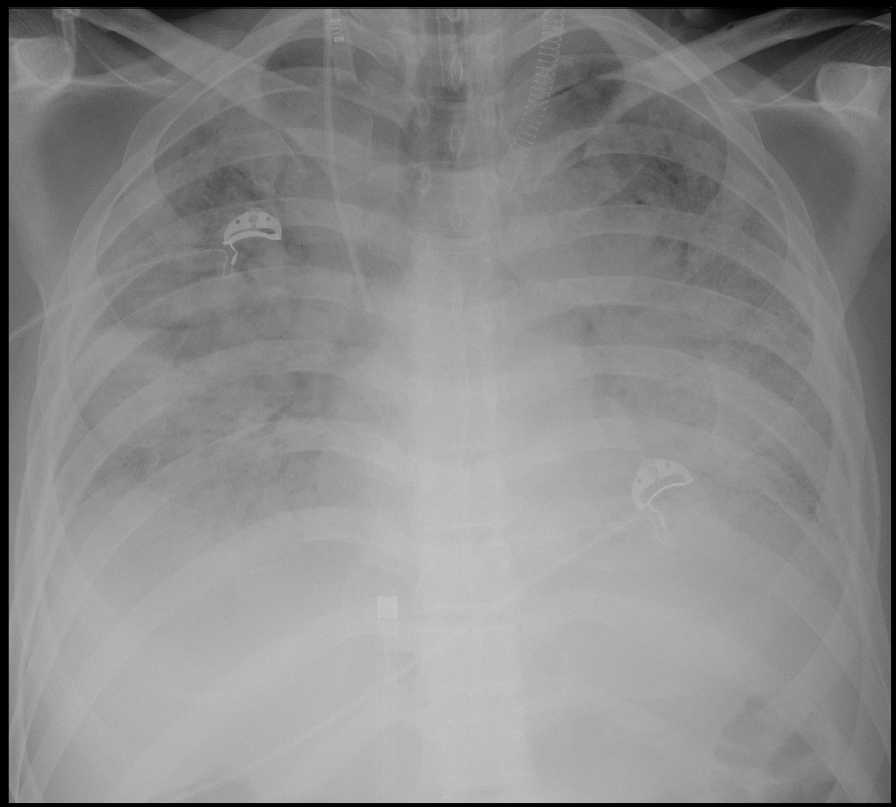
SARS-CoV-2

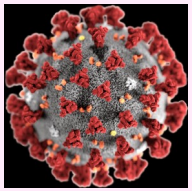


těžké formy chřipky/komplikované formy chřipky

těžká bilaterální pneumonie
akutní respirační selhání
ARDS







terapie

UPV

konsekvence: rizika managementu IM

podpora oxygenace

vs.

podpora ventilace

SARS-CoV-2

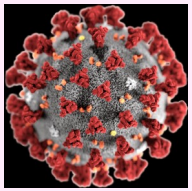
WHO klasifikace dle závažnosti

nekomplikované onemocnění	Pacient s nekomplikovaným zánětem horních cest dýchacích s nespecifickými příznaky (horečka, kašel, únava, cefalea, artralgie, myalgie), nejsou známky dehydratace a dušnosti.
lehká pneumonie	pacient s pneumonií , ale bez známek těžké pneumonie.
těžká pneumonie	Horečka + pneumonie + jeden z příznaků: **dechová frekvence > 30/min**, **respirační distress**, **SpO_2 na vzduchu < 90 %.**
ARDS	Berlínská definice (2012) bilaterální opacity **mléčného skla.** PaO_2/FiO_2 < 300 mmHg
sepse	Život ohrožující orgánová dysfunkce způsobená dysregulovanou odpovědí organizmu na infekci: známky orgánové dysfunkce charakterizované alterací vědomí, ztíženým/zrychleným dýcháním, poklesem diurézy, tachykardií, oslabením pulzu, mramorováním kůže, chladnými končetinami a laboratorně vyjádřenými příznaky koagulopatie, trombocytopenie, acidózy, hyperbilirubinémie a zvýšeného laktátu
septický šok	Přetrvávající hypotenze navzdory adekvátní tekutinové resuscitaci, nutnost podávání vazopresorů ke střednímu arteriálnímu tlaku nad 65 mmHg a hodnotě sérového laktátu nad 2 mmol/l

podpora oxygenace vs. podpora ventilace

nekomplikované onemocnění	
lehká pneumonie	nic/O_2
těžká pneumonie	O_2/HFNO/NIV/(UPV)
ARDS	**UPV** (HFNO, NIV)
sepse	**UPV**
septický šok	**UPV**

SARS-CoV-2



HFNO

NIV

UPV

kdy?

pronace

jak? kdy? komu?

ECMO

kdy? komu?

SARS-CoV-2

časná intubace

PRO

Zuo et al, 2019; Meng et al, 2020

HFNO a **NIV** jsou aerosol generující proceury (AGPs), izolace DC

opožděná intubace zhoršuje prognózu

riziko **rychlé deteriorace** klinického stavu (hodiny) + logistika intubace (transport a dostupnost PPE)

klinicky významná tichá „silent“ hypoxémie

redukovaný efekt preoxygenace, periintubační riziko CA

patients showing no improvement in respiratory distress, tachypnea (respiratory rate greater than 30 per minute), and poor oxygenation (PaO_2/FiO_2 ratio less than 150 mmHg) after 2-h high-flow oxygen therapy or NIV

The Chinese Society of Anesthesiology Task Force on Airway Management's, 2020 Feb 27

časná intubace – how early?

"timely, but not premature, intubation" is vital

rate of deterioration and severity of illness

altered mental state and agitation, especially when they prevent compliance with existing oxygen therapy

anatomically difficult airway requiring awake intubation

need for untolerated diagnostic procedures

ANESTHESIOLOGY

Intubation and Ventilation amid the COVID-19 Outbreak

Wuhan's Experience

Lingzhong Meng, M.D., Haibo Qiu, M.D., Li Wan, M.D., Yuhang Ai, M.D., Zhanggang Xue, M.D., Qulian Guo, M.D., Ranjit Deshpande, M.D., Lina Zhang, M.D., Ph.D., Jie Meng, M.D., Ph.D., Chuanyao Tong, M.D., Hong Liu, M.D., Lize Xiong, M.D., Ph.D.

ANESTHESIOLOGY 2020; XXX:00–00

increased work of breathing (dyspnea), **fatigue**, with **worrying trajectory**

„if a patient asks to be intubated for these reasons, we should listen!"

SARS-CoV-2

Intensive Care Medicine

EDITORIAL Un-edited accepted proof

COVID-19 pneumonia: different respiratory treatment for different phenotypes?

L. Gattinoni[1], D. Chiumello[2], P. Caironi[3], M. Busana[1], F. Romitti[1], L. Brazzi[4], L. Camporota[5]

fenotypy

H
high

L
low

SARS-CoV-2

H
high

Intensive Care Medicine

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The Type H patient

- High elastan… …the increased lung elastan…
- High right-t… …non-aerated tissue whic… …edema and superimpos…
- High lung w… …crease in lung weight (> 1.…
- High lung recruitability. The increased amount of non-aerated tissue is associated, as in severe ARDS, with increased recruitability [12].

- ↑ elastance
- ↑ PL shunt
- ↑ váha plic
- ↑ recruitabilita

SARS-CoV-2

L
low

Intensive Care Medicine

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- Low elastance: the nearly normal compliance indicates that the amount of gas in the lung is nearly normal [3].
- Low ventilat…ormal, hypoxemia may be be… loss of hypoxic vasoconstric…re, should be near normal.
- Low lung w… primarily located subpleurally… only moderately increased.
- Low lung recruitability: the amount of non-aerated tissue is very low, consequently the recruitability is low [4].

- ↓ elastance → ↑ poddajnost
- ↓ V_A/Q
- ↓ váha plic
- ↓ recruitabilita

SARS-CoV-2

treatment

Intensive Care Medicine

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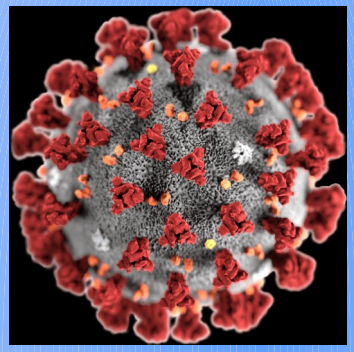
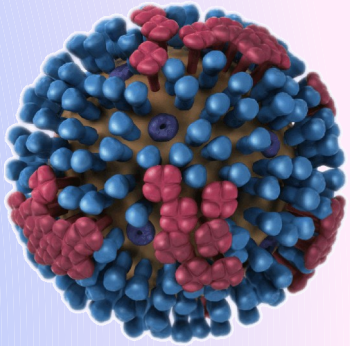
H high	L low
HFNO	**UPV:** ↓ Vt, ↑ PEEP, ↓ DP
NIV	**pronace**
UPV, pronace, (ECMO)	**ECMO**

cíl je ↑ FiO_2 a ↓ WOB





UPV u COVID-19

vs.

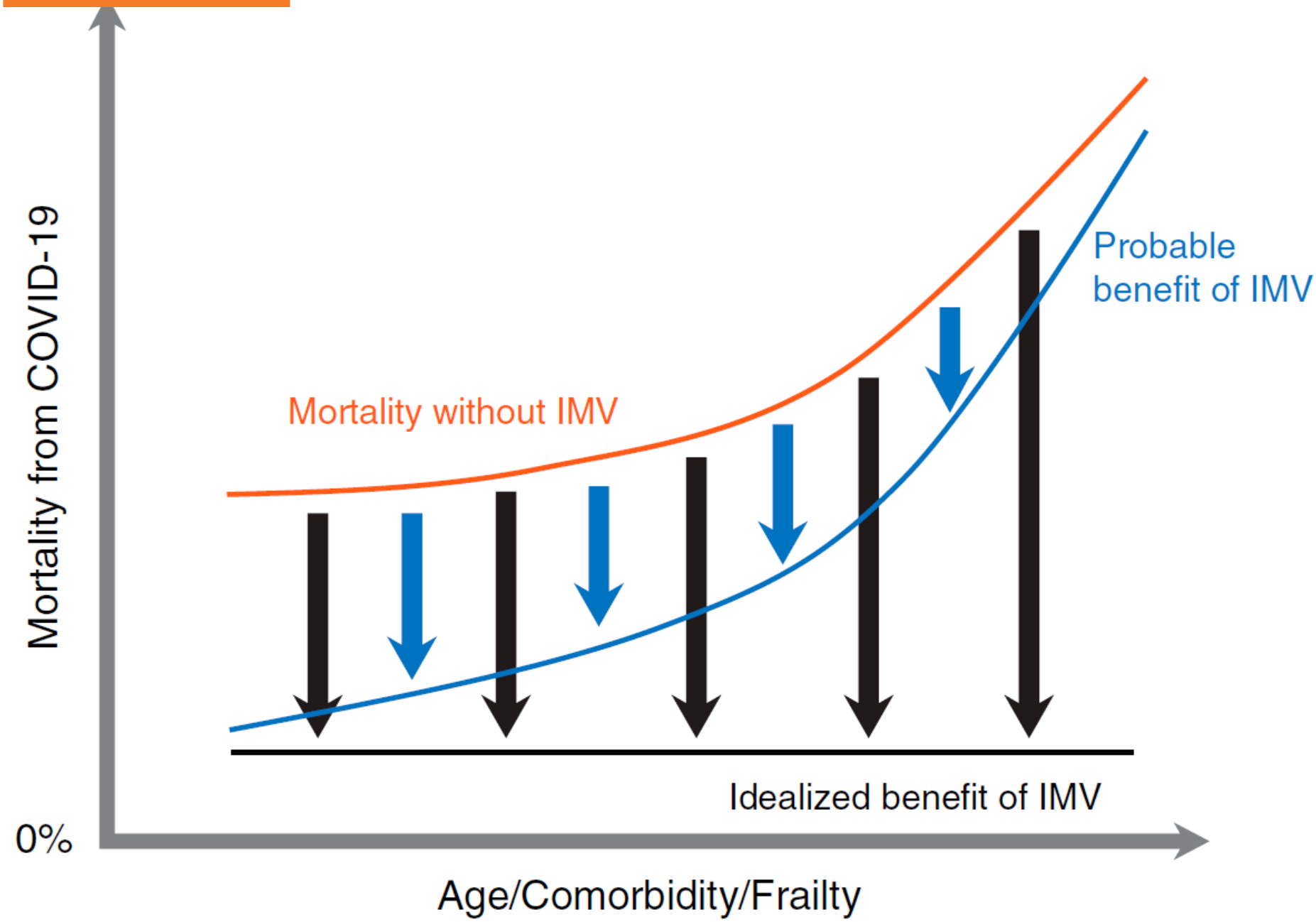
UPV u chřipky

obdobná strategie

roli hraje kvantita pacientů

perspektivnost pacienta

SARS-CoV-2


Mortality from COVID-19
0%
Age/Comorbidity/Frailty
Mortality without IMV
Probable benefit of IMV
Idealized benefit of IMV

SARS-CoV-2

UPV management

- obecné zásady protektivní ventilace
- snaha o časný weaning
- prevence VILI, P-SILI, HALI
- pronace u responderů
- ECMO

závěr

COVID-19 není chřipka

existují podobné klinické rysy

1. epidemiologické (inkubace, transmise, nesezónnost, R)
2. patofyziologie (cílové bb, koagulopatie, „silent hypoxia!“)
3. klinická specifika (UPV, délka hospitalizace)
4. …

děkuji za pozornost